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WELCOME MESSAGE

Prof Dr Saleem Ahmed Khan
President Pakistan Society of Haematology

It is a great pleasure for me to formally welcome you to our much-awaited conference of Pakistan Society of haematology. This scientific abstract book is a testament to the remarkable research presented by our esteemed members. Your contributions demonstrate the ongoing commitment to advancements in the field of haematology. May this conference foster collaboration and inspire new avenues of exploration in our shared pursuit of improving patient care and scientific knowledge.

Best Regards

MESSAGE BY CHAIRPERSON

Prof Dr Hafeez Ud Din
Chairperson HaemCon 2024

As Chairperson HaemCon 2024, I extend a warm welcome to all participants of this year's conference. The scientific abstract book showcases the depth of knowledge and innovation within our community. Your invaluable contributions pave the way for advancements in haematology. I appreciate your dedication to the field and look forward to a fruitful exchange of ideas.

Best Regards

MESSAGE BY CHAIRMAN ORGANIZING COMMITTEE HAEMCON 2024

Prof Dr Hamid Saeed Malik
Chairman Organizing Committee

It is indeed a pleasure for me to welcome all the participants to our annual Haematology Society Conference. This scientific abstract book reflects the cutting-edge research and advancements in haematology. Your contributions have enriched our community, fostering collaboration and progress in our field. Thank you for your dedication to advancing haematology.

Best Regards

IBN-E-SINA LECTURE

Challenges in Diagnosis of Haematological Malignancies in under-resourced setting

Prof Dr Hamid Saeed Malik
Head of Haematology Department
AFIP, Rawalpindi - PK

Over time, there has been a notable rise in the incidence of haematological malignancies, encompassing various blood cancers such as leukaemia, lymphoma and myeloma. The rise in haematological malignancies presents a significant healthcare challenge. Advancements in diagnostics have played a pivotal role in identifying and characterizing these with greater accuracy. Traditional methods such as blood smears and bone marrow biopsies have been complemented and often surpassed by flow cytometry and molecular testing, allowing for earlier detection and monitoring of haematological cancers.

The developed world has witnessed significant advancements in haematological malignancy diagnosis, leveraging cutting-edge technologies and research to formulate comprehensive guidelines. These guidelines often incorporate advanced molecular diagnostic tools, enabling precise identification and characterization of haematological disorders. The guidelines are crafted with access to state-of-the-art equipment, skilled professionals and continuous training.

However, the translation of these advancements to under-resourced countries encounters formidable challenges. Contrastingly, under-resourced countries grapple with limited financial means, hindering the acquisition of advanced diagnostic technologies. The lack of well-established infrastructure and trained personnel further compounds the challenge. Overcoming these challenges requires a multifaceted approach, including targeted investments in infrastructure, educational programs and collaborative efforts to ensure equitable access to advanced haematological malignancy diagnosis globally.

In Pakistan, in spite of the constrained resources and lack of national support, few

centers have successfully established advanced testing facilities, offering a fragmented yet comprehensive range of advanced diagnostics. The fragmented nature of the facility implies a diverse set of tests tailored to address specific diagnostic needs. While these advanced testing facilities are often found in specialized centers or research institutions, the challenge remains in expanding such capabilities to more healthcare settings throughout the country, ensuring broader access to advanced diagnostics for a wider population.

PLENARY TALK

Practical demonstration of using AI for molecular pathology self learning and teaching

Dr Rizwan C. Naeem
Professor of Pathology, Director of molecular pathology and serves as founding and current program director for Laboratory Genetics and Genomics (LGG) and Molecular Genetics Pathology (MGP) fellowship programs at the Albert Einstein College of Medicine and Montefiore Medical Center in NY

In this presentation, we will present a practical demonstration of generative AI tools like ChatGPT and Bard. We are hoping to show how people can save time using these tools to help with preparation of lectures and course material, journal club, and self-directed learning. We will discuss learning about these tools and how to employ them in molecular education. We will discuss pros and cons for ChatGPT and BARD.

Given the increasing workload that many of us are experiencing, the purpose of this presentation is to allow educators to identify resources more efficiently from a list that may be useful to include as part of a teaching program.

Given the recent strong interest in AI we will discuss and refine potential uses of AI in molecular pathology education. For example, how to generate test questions and learning objectives. Are there other applications of AI that would be useful for the education community? How can you try them out?

ORAL PRESENTATION

Evaluation of Circulating Syndecan-1 As A Diagnostic Marker of Disseminated Intravascular Coagulation

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Objective: To evaluate circulating syndecan-1 as a diagnostic marker of disseminated intravascular coagulation

Methods: A descriptive cross-sectional study conducted at LUMHS hospital Hyderabad from 01-01-23 to 31-06-2023 on 90 DIC patients admitted in ICU with data collection done on structured proforma. (SPSS-20) version was used to analyze the data.

Results: In this study, total 90 patients of DIC were studied for serum Syndecan-1 level. Mean age of patients were 39.64± 17.32 years. Among patients most common cause of DIC were sepsis (36.67%) and obstetric complications (35.56%). Mean Platelets was 99.05 ± 24.04, PT was 20.13 ± 7.11, Fibrinogen was 141.8± 28.40, D. Dimer was 0.56± 0.23. Among patients at time of DIC diagnosis, serum Syndecan-1 level of 40 (44.44%) were in normal range group(0-45ng/ml), 19 (21.1%) were in mild range group(45-60ng/ml), 28 (31.1%) were in moderate range group(60-85ng/ml), & 3 (3.3%) were in severe range group(>85ng/ml).

Conclusion: Endothelium is a main contributing factor in pathogenesis of DIC so its biomarker (serum Syndecan-1) can be used as a diagnostic tool for Disseminated Intravascular coagulation that can help to assess endothelial injury in early phase of DIC and in early management to prevent mortality.

ORAL PRESENTATION

Emicizumab: Revolutionizing Management in Persons with Haemophilia A in Pakistan

Dr Muhammad Usman Siddique
Co-Authors Dr. Ayisha Imran (MBBS; FCPS) Dr. Shahla T. Sohail (MBBS; MRCPCH)
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Objective: The aim of this prospective cohort study is to determine the effectiveness of Emicizumab in patients with inhibitors and high annual bleeding rate (ABR) along with any side effects.

Methods: 38 PwH who were on Emicizumab for at least 1 year were studied at Hemophilia Patients Welfare Society (Lahore Chapter). Following parameters were keenly monitored: Inhibitor status; ABR before (mean of 2 years) and after and any breakthrough bleed(s). These patients were also observed for any side effects.

Results: Out of 38 PwH, 5 had developed inhibitors and were not responding to Factor VIII concentrates even on high doses. These 5 PwH after being shifted to Emicizumab had no bleeding episodes (P-value <0.05). 19 PwH had high ABR but after starting Emicizumab only 1 had high ABR (P-value <0.05). None of the 38 PwH had any serious side effects.

Conclusion: PwH who are on Emicizumab are now experiencing lives which are almost near to normal with remarkable improvement in their quality of life. Using Emicizumab as prophylaxis with and without inhibitors led to time & cost saving for the beneficiary & treatment center (HTC) along with saving in IUs of other products (factor concentrates). This further led to less patient visit and less burden at HTC. On top of that, there were no side effects observed in any of the PwH making it an ideal product for PwH with inhibitors and for those who had high ABR.

ORAL PRESENTATION

Frequency of Inhibitors and homozygous gene (c.3622delT) in Patients with Type III von Willebrand Disease

Mr. Muhammad Yaqoob Hassan (M. Phil MLS Haematotechnology), Prof. Dr. Muhammad Asif Naveed (FCPS & PhD Haematology), Ms. Khanasa Qamar (M. Phil Haematology), Ms. Madiha Shakoor
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Background: Von Willebrand disease (vWD) is an inherited bleeding disorder due to von Willebrand factor (VWF) deficiency or dysfunction, crucial for primary hemostasis. vWD has three types: Types 1 and 3 involve quantitative defects, while Type 2 has functional abnormalities. Severe Type 3, often caused by large VWF gene deletions like c.3622delT, poses challenges with potential antibody development.
Objective: The present study aimed to assess the prevalence of inhibitors and the homozygous gene mutation (c.3622delT) in patients diagnosed with Type III vWD in the Pakistani population, considering both individuals with and without inhibitors.

Methods: Total 71 patients diagnosed with type III vWD participated in research. Prior diagnoses were confirmed through various laboratory tests, including Platelet counts, Bleeding Time, Prothrombin Time, APTT, FVIII levels, vWF: Ag levels, and Ricof levels at Department of Hematology, University of Health Sciences Lahore. vWD antibody assessment employed ELISA on plasma samples, while mutational analysis of DNA extracted from whole blood was conducted via PCR.

Results: In our study, the mean PT and APTT for all patients were 12±0.9 and 54.8±5.7 sec, respectively, while the mean FVIII level was 2.5±1.49, and vWF: Ag levels measured 1.8±0.9. Notably, 7% of participants exhibited alloantibodies against vWF. Importantly, no homozygous gene mutation (c.3622delT) associated with Type III vWD was detected in this cohort.

Conclusion: These results enhance comprehension of the clinical characteristics of Type III vWD patients in this area, underscoring the prevalence of inhibitors (7%) and the lack of a distinct gene mutation (c.3622delT) associated to Type III vWD.

ORAL PRESENTATION

Clinicopathological Spectrum of Paediatric Thrombocytopenia During Hospital Stay

Haleema Urooj, Bushra Moiz, Mohammad Shahzaib, Eisha Saadat, Sadaf Altaf
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Objective: This study aimed in evaluating the severity and outcome of thrombocytopenia in children admitted in non-critical setting.

Methods: During August to December 2022, admitted patients (age 2-18 years, both sexes) were evaluated for thrombocytopenia (< 150 x 10E9/L). Electronic records were reviewed for etiology, length of stay (LOS), outcome, and platelet transfusions. Complete blood count or CBC (Sysmex, XN 9000), peripheral film-review and routine coagulation profile (where available) were obtained from computerized system. CBC was compared in patients with and without dengue using Mann Whitney (SPSS 19). ERC approval # was 2022-8044-23395.

Results: Overall, 200 (131M/69F) of 2318 patients had thrombocytopenia (8.6%). Etiology included infections (n=175), malignancy (n=5), surgery (n=11) and other causes (n=9). NS1 antigen/IgM confirmed dengue fever (DF) was predominant as observed in 93 (46.5%) patients while systemic infection was the next common cause (46.0%). Severe thrombocytopenia (<20x109E/L) and bleeding were observed in 27 (13.5%) and 16 (8.0 %) patients respectively. Platelet transfusions were required in 2 patients only. LOS was 1-30 days and mortality was 2%. Statistically significant difference (p-value <0.05) was observed in haemoglobin (0.000), platelet count (0.019), prothrombin time (0.024) and haemoglobin-platelet ratio (0.004) in patients with and without dengue DF.

Conclusion: Infection was the most frequent cause of low platelets in children in a non-critical setting. However, majority of the patients had non-severe thrombocytopenia with a low risk of bleeding and mortality.

ORAL PRESENTATION

Management of severe hemophilia a: low-dose prophylaxis vs. On- demand treatment

Dr. Rabeea Munawar Ali, Madiha Abid, Sidra Zafar
National Institute of Blood Disease and BMT, Karachi, PK

Objective: Prophylactic clotting factor infusion regimens to prevent bleeding and joint deformity has become the standard of care in severe hemophilia A patients. The aim of this study is to assess low-dose factor prophylaxis in our population as an alternative approach to managing severe hemophilia A.

Methods: A prospective cohort study that included 68 hemophilia A patients divided into two groups, i.e., Prophylaxis and on-demand. The two groups were compared for annualized bleeding rate (ABR), hospitalization, units of factor VIII (FVIII) infused, or plasma products transfused, i.e., fresh frozen plasma (FFP) and cryoprecipitate (CP), and development of FVIII inhibitors.

Results: Of the 68 patients recruited in this study, 25 (36.7%) were in the prophylaxis group, and 43(63.3%) were in the on- demand group. The on-demand group presented a higher median-IQR ABR [8(20-3) vs. 5(10-1.5), p-value 0.024], several hospitalizations (39.7% vs. 0, p-value 0.001), and inhibitor development (9.3% vs. 0, p-value 0.289) compared to the prophylaxis group. The prophylaxis approach demonstrated a significant negative correlation of ABR with FVIII prophylaxis (r=-0484, p=value=0.014). Moreover, no hospitalizations or inhibitor development was observed in the prophylaxis group. The estimated annual consumption of FVIII was 328 IU/kg/year in the on- demand group and 1662.6 IU/kg/year in the prophylaxis group. However, a highly significant difference in plasma product utilization was observed between the two groups, i.e., p-value <0.001 and 0.038 for FFP and CP, respectively.

Conclusion: Low-dose factor prophylaxis resulted in improved outcomes compared to on-demand treatment in terms of ABR, joint bleeding, hospitalization, and the development of inhibitors. This treatment approach should be adopted as an economically feasible alternative to high-dose Prophylaxis in resource-constrained countries.

ORAL PRESENTATION

Emicizumab prophylaxis: a novel alternative therapy for severe Hemophilia A patients with and without inhibitor

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Objective: Assessment the efficacy of Emicizumab prophylaxis in terms of bleeding, safety, and quality of life of severe hemophilia A (HA)

Methods: n this prospective study, severe HA patients were recruited from January 2022 to June 2023. Inhibitor positive and inhibitor negative patients with annual bleeding rate (ABR) 8 or greater and past histories of bleeding like intra cranial, intra-abdominal, and pseudo-tumors were included. Emicizumab loading dose was 3mg/kg in the first 4 weeks and the maintenance dose was started at week 5 at 6mg/kg/month. Patients detail bleeding history, demographics were recorded. The five-level five-dimensional questionnaire (EQ-5D-5L) were used to evaluate patients. Furthermore, Hemophilia Joint Health Score (HJHS) and Functional Independence score in Hemophilia (FISH) were applied for the assessment of joints at different time points. Results were analyzed by SPSS version 21.

Results: A total of 36 HA male patients with mean age of 19.7 ±14.42 years were recruited in the study among them 19 patients were inhibitor positive while 17 were negative. Patients clinically presented with bleeding symptoms which includes: hemarthrosis >95%, GI bleeding 13.8 %, bruises and gums bleeding 13.8%. Significant reduction was observed in the bleeding episodes after the therapeutic intervention, joints assessment and EQ VAS analog scores which showed a significant improvement in health state after treatment, similarly, there was a remarkable reduction in bleeding episodes and increased Quality of life, among the patients. The annualized bleeding rate (ABR) decreased from 53.6% episodes per year prior to treatment to 2.4% during Emicizumab therapy. Prior to initiating

Emicizumab therapy, participants exhibited an average FISH score of 16 and HJHS score of 10, indicating moderate limitations due to joint-related issues. After treatment, the mean FISH score improved to 9 and HJHS score to 4 reflecting a substantial enhancement in participants' ability to perform daily activities ($p < 0.0057$)

Conclusion: Our results showed that patients on prophylactic treatment with Emicizumab were less restricted and had improved quality of life due to marked decrease in bleeding episodes which resulted in improved health and social lives. In addition, it was well tolerated, and no participant discontinued treatment because of adverse events.

ORAL PRESENTATION

Incidence of Thrombosis in patients undergoing hemodialysis at Multan Institute of Kidney Diseases

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Background: Chronic kidney disease (CKD) presents global health and economic challenges, especially in resource-limited regions like Pakistan. Owing to the complexities associated with transplantation, hemodialysis (HD) stands as the principal mode of management. It alters platelet function and coagulation, impacting clot formation at access sites and leading to thrombosis & its associated complications. This study explores changes in coagulation profile with a main focus on the incidence of thrombosis in patients on maintenance HD, aiming to fill knowledge gaps for targeted prevention and treatment strategies in this population.

Methods: A retrospective study was conducted at the Multan Institute of Kidney Disease, after retrieving the data from Laboratory Information System (LIS). The study comprised a total sample size of 85 individuals, with 54% males (n=46) and 46% females (n=39). This cohort consisted of chronic kidney disease (CKD) patients undergoing thrice- weekly dialysis, spanning from August 2017 to August 2022. Various variables were collected, including age, gender, height, weight, BMI, co-morbidities (such as diabetes mellitus, hypertension, ischemic heart disease, connective tissue disorders, and malignancy), risk factors (AVF, Catheter, DVT, PE), PT, APTT, INR, and platelet count before the initiation of dialysis.

Results: In a cohort of 85 patients, it was noted that 33 individuals (38.8%) developed thrombosis during the progression of their illness. Among them, 20 experienced thrombosis once, 4 had it twice, 8 encountered it thrice, and 1 suffered from it four times.It was unexpected to discover that all these patients exhibited

normal coagulation profiles, with the highest prothrombin time (PT) value recorded at 38 seconds and an international normalized ratio (INR) of 2.9.

Conclusion: The findings indicate an overall thrombosis incidence of 38.8% in CKD patients on maintenance hemodialysis. Despite apparent normalcy in the coagulation profiles of dialysis patients, there exists a notably high occurrence of thrombosis within this patient group.

GUEST SPEAKER

Many faces of lupus: unfolding diagnostic challenges

Dr Bushra Moiz
Head of Haematology and Transfusion Medicine services and Department of Pathology and Laboratory Medicine, Aga Khan University, Karachi - PK

Anti-phospholipid syndrome (APS) is an autoimmune disorder, though rare but can be life threatening. It is characterized by the presence of autoantibodies against negatively charged phospholipids and in complex of proteins like prothrombin and beta2 glycoprotein-I (β2-GPI). These include lupus (LUP), anticardiolipin antibodies (ACA) and β2GPI. Clinical presentation of APS is either as thrombotic APS (arterial or venous) or as obstetric APS. International Society of Thrombosis and Haemostasis (ISTH) requires one clinical event with the concomitant presence of any of the three antiphospholipid antibodies for establishing the diagnosis of APS. It is imperative for laboratories to give correct diagnoses as these patients need lifelong anticoagulation to prevent future thrombotic events. While testing for ACA and β2GPI is straight forward using CLIA, the case is not same for LUP. Laboratories face challenges in standardization and interpretation of results for patients already on anti-coagulants. LUP is the most mysterious of all antibodies as it not only interferes with clotting factors but also with other laboratory tests such as activated protein C resistance etc. In this talk, various faces of lupus will be discussed through clinical scenario and how laboratories can help the clinician in correct diagnosis of APS.

GUEST SPEAKER

Recent Advances, Challenges and Way Forward in Management of Hemophillia A in Pakistan

Dr Ayisha Imran
Consultant haematologist & HOD blood bank Chughtai Healthcare, Lahore - PK

Hemophillia A is a prevalent disorder in our country and many organizations are working in collaboration with World Federation of Hemophilia (WFH). Pakistan is a country with a low Human Development Index and thus there are many challenges in diagnosis and management of Hemophilia A due to lack of awareness, variable presentation of the disease and cost constraints.

Diagnosis has always been a challenge in our country due to lack of awareness and limited diagnostic facilities. It is high time that we should be focusing more on recent developments like, chromogenic assays, carrier detection and genetics. The traditional approach to management of Hemophilia A in our country has been shifting towards plasma derived products and recombinant concentrates over the last few years. With the introduction of Emicizumab in Pakistan through humanitarian aid, patients have been experiencing lives which are almost near to normal with remarkable improvement in their rehabilitation be it physical, economic or psychosocial. My proposal is adjusting the dosage of Emicizumab such that maximum number of patients can benefit from this game changer product. But with uncertainty about how long this aid by WFH will continue and with increasing burden of the disease, we should be mentally prepared and have a backup plan as we move forward.

GUEST SPEAKER

Platelet Aggregation Studies of Thrombocytopenic Patients: Updates on Evidence and Recommendations

Dr Catherine Hayward
Professor of Pathology and Molecular Medicine, and Medicine, at McMaster University, and the Head of Coagulation for the Hamilton Regional Laboratory Medicine Program in Canada

Light transmission aggregometry (LTA) is important for diagnosing platelet function disorders (PFD) and forms of von Willebrand disease (VWD) that affect ristocetin-induced platelet aggregation (RIPA). Nonetheless, data has been lacking on the utility of LTA for investigating thrombocytopenic patients and platelet rich plasma samples with low platelet counts (L-PRP). Previously, we developed a strategy for diagnostic LTA assessment of L-PRP that included: 1) acceptance of referrals/samples, regardless of thrombocytopenia severity; 2) tailored agonist selection, based on which are informative for L-PRP with mildly or severely low platelet counts, and 3) interpretation of maximal aggregation (MA) using regression-derived 95% confidence intervals, determined for diluted control L-PRP (C-L-PRP). We recently reevaluated the strategy, and improvements to testing recommendations, including test interpretation. The use of L-PRP specific-RI helped diagnose PFD of diverse types, and it did not result in any false negatives for patients who had a PFD or VWD diagnosis verifiable by other tests (e.g., VWD screens, flow cytometry, genetics, etc.). In contrast, the expert consensus recommendations, to assess PRP with 150-250 X 109 platelets/L by usual procedures, significantly increased the proportion of findings considered abnormal, making it more difficult to exclude PFD and VWD affecting RIPA, particular for the subgroups with ITP or thrombocytopenia of unknown cause, many of whom had minimal bleeding symptoms. Additionally, the recommendation to first test lower concentrations of agonists, such as collagen, ADP, and epinephrine, and only higher concentrations if the findings are abnormal,

was problematic for L-PRP. While only few agonists (collagen, ristocetin) were informative for L-PRP with ≤80 X 109 platelets/L, we found paradoxically a greater LTA diagnostic yield for the patients with the lowest platelet counts. The L-PRP strategy helped rule in, or rule out, Bernard Soulier syndrome (BSS), type 2B and platelet type-VWD, and suspected ITGA2B/ITGB3-RT. LTA abnormalities were also present in some patients with acquired thrombocytopenia, including immune thrombocytopenia complicated by acquired BSS. Diagnostic LTA with L-PRP, using a strategy that considers thrombocytopenia severity, is feasible and informative.

GUEST SPEAKER

Between a rock and a hard place

Dr. Abdul Mannan
Consultant Haematologist at North Wales Cancer Treatment Center, Director at Bangor Haemophilia Center, and Clinical Haematology Lab Lead for Betsi Cadwaladr University, UK

Direct oral anticoagulants (DOACs) are established as the preferred anticoagulation strategy for atrial fibrillation (AF) and venous thromboembolism (VTE), surpassing vitamin K antagonists (VKAs). DOACs demonstrate superior or non-inferior efficacy with a lower risk of intracranial hemorrhage. Despite their advantages, practical considerations include issues like drug–drug interactions, transitions to alternative therapies, and challenges in specific patient populations. This talk aims to provide a practical guidance for DOAC prescription and address challenging scenarios in clinical practice.

Additionally, resuming anticoagulation after severe bleeding challenges, prompts a careful decision-making process. Evidence supports resuming anticoagulation for gastrointestinal and intracranial hemorrhage survivors, with a default plan of resumption. Collaborative decision-making is crucial considering factors like the index bleeding event, thromboembolic risk and comorbidities. While optimal timing for resumption requires further research, waiting approximately 7- 14 days is suggested after gastrointestinal bleeding, and within the first month post-discharge for intracranial hemorrhage, for a balanced approach to recurrent bleeding, thromboembolism, and mortality risks.

GUEST SPEAKER

Metabolic Syndromes associated with increased thrombotic tendency

Prof Waseem Iqbal
Professor and Chairman Department of Pathology FRPMC,
Air University, Karachi - PK

Metabolic syndrome (MetS) is characterized by visceral obesity, insulin resistance/Type II Diabetes, hypertension, and dyslipidemia (HDL: low, triglycerides: increased) . It is significantly associated with increased thrombosis in the body causing high mortality and morbidity as a result of cardiovascular disease. Clinically MetS is defined by presence of three or more above mentioned disorders.

Complications of MS include hyperinflammatory state due to cytokine storm, cardiovascular and cerebral artery disease due to increased thrombosis, and chronic liver and kidney diseases. Other complications include, fatty liver/NAFLD, polycystic kidney and increase incidence of cancer. There is a cross-linkage between inflammation and coagulation in patients of MetS particularly when suffering from overwhelming infections like COVID-19. The disease may be associated with high levels of inflammatory markers such as CRP, ferritin IL-6, and D-dimers. Vascular endothelial cell dysfunction mainly due to cytokine insult plays a key role to promote hypercoagulable state in such patients.

Patients with visceral obesity have higher risk of thrombosis and its complications They suffer from chronic inflammatory state characterized by increased levels of adipokines and pro inflammatory cytokines such as TNF-a, IL-1b, IL-6, MCP-1 and leptin produced by adipose tissue leading to deregulatory immune response, endothelial dysfunction and thrombosis. There may also be high levels of CRP, ferritin and D-dimers.

Patients with insulin resistance/D.M Type 2 with or without systemic hypertension have more tendency towards thrombosis. A major cause of death in diabetic

patients is coronary and cerebral artery thrombosis due to hypercoagulable state as a result of endothelial dysfunction, increase VWF, tissue factor release, multiple clotting factors activation, decrease in protein C and S activity. This triggers fibrinolysis, marked by increased tissue plasminogen activity(tPA), and secondarily increase in PAI-1, and a-2 anti-plasmin.

Conclusion

Patients of MetS with obesity and DM with or without hypertension having poor glycemic control in the presence of overwhelming infection have higher levels of CRP, IL-6, ferritin and D-dimers, signifying the presence of hyperinflammatory and hyper coagulable state.

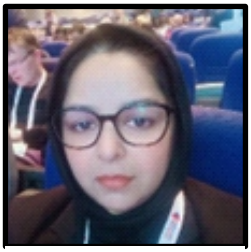
Life style modifications and foods such as carbohydrates, fatty meals, junk food should be restricted. Fruits, vegetables, nuts, fish olive oil should be added in the diet. Likewise, by adding Vitamin D and C, Zinc, supplements having anti-inflammatory, immune-modulatory effect can be helpful

These dietary products and supplements and use of anti-inflammatory and anti-coagulation drugs can fight inflammation, thrombotic tendency and reduce morbidity due to cardiovascular and cerebral disease in MetS.

Key words

Metabolic Syndrome, Hypercoagulable state, Hyper-inflammation, Visceral obesity, Insulin resistance

GUEST SPEAKER



Beyond rearrangement: novel insights into the diverse role of mll (kmt2a) gene alterations in acute leukemia

Dr Shawana Shahid
Consultant Hematologist, Assistant Professor of Pathology, Associate program Director Hematology, Section Head cytogenetics lab, Shifa International Hospital, Islamabad - PK

The Mixed Lineage Leukemia gene (MLL), also known as KMT2A, is crucial for maintaining normal hematopoiesis. Located in chromosome band 11q23, this gene codes for a histone methyltransferase which regulates gene transcription.

The prognostic implications of MLL gene rearrangement are well described in leukemic patients. An estimated 10% of all leukemias harbour MLL1 translocations. A recent study identified a total of 135 unique MLL gene rearrangements in a study population of 2345 pediatric and adult patients from several countries. KMT2A rearrangements are associated with unfavourable outcomes in patients with Acute Lymphoblastic Leukemia (ALL) and Acute Myeloid Leukemia (AML), regardless of the specific gene partner.

More recently, it is becoming evident that the role of MLL gene extends beyond the impact of gene rearrangement. Various other genetic alterations such as MLL gene amplification, inversion, deletion and partial non-tandem duplication have also been documented in patients with leukemia. However, these genetic abnormalities are rare as compared to rearrangements. Thus, data available is scarce

The aim of our study is to report the variety of MLL gene rearrangements including copy number variations in patients with acute leukemia. We would also be reporting the impact of these genetic aberrations on patient outcomes, including remission status and survival. We hope our data would guide hematologists in the risk stratification and management of patients with leukemia.

GUEST SPEAKER

Challenges in hematopathology with highlight of the new WHO guidelines

Dr. Heba Raslan
Consultant Hematopathology at KFSH KSA

The field of hematopathology is continually evolving and with the release of the new World Health Organization (WHO) classification of tumors of the hematopoietic and lymphoid tissues, there are new challenges and opportunities in the diagnosis and management of hematologic malignancies. This lecture will present case studies that highlight some of these challenges, including the accurate classification of rare and complex hematologic neoplasms, the integration of molecular and genetic data into the diagnostic process, and the importance of applying the WHO criteria in the evaluation of these cases and demonstrate the significance of the updated WHO classification in guiding clinical decision-making and improving patient outcomes in hematopathology.

GUEST SPEAKER

Clinical Application of FISH and Karyotyping in diagnosis for Hematological Neoplasms

Dr Zeeshan Ansar
Assistant Professor, Section Head Molecular Pathology, At the Department of Pathology and Laboratory Medicine, The Aga Khan University Hospital, Karachi - PK

Over the past five decades, innovative technical advances in the field of Hematological cancer cytogenetics have greatly enhanced the detection of chromosomal alterations and have facilitated the research and diagnostic potential of chromosomal studies in Haempathology. Karyotyping of a single cell is still the easiest way to understand the relationship between clonal evolution and disease progression. The use of advanced FISH techniques allows for the identification of chromosomal alterations that are unresolved by karyotyping. The main goal of the Karyotyping and FISH laboratory is to identify the techniques that are most useful and informative for a particular study and perform thorough analyses to arrive at an interpretation that is useful for research and diagnostic purposes. IF the morphologic, cytogenetic, and molecular findings are inconsistent. It is envisaged that efforts made towards the characterization of molecular defects in neoplasms will ultimately be translated into better clinical outcomes for patients. Taken together, the morphologic, karyotyping, FISH, and molecular features should all be considered to obtain accurate diagnoses of malignancies. This highlights the clinical importance of a combined modality approach for the accurate diagnosis and classification of cancers.

GUEST SPEAKER

Genetic Landscape of AML: Decoding the Complexity

Dr Rafia Mahmood
Consultant Haematologist
Armed Forces Institute of Pathology
Rawalpindi - PK

Acute myeloid leukemia is a heterogeneous disease characterized by increased proliferation and impaired differentiation with a spectrum of clinical presentations and outcomes. While age, performance status and concomitant comorbidity are factors that affect outcome, well known recurrent gene fusions have a significant role not only in diagnosis but also in prognosis. However, discovery of new genetic mutations and recent advances in diagnostic modalities have led us to know that many other genes may be involved in the process of leukemogenesis. These include the genes associated with DNA methylation, chromatin remodeling, transcriptional deregulation and activated signaling. Each patient is unique and the genetic profile determines disease course and response to treatment. Disease biology, clinical presentations, severity and outcome of AML are different and distinctive for different geographic/ethnic population groups. These include the genes associated with DNA methylation (DNMT3A, TET-2, IDH 1, IDH 2), chromatin remodeling (ASXL1, EZH 2, BCOR, KMT2A), transcriptional deregulation (CEBPA, WT 1, RUNX1) and activated signaling (NRAS, KRAS, FLT3, JAK 2, CBL, KIT). Recent advancements and new technologies like next generation sequencing (NGS) have enabled the detection of these mutations.

European Society for Medical Oncology (ESMO) guidelines for risk stratification are only based on NPM1 mutations. Acknowledging the role of molecular events in AML, the European Leukemia Net (ELN) revised the prognostic classification for leukemia to add new clinically significant mutations (RUNX1, ASXL1 and BCR-ABL1) to the previously identified molecular risk categories defined by mutations in NPM1, CEBPA, FLT3-ITD and TP53. NCCN 2020 guidelines also recommend testing for actionable mutations (CEBPA, ASXL1, IDH1 and IDH2) associated with

specific prognosis and having therapeutic implications to guide medical decision making. The American Society of Clinical Oncology (ASCO) clinical practice guidelines recommend additional testing to identify mutations in KIT, DNMT3A and IDH1/IDH2 genes.

GUEST SPEAKER

Choosing Wisely Campaign for Hematologists: Is it more pertinent to low and middle income countries

Dr. Syed Muhammad Irfan
Professor of Hematology at Liaquat National Hospital and Medical College, Karachi - PK

Choosing Wisely, an international medical campaign, is a review of Hematology practices with main role being played by American society of Hematology. The aim has been to identify tests / treatments / procedures, based on evidence and cost that could best be avoided in the genomic era. For obvious reasons, campaign appears more relevant to low and middle socio-economic countries like Pakistan.

Following are the recommendations given by international haematology societies:

1. Don't transfuse more than the minimum number of RBC units necessary to relieve symptoms of anemia (7-8 g/dl)
2. Don't test for thrombophilia in adult patients with VTE occurring in setting of major transient risk factors.
3. Don't use IVC filters routinely in patients with acute VTE.
4. Don't administer plasma or PCC for non-emergent reversal of vitamin K antagonists.
5. Limit surveillance CT scans in asymptomatic patients following aggressive lymphoma treatment.
6. Don't treat with an anticoagulant for more than three months in patients with a first VTE occurring in setting of major transient risk factor.
7. Don't routinely transfuse patients with SCD for chronic anemia or uncomplicated pain crisis.
8. Don't perform baseline or routine surveillance CT in patients with early stage CLL.
9. Don't test/treat suspected HIT in patients with low pre-test probability.
10. Don't treat patients with ITP in absence of bleeding or very low count.
11. Don't give IVIG as first line treatment for patients with asymptomatic ITP.
12. During interruption of warfarin anticoagulation for procedures, don't 'bridge'

with heparin unless risk of thrombosis is high.

13. Don't order thrombophilia testing in women with 1st early pregnancy loss.
14. Do not treat patients with immune thrombocytopenic purpura (ITP) in the absence of bleeding or a platelet count <30,000/L without risk factors for bleeding.
15. Do not conduct thrombophilia testing in adult patients under the age of 50 years.
16. So, we need to practice wisely and work in the larger interest of our patients, community and profession.

GUEST SPEAKER

Diagnostic Spectrum of Sickle Cell Disorders: The Local Perspective

Dr Manzar Bozdar
Consultant Haematologist and Assistant Professor of Pathology, AFIP, Rawalpindi - PK

Sickle cell disease (SCD) usually affects African people but is also prevalent in South East Asia, Indian subcontinent, Saudi Arabia, and Mediterranean countries. In Pakistan the provinces of Baluchistan and Sindh have the most cases of SCD. These disorders can be diagnosed by neonatal screening which ensure provision of comprehensive care from an early stage, but due to resource constraints low and middle-income countries cannot implement the newborn screening programs. Patients with SCD often present with painful episodes and children with haemolytic anemia must be screened for Sickle cell disorders. Various diagnostic modalities and the spectrum of sickling conditions being diagnosed in our set ups will be discussed as clinical case scenarios and the local and regional data for the disease will also be highlighted in this talk.

GUEST SPEAKER

Artificial Intelligence and Red Cell Disorders: Recent Updates

Dr Muhammad Asif Naveed
Professor of Haematology and Director of the Directorate of Postgraduate Studies at the University of Health Sciences, Lahore - PK

In recent years, the intersection of Artificial Intelligence (AI) and the study of Red Cell Disorders has yielded significant advancements, potential of revolutionizing diagnostics and treatment strategies. AI technologies, such as machine learning algorithms, are proving instrumental in analyzing vast datasets related to hematological disorders. These tools enable more accurate and rapid identification of markers, aiding in early detection and personalized medicine approaches. Additionally, AI is enhancing the understanding of complex molecular pathways involved in red cell disorders, facilitating drug discovery and the development of targeted therapies. The synergy between AI and hematology holds promise for improved patient outcomes, as researchers leverage cutting-edge technology to unravel the intricacies of these disorders and pave the way for innovative interventions. As this interdisciplinary collaboration continues to evolve, the integration of AI in hematological research promises a brighter future for individuals affected by red cell disorders.

ORAL PRESENTATION

Serum ferritin trends and growth impairment in thalassemia major; a scientific exploration.

Dr Amara Urooj, Dr Kiran Amir, Professor Dr. Ikram Din Ujjan
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Background: Beta Thalassemia major prevalence in Pakistan ranges from 5.0-7.0%. Thalassemia is the most common monogenic inherited disorder and is associated with reduced synthesis of structurally normal Haemoglobin. The patients require lifelong sequence of multiple blood transfusions leading to the inimical condition of iron overload making iron chelation therapy imperative. Iron overload and high serum ferritin levels have been implicated in physical growth impairments.

Objective: To determine the trends and impact of serum ferritin levels on physical growth in Thalassemia major patients, using height and weight Z-scores.

Methods: This cross-sectional study was conducted at the thalassemia center, LUMHS, Hyderabad on 100 Thalassemia major patients enrolled for regular blood transfusions, of both genders aged 2-20 years, excluding those with other congenital disorders and acute or chronic illness other than thalassemia. Interviews yielded demographics. Anthropometric measurements were taken. Serum Ferritin was measured using Cobas 411 Hitachi analyzer. Height and weight Z-scores were calculated according to WHO and CDC standard growth charts. Height and weight Z-scores less than -2 were labeled short stature and underweight for age respectively.

Results: Subjects were aged 2-9 years with 60 males and 40 females. Mean serum ferritin was 2235.9 ng/ml and the values ranged from 69- 9140.4 ng/ml. 98% subjects had raised serum Ferritin levels. 60% subjects had height Z-scores <-2(short stature) and 74% had weight Z-scores <-2(underweight).

Conclusion: Raised serum ferritin levels play a role in impairing growth in thalassemia major patients. Effective, early and regular iron chelation therapy and regular serum ferritin level monitoring is necessary to prevent growth failure.

ORAL PRESENTATION

Hb E syndrome, Unfolding of a new haematological challenge

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Objective: Hemoglobinopathies are genetic defects resulting in abnormal formation and function of globin chains in hemoglobin synthesis. Hemoglobin E is a common variant with high frequency in Asia. The objective of this study is to elaborate hemoglobin E disorders based on hematological parameters and HPLC.

Methods: This cross sectional study was based in Diagnostic and Research Lab, Liaquat university of medical and health sciences Jamshoro/Hyderabad. The study was extended to period of two years i.e. 1 January 2021- 31 December 2022. We analyzed 9690 EDTA blood samples for complete blood count and hemoglobin variants by automated analyzers through sysmex XN1000 and variant II Bio-Rad hemoglobin testing system respectively.
inclusion criteria:
Patients with: Age > 6months, history of recurrent PCV transfusion, Family history of hemoglobinopathies. exclusion criteria:
Patients with: Age <6 months or > 60 years. Patient with known hemoglobinopathy, patients with history of recent PCV transfusion.

Results: 9690 chromatographs were analyzed and Hb E was detected in (n= 19 or 0.19%). HbEA in (n=10 or 0.10%) and HbE/B- Thalassaemia in (n=09 or 0.09%). Hb E/B Thalassaemia was found to be severely affected hematologically.

Conclusion: Hemoglobin E variants are common in Pakistan with HbEA and HbE/B Thalassaemia being reported the most. HPLC is an easy and cost effective method for detection of hemoglobinopathies. Furthermore molecular diagnosis of Hb E can be made.

ORAL PRESENTATION

Clinico haematological Characteristics and Survival Analysis of Aplastic Anemia in Pakistan; a Single Centre Experience

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Background: Aplastic Anemia (AA) is characterized by pancytopenia and hypocellular bone marrow. Several factors like infections and toxins can suppress hematopoietic cells with an unknown exact cause. The study aims to analyze demographics, lab data, clinical features, and cytogenetic profiles of aplastic anemia patients.

Methods: A retrospective cohort study conducted at NIBD Hospital Karachi after approval by Institutional Ethics Committee. In this study, AA patients were enrolled from January 2013 to December 2021. Data collection included demographic, laboratory, and clinical characteristics including age, gender, symptoms, treatment, and blood counts. Data analysis was by using SPSS v23.

Results: Based on camitta classification, a total of 362 AA patients were enrolled in the study. The frequency of severe AA was most common 199(55%). Median and interquartile range (IQR) age of overall patients was 17(11-26) years, for children and adult population were 12(9-14) years and 28 (21-43) years respectively. Male predominance was observed i.e.251 (69%). The most common presenting complaint was fever 202(55.8%). The median and IQR of hemoglobin (Hb) was 7.8(5.8-9.4) g/dl, MCV 90(83-91) fl, total leucocyte count (TLC) 2.6 (1.9-3.6) x 109/l, absolute neutrophil count (ANC) 0.64(0.27-1.2) x109/l and platelet count 13 (5-27) x 109/l. Bone marrow cytogenetics was done and 76 (67%) patients were found to have normal karyotype. CMV was positive in 24(6.6%). Majority of patients were treated with blood transfusion and supportive care 230(64%) and the survival was 84%.

Conclusion: The study reveals a substantial cohort of severe acquired AA. Limited standard treatment uptake suggests financial constraints. Larger collaborative studies are needed for comprehensive analysis.

ORAL PRESENTATION

HOMA-IR & HOMA-BETA as a predictor of prediabetes & diabetes in transfusion dependent Beta Thalassemia Major patients, along with association of iron overload.

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Objective: To determine
*Incidence of DM in transfusion dependent Beta-Thalassemia patients.
*Beta-cell function of pancreas by HOMA-Beta & insulin resistance by HOMA-IR.
*Relation of Beta-cell function & insulin resistance with iron overload status.

Methods: This cross sectional study was conducted in Baqai Medical University & Muhammadi Thalassemia Center Karachi. 100 patients between the age of 3 to 16 years were recruited for this study. Lab investigations Serum Ferritin, Plasma Insulin, FBS & HbA1c were performed on Roche Cobas e411 & c111. HOMA-IR and HOMA-Beta were calculated.

Results: In accordance with HOMA-IR, 13% of patients had optimal (Mild) insulin resistance, 15% had early (Moderate) IR, 48% had significant(Severe) IR, 24% had normal insulin. HOMA-Beta was significantly low in diabetic than non- diabetic patients ($p<0.01$). Incidence of diabetes mellitus in transfusion dependent beta thalassemia major patients was 15% and 10% patients were pre-diabetic.

Conclusion: HOMA-Beta & HOMA-IR are useful predictors of insulin resistance, there is an association of iron overload with insulin resistance as Beta-Thalassemia patients developed insulin resistance because of increase frequency of blood transfusions.

ORAL PRESENTATION

Markers of Endothelial Dysfunction and Iron Deficiency in Patients with Polycythemia

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Objective: The objective of the study was to determine and compare the levels of iron deficiency and endothelial dysfunction markers i.e., TM and vWF in polycythemia vera, secondary polycythemia and healthy control group.

Methods: A total of 60 participants was included comprising 20 in each group. The blood samples were collected in EDTA, gel vials and tri-sodium vials. Biochemical markers include iron deficiency markers i.e., iron, ferritin, erythropoietin and endothelial dysfunction markers i.e., thrombomodulin (TM) and vWF. These markers were measured by ELISA while plasma vWF levels were determined by Stago instrument (Coagulation analyzer).

Results: Current study results revealed that mean serum iron, ferritin and erythropoietin levels were significantly lower in polycythemia vera as compared to secondary polycythemia but no significant difference was shown in the healthy control ($p<0.005$). The median (IQR) thrombomodulin levels were significantly higher than those compared in secondary polycythemia patients and healthy controls however, no significant difference was observed in median TM among secondary polycythemia and healthy controls. Similarly, plasma vWF levels were higher in PV as compared to secondary polycythemia & healthy controls and statistically showed significance ($p<0.001$). However, no significant difference was observed in mean plasma vWF among secondary polycythemia and healthy controls ($p=0.686$).

Conclusion: Therefore, we propose that serum TM and vWF could serve as more effective and early diagnostic tools for understanding polycythemia.

ORAL PRESENTATION

Platelet Concentrate Utilization Trends in a Tertiary Care Hospital: A Comprehensive Analysis

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Objective: The objective of the study was to determine frequency of the appropriate utilization of platelet concentrates in a tertiary care hospital..

Methods: It was a descriptive cross-sectional study that was conducted in Diagnostic &Research Laboratory Liaquat University Of Medical and Health Sciences Jamshoro from January 2022 to June 2023. Patients of both genders, above five years of age receiving platelets transfusions during the study period were included in this study. An informed consent was obtained from the patients. The data was collected on a predesigned form that included patient demographic and clinical details. All patients were categorized whether the platelet transfusion was appropriate or inappropriate according to the mentioned definitions. T test was applied to find statistical difference between appropriate and inappropriate transfusions. .

Results: Out of total 165 patients,85 (52%) were females while 80 (48%) were males. Mean age was 41.75 + 23.1 years with a range of 6-92 years. Maximum patients were in 31-40 years age group. Single donor platelet units were transfused to 27(16.4%) patients while rest 138 (83.6%) patients received random donor platelets. 145 (87.9%) had appropriate transfusion while 20 (12.1%) patients received blood transfusion due to inappropriate indications. ($p < 0.0001$).

Conclusion: From this study it was concluded that a considerable number of patients in hospital setting receive inappropriate platelet transfusions.

ORAL PRESENTATION

Spectrum Of Causes Of Pre-donation Deferrals Based On Donor History Questionnaire At Jinnah Hospital, Lahore

Mr Umer Farooq, Dr Tooba Fateen, Prof Shabnam Bashir, Prof Muneeza Natiq
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Objective: To investigate and identify the diverse spectrum of causes leading to pre-donation deferrals in a tertiary care hospital setting using a donor history questionnaire.

Methods: It is a prospective descriptive cross-sectional ongoing study started from July 2023 at the Blood Bank, Jinnah Hospital, Lahore. Initial three months data is collected from 200 donors aged, 18-65 years, both males and females through consecutive sampling after the informed consent through a structured questionnaire. It has with predefined questions which assess relevant information. This data was analyzed using SPSS.

Results: Among 200 blood donors, predominantly males 71% having mean age of 40±1.2 years. 60(30%) of the donors were deferred from donating blood. Of these,15(8.5%) were temporary deferrals due to recent surgical procedures (1%), recent blood donations (4.5%), ear piercings (1%) and tattoos (2%). The remaining 45(22.5%) were deferred permanently attributed to positive for HCV (8%), HBsAg (4.5%), malaria (1%), and syphilis (2%). Health-related factors leading to deferral encompassed underweight (2%), low hemoglobin in female donors (3%), and jaundice (2%). As this study is ongoing, and future analyses for additional six months aim to provide a more comprehensive understanding of pre-donation deferral patterns.

Conclusion: Blood donor deferral is a crucial step in donor selection and Permanent deferrals causes being more prevalent in our society needs proper education, intervention and treatment for ensuring safe blood donations.

ORAL PRESENTATION

Analysis Of Causes Of Wastage Of Blood & Blood Components In Blood Unit Jinnah Hospital Lahore

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Objective: It is important to maintain the quality and quantity of blood and blood products with minimal or no wastage. The present study was carried out to analyze the main causes of wastage of whole blood & blood products.

Methods: This retrospective study was done in the blood bank of Jinnah Hospital Lahore from Oct-2022 to Oct-2023. Reasons for wastage of 45264 units of blood products were analyzed and data was analyzed using SPSS software. Taking this study as a baseline there will be active intervention in the form of awareness lectures addressing this issue for a month and follow up data will be collected prospectively for next six months after Oct 2023.

Results: 45264 blood units were collected out of which 30495(67.3%) were whole blood and 14769 (32.6%) blood components Out of which PRBCs constituted (44.1%), FFPs (28.5%) & Platelets (27.3%). Total Discarded blood bags was 877 (1.93%). Among the main causes of discard were near to expiry blood bags (41.4%) followed by wastage of unused blood products from end-users due to failure to maintain cold chain ((29.53%). Hemolysis, Leakage, Lipemic & Polycythemic blood bags were other reasons for wastage (29.07%).

Conclusion: Maximum utilization, implementation of blood transfusion services guidelines, maintenance of cold chain, education & training of blood bank staff and liaison with clinical departments of Jinnah Hospital, all can reduce wastage of blood & blood products. After the intervention our follow up study can give us better insight into the improvement in this present percentage of wastage.

ORAL PRESENTATION

Are We Facing An Upsurge In Window Period Donations?

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Objective: Nucleic Acid Testing (NAT), performed individually (ID-NAT) or in minipools (MP-NAT), is a crucial tool for blood transfusion safety, particularly valuable in regions with high incidence of infection on seroreactive donations in resource-constrained environments, minimizing the window period and identifying false positives for transfusion transmitted viral infections like HBV, HCV, and HIV. The objective of this study was to compare the impact of ID- NAT and MP-NAT in Southern Pakistan and to estimate NAT yield and residual risk of TTVIs in the blood units.

Methods: The study collected whole blood units, conducting serological tests on (Vitros, Johnsons and Johnsons, Germany) and nucleic acid testing (MP- and ID-NAT) for HIV-1, HBV, and HCV on Cobas 201 and 6800 automated platforms (Roche diagnostics, Switzerland) respectively during two periods (2016-2018 and 2019-2022). The analysis focused on comparing serological and NAT results to assess the variance in the window period donation for each virus and calculating NAT yield percentage and yield rate.

Results: A total of 77683 and 94674 blood units were collected between 2016-2018 (phase 1) and 2019-2022 (phase 2) respectively. A decline in sero-reactivity % was observed for anti-HIV-1(0.05 to 0.04), HBsAg (1.26 to 0.96) and anti-HCV (1.58 to 0.89) during these two time points. NAT was performed on sero-negative donor units which were 75214 and 92379 in phase 1 and 2 respectively. In contrast to serology, NAT yield % increased for HIV (0.003 to 0.011), HBV (0.101 to 0.228) while decreased for HCV (0.057 to 0.053) when ID-NAT was used. Window period

donations showed 4 folds increase for HIV-1 and 2.2 folds for HBV with a decline of 0.9 for HCV.

Conclusion: The study showed an alarming upsurge in window period donations for HIV and HBV raising a concern for patients's safety. ID-NAT increases the efficacy of donor screening for preventing TTVIs.

ORAL PRESENTATION

Adverse Donor Reactions And Wastage Of Plateletpheresis In A Tertiary Care Hospital

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Objective: Plateletpheresis procedures are generally safe but it is important to identify the adverse reaction and address the factor related to wastage of this expensive product. This study was designed to assess the frequency of adverse reactions in donors undergoing apheresis, so the donor may not discourage from future donations and also delineate the factors associated with wastage of platelets mega units prepared by apheresis as kits are very expensive now a days.

Methods: This retrospective cross-sectional study was performed with a quantitative approach by analyzing 468 individuals from January 2022 to November 2023 at blood bank of Pakistan Institute of Medical Sciences (PIMS) Islamabad (Pakistan). Out of 468 donors, 396 met the criteria for plateletpheresis procedure. 395 (99.75%) donors were male and 1 (0.25%) was female. Plateletpheresis procedures have been performed on Fresinius Kabi (USA) (87.88%) and Trima Accel () 12.12% analyzers.

Results: Out of 468 donors, 72 have been deferred. Number of replacement and volunteer donors is 381 (96.21%) and 15 (3.79%) respectively. Rh positive donors were 361 (91.16%) and Rh negative donors were 35 (8.84%). Blood group B positive (n=124, 31.31%) is most common. 21 adverse reactions were reported in relation to the 396 procedures. The rate of vascular injury, citrate reaction and presynocopal/ synocopal in platelet pheresis procedure was 1.52% (n=6), 0.51% (n=2) and 3.2% (n=13) respectively. 5 units have been wasted due to greenish discoloration (n=2), incomplete donation due to vascular injury (n=1), hyperlipidemia (n=1) and mixing of blood (n=1).

Conclusion: Apheresis procedures on cell separator are safe with low incidence of significant adverse reactions. No significant difference between both cell separators. Auditing the factors associated help us review the policies and improve competency among the staff and helps to encourage the voluntary donors as well. Wastage of mega unit could easily be prevented by improving competency among the staff and it is recommended that there should be national guidelines regarding the use discoloration platelets/ plasma

ORAL PRESENTATION

Pattern Of Blood Components Utilization In Hayatabad Medical Complex: A Provincial Tertiary Care Hospital Of Pakistan

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Objective: The objective of the present study was to review the blood components acquisition patterns and practices of transfusion in a tertiary care hospital.

Methods: An observational cross sectional retrospective study was conducted in the blood bank of Hayatabad Medical Complex (HMC) Peshawar, for a period of six months. The requisition forms for blood components and details of patients acquiring blood products for transfusion recorded in HMC blood bank Blood components issue register were the sources of data. The data was analyzed using software SPSS version 20.

Results: In the study period of six months a total 16025 blood components were transfused with an average of 2670 units per month. whole blood was the maximum blood product transfused and followed by RCC, platelets and FFPs are least utilized blood products. Among total patients 50 % were males while 50% were females. Pediatric units utilized maximum (21.2%) units followed by Gynae/Obs. (19.1%), Medical units demanded 16.7%, Accident and Emergency (A&E) unit 14.1%, surgical units 8.8%, intensive care unit (ICU) 6.8%, Orthopedic units consumed 3.3%, cardiology 3.1%, gastroenterology 2.6 %, oncology 2.4% and endocrinology consumed 1.5 %. Among the positive blood groups B+ was the most frequently utilized contributed 35.7% followed by O+ (25.3 %), A+ (23.9%) and AB+ was the least utilized blood group contributing 8.4% of the total blood components. Among the negative blood groups, A- (2.4 %) > O- (2 %) > B - (1.3 %) and B- (0.9 %) was the least utilized blood group in our study

Conclusion: The study statistics on the usage of blood component are highly valuable to plan awareness sessions in the units of maximum consumption for reducing the overutilization and thus can be available in units for essential needs. Also, it provides a data of blood groups most frequently utilized, which is of great help to maintain the blood components stock in the blood bank for a smooth response of blood components availability in an emergency situation.

GUEST SPEAKER

Clinical & lab evaluation of blood transfusion reactions

Prof Dr Fahim Akhtar
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Armed Forces Institute of Transfusion, Rawalpindi,
Pakistan

The presentation provides a comprehensive overview of blood transfusion reactions, including their definition, epidemiology, classification, evaluation, and workup. It covers various types of transfusion reactions, such as acute hemolytic reactions, febrile non-hemolytic reactions, anaphylactic reactions, transfusion-related acute lung injury (TRALI), transfusion-associated circulatory overload (TACO), and others. The presentation also includes data from the SHOT 2022 report, highlighting the total transfusions, reported events, deaths, and major morbidity events and its comparison to the reactions observed at AFIT. Additionally, it offers recommendations for the management of transfusion reactions, emphasizing the importance of training and immediate recognition of acute transfusion reactions.

GUEST SPEAKER

Neonatal And Paediatric Transfusion

Prof Dr Ayesha Junaid
Consultant Haematologist
Shifa International Hospital, Islamabad, Pakistan

The talk would encompass indications, transfusion reactions, common practical problems / issues in neonatal and paediatric transfusion. Neonatal intensive care unit at Shifa International hospital daily deals with very complicated and delicate underweight septic patients with premature lungs. Providing the gift of life to these tiny humans is challenging and always an uphill task with twins and at times triplets struggling to win the battle of life with rightly selected, timely delivered blood products. With an ambition to soon start with intra-uterine transfusion in this high prevalent thalassemia region, we would be sharing with you some important tasks and goals

GUEST SPEAKER

Patient Blood Management (PBM)

Dr. Muhammad Hasan
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Patient blood management (PBM) is a patient-centred, systematic, evidence-based approach to improve patient outcomes by managing and preserving a patient's own blood, while promoting patient safety and empowerment Successfully implementing a PBM program requires planning, education, teamwork, and resources with support from institutional leadership. It is more than just transfusion avoidance. It includes the use of pharmaceutical agents, blood recovery techniques, surgical tools to limit blood loss, limiting phlebotomy for laboratory testing, adherence to transfusion guidelines, and medical education.

GUEST SPEAKER

Indications and Transfusion Thresholds of blood products: When and How to use

Dr Raheel Iftikhar
Consultant Clinical Haematologist & Transplant Physician
Armed Forces Bone Marrow Transplant Center,
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Over last decade, a number of randomized trials have been done to identify the timing and indications of blood product transfusion. This evidence-based data is now useful in deciding when and how to use blood products in clinical practice to reduce cost, side effects and saving blood inventory.

GUEST SPEAKER

From AA, AB, AO to AI

Dr Mohammad Abdul Naeem
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Artificial Intelligence (AI) has been increasingly integrated into various aspects of healthcare, including blood transfusion services, to enhance efficiency, accuracy, and safety. Here are several emerging roles of AI in blood transfusion services:

Inventory Management: AI can optimize blood inventory by predicting demand based on historical data, current usage patterns, and upcoming events. Machine learning algorithms can forecast the need for specific blood types and quantities, reducing wastage and shortages.

Matching Blood Donors and Recipients: AI algorithms assist in matching compatible blood donors with recipients by analyzing complex genetic and immunological data. This helps in finding the most suitable matches, reducing the risk of transfusion reactions.

Quality Control and Testing: AI systems can improve the accuracy and speed of screening donated blood for infectious diseases, ensuring higher levels of safety. With Image recognition and pattern detection AI can aid in analyzing blood samples for abnormalities or irregularities.

Decision Support Systems: AI-powered decision support tools provide recommendations to healthcare professionals regarding transfusion strategies based on individual patient data, medical history, and best practices, leading to more personalized care.

Real-time Monitoring: AI facilitates real-time monitoring of patients during and after transfusions, flagging any adverse reactions or complications allowing immediate intervention for improving patient safety.

Workflow Optimization: AI streamlines the workflow in blood banks and transfusion services, automating routine tasks like documentation, scheduling, and data entry. This enables staff to focus more on critical aspects of patient care.

While AI offers significant potential benefits in blood transfusion services, its integration should be accompanied by rigorous testing, validation, and continuous monitoring to ensure accuracy, reliability, and ethical use in healthcare settings. Additionally, maintaining patient privacy and confidentiality is crucial when handling sensitive health data through AI systems.

GUEST SPEAKER

The Role of National Blood Policy in Ensuring Safe and Adequate Blood Supply in Low to Middle-Income Countries

Prof Dr Nuzhat Mushahid
Consultant Haematologist & Blood Transfusion Specialist
Mega Medical Complex, Rawalpindi, Pakistan

National policies in healthcare serve as crucial governance tools for states and governments to ensure the safety, quality, and availability of healthcare services, including blood transfusion services. These policies address key organizational, financial, technical, and legal issues to establish and develop a national health system, including "National Blood System ". WHO states that "Establishment and maintenance of a national blood system requires a broad range of societal, scientific and medical competencies that span behavioral science, epidemiology, serological and gene-based diagnostic methods, operational and quality systems management, risk-based decision-making, clinical training, surveillance tools, and business skills, all of which must operate under local physical, social, political and financial conditions and constraints. Given the breadth and scope of the issues and challenges, an interactive set of strategies is needed." All set of strategies should ideally be part of National Blood Policy.

In the absence of a national blood policy, several challenges may arise including, a deficit in blood supply, particularly in remote and rural areas, an increased risk of transfusion-transmitted infections, such as: HIV, hepatitis, and other blood-borne pathogens; collection and distribution of blood will become inefficient and fragmented ; wastage in some areas and shortages in others; a lack of quality management; un fair prices for blood services; absent comprehensive transfusion reporting; system-wide transparency and accountability.

In LMIC the access to safe blood is often limited, particularly in rural areas in. Challenges arise in blood collection, testing, processing, storage, and distribution. As of 2018, only 125 out of 171 countries had a national blood policy, and only 113

out of 171 countries had specific legislation covering the safety and quality of blood transfusion.

A national blood policy explicitly spells out the will of Government for establishing National Blood System and must address several key aspects to ensure a safe and adequate blood supply for all of its population. The aspects include:

1. Organizational structure: Establishing a national blood commission or authority with an appropriate mandate, and delegating defined responsibilities to institutions and/or non-governmental, not-for-profit organizations.

2. Financial basis: Defining the sources of funding for a sustainable national blood program.

3. Quality management: Providing a framework for quality management and ensuring fair prices for blood services, comprehensive transfusion reporting, and system-wide transparency and accountability.

4. Blood donor selection: Implementing guidelines and recommendations for assessing donor suitability and ensuring voluntary unpaid blood donations as the primary source of blood supply.

5. Blood safety and availability: Coordinating blood collection, testing, processing, storage, and distribution at the national level through effective organization and integrated strategies.

6. Oversight on usage of blood, surveillance mechanisms and preventing wastage: Defining all measures for regulating the clinical usage of blood for recipient safety, preventing wastage at all levels and defining surveillance structures and mechanisms.

In conclusion, a national blood policy designed in a local context, with interactive set of strategies that plays a crucial role in ensuring a safe and adequate blood supply in low to middle-income countries. Implementation of the strategic objectives, usually stated in policy, remains the only means to achieve the desired outcomes expected from a National Blood System.

GUEST SPEAKER

Haemovigilance. Past, Present and Future.

Peter J.M. Van Den Burg
Chair of ISBT WP for Haemovigilance
Vitalant, USA

Haemovigilance is the system to monitor the quality of blood transfusion by reporting, analysing and publishing the outcomes and advices related to reactions and events in blood transfusion. Since the practice of blood transfusion, the quality has always been monitored but incidents related to HIV gave an extra trigger to monitor in a more organised way: haemovigilance.

Haemovigilance systems started in Japan and France in 1993/1994, more countries followed and in 2009 many organisations collaborated in the IHN (International Haemovigilance Network). Haemovigilance systems have many monitoring tools in common e.g. grading of serious adverse reactions and events by severity and imputability. An example of the added value of haemovigilance is the monitoring of 'male-only' plasma in relation to the incidence of TRALI, as a result the relation between HLA-antibodies and TRALI became more clear. Another example is the follow-up and look back in cases of hepatitis B that lead to the insight of occult hepatitis B. In addition, in many countries additional anti-HBc tests were implemented. Also based on the success of haemovigilance systems other systems related tot tissues (biovigilance) and donor monitoring and follow up (donorvigilance) were introduced and upcoming regulations give more attention to implement vigilance systems.

Haemovigilance gave us insight and answers but still various aspects need to be explored. For the future the strength of hemovigilance will be more uniform coding and international cooperation. Big data will give us more power to answer questions that could not be answered until now.

GUEST SPEAKER

Navigating CML — Strategies for Management and Overcoming Challenges.

Dr Munira Borhany
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Dr. Ziauddin Medical University Hospital and the Midciti Hospital

Chronic Myeloid Leukemia (CML) is a clonal myeloproliferative disorder characterized by the presence of BCR-ABL oncoprotein carrying markedly enhanced tyrosine kinase activity. Treatment outcomes and survival rates for patients with chronic myeloid leukemia in chronic phase (CML-CP) have substantially improved with the emergence of tyrosine kinase inhibitors (TKIs) and patients with CML can have an average life expectancy near that of the general population. Currently, guidelines endorse all four TKIs — Imatinib, Dasatinib, Bosutinib and Nilotinib — for first line treatment of newly diagnosed CML in chronic phase. However, clinical trials with second generation TKIs have shown significantly deeper and faster responses but had no impact on survival prolongation. Furthermore, generics have entered the market recently for Gleevec and Tasigna that offer more cost-effective therapy and studies have shown good safety profile, with similar results in terms of response in patients treated with generics as compared to reference drugs. In conclusion, with more approved TKIs being available, treatment decisions have become more complex. Treatment choice in the first line is not only influenced by efficacy and safety of the TKIs, but also by patient-specific factors and real-world considerations. A domestic registry to understand the prevalence and outcome of the disease in our setting is the need of the time.

ORAL PRESENTATION

Successful Strategies and Challenges Establishing a Paediatric Acute Leukaemia Biobank in Pakistan

Javeria Aijaz, Muhammad Rafie Raza, Thomas Alexander, Fouzia Naseer, Shakir Hussain, Omer Javed, Maqboola Dojki, Nazia Khursheed, Nickhill Bhakta, Saba Jamal, Muhammad Shamvil Ashraf
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Objective: The presentation will outline the methodology, procedures, challenges, and implementation strategies of setting up a pediatric acute leukemia biobank at Indus Hospital & Health Network (IHHN) in Karachi. Additionally, and with the goal of assisting comparable initiatives in lower-middle-income countries, the approaches and experiences that proved successful in the initialization stage, spanning approximately one year, will be described.

Methods: Key methodological steps include feasibility assessment, budget preparation, facility setup, ethical considerations, staff training, and development of process flows. The primary facilitators of the undertaking included early stakeholder engagement and leveraging IHHN's substantial pediatric cancer patient base. Moreover, embedding of the biobank in an ISO15189 accredited clinical laboratory facilitated seamless integration with routine clinical processes by trained staff. The importance of commencement with minimum initial investments of time, training, budget, and new processes, along with some local successful strategies, will be discussed.

Results: The accomplishments of the biobank thus far include an active process of pediatric acute leukemia specimen collection, swiftly conducted prior to the commencement of treatment, and preceded by obtaining informed consent. The ancillary processes of pre-defined quality indicator monitoring, and storage of two different specimen types and storage temperatures will be described and related data presented. Additionally, the distribution of the pediatric cancer biobank

specimens to date will be specified. Some of the future initiatives include expanding the biobank's scope to frozen tissues and treatment follow-up specimens. Additionally, plans for accreditation, expansion, as well as sustainability measures, including financial management and data security, will be briefly outlined.

Conclusion: We conclude that the establishment of a pediatric acute leukemia biobank is a pioneering effort in Pakistan. With sustained dedication, it may serve as a resource for diverse scientific inquiries in the field of pediatric oncology in Pakistan.

ORAL PRESENTATION

Induction Outcome of Acute Lymphoblastic Leukaemia- Real World Experience

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Objective: To analyze the outcome of induction chemotherapy in patients with acute lymphoblastic leukaemia (ALL) in a low-resource setting.

Methods: Retrospective observational analysis

Patients and Methods: Consecutive patients of any age diagnosed with ALL from March 2022 to October 2023 were included in this analysis. Data included mean age, gender, and physical examination at presentation, disease subtypes, response to induction chemotherapy and complications. SPSS 23 software was used for data analysis.

Results: A total of 51 patients with Acute lymphoblastic leukemia were seen at PCH&BMT, Rawalpindi during the study period. Clinical data and treatment response of 31 patients was available and these patients were included in this analysis. Out of 31 patients, 29 were male and two were female. Median age was 20 years (range 5 – 58 years). Twenty-one patients out of 31 (67.7%) were newly diagnosed, 6 (28.5%) were in first relapse, 3 (9.6%) patients had refractory/relapsed disease and 1 (3.2%) patient was in lymphoid blast transformation of chronic myeloid leukemia (CML). Twenty patients (64.5%) had B-ALL, 1 (3.2%) T- ALL and 1 (3.2%) patient was in B lymphoid blast phase of CML. Molecular workup was available for 25 (80.6%) patients. Three patients were BCR-ABL positive (2 (8%) with de novo ALL, 1 in CML blast transformation). All patients except 7, received multiagent induction chemotherapy based on UK-ALL2011, 6 patients received Fludarabine, cytarabine and daunorubicin/Idarubicin (FLAG-Dauno) and 1 patient received high dose cytarabine, vincristine, daunorubicin and

dexamethasone (Hyper CVAD). Additionally, BCR;ABLl positive patients received a tyrosine kinase inhibitor (TKI) . The complications were mainly infectious. Eighteen patients (58 %) experienced complications during induction therapy-febrile neutropenia in 10 patients (32.2 %), 4 (12.9%) pneumonia, viral encephalitis 1 (3.2%), bacterial meningitis 1 (3.2%), otitis media 1 (3.2%), neutropenic enterocolitis 2 (6.4%). Twenty-three (74.1%) achieved remission after induction, 6 (19.3%) had refractory disease, and 2 (6.4%) patients died during induction treatment.

Conclusion: Our data show that excellent results with an acceptable complication rate can be achieved in a low resource setting. This is significant as this was a diverse patient population including relapsed refractory patients. Longer term outcomes and larger studies may help to refine optimal treatment approach for patients in limited resource settings.

ORAL PRESENTATION

Mitigating Febrile Non-Haemolytic Transfusion Reactions in Thalassemia Major: Clinical Experience of Bedside Leukoreduction Filters in a Resource-Limited PublicSector Hospital

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Objective: The incidence of Febrile Non-Haemolytic Transfusion Reaction (FNHTR), which result from the immune response of the recipient to donor leukocytes, in Beta Thalassemia Major patients ranges from 0.5%-6.8%. Leukodepletion, involving the removal of leukocytes from donated blood, can be implemented during blood collection, processing, or at the bedside. This study aimed to assess the clinical effectiveness of bedside leukoreduction filters in reducing the occurrence of FNHTRs in individuals with thalassemia major.

Methods: A cross-sectional retrospective study was conducted at the Thalassemia Centre, in collaboration with the Blood Bank of Pakistan Institute of Medical Sciences (P.I.M.S). It spanned from August to October 2023, involving 500 multi-transfused thalassemic patients who had previously experienced FNHTRs. Ethical approval was obtained from the review board of P.I.M.S. The selected patients received transfusions through leukoreduction filters. Transfused red cell concentrates varied in age from 2-14 days. Data analysis utilized SPSS Version 20.

Results: Among the 500 patients receiving bedside leukoreduced blood, 7 (1.4%) experienced FNHTR during transfusion, manifesting symptoms such as fever, chills, cold extremities, abdominal pain, and facial flushing.

Conclusion: The incidence of FNTHRs significantly decreased with the transfusion of bedside-filtered leukoreduced blood compared to non-leukoreduced blood. Implementing this practical strategy in resource-constrained settings may prove advantageous in preventing transfusion reactions, enhancing patient and staff satisfaction, and reducing the risks of discontinuation of transfusion, prolonged

hospital stay, and the need for laboratory evaluation. This evidence further suggests the potential extension of this approach to other patient populations, including multiparous females and leukemia patients requiring transfusions.

ORAL PRESENTATION

Development of Cost Effective Real Time PCR Using Sybr Green Method for Donor Chimerism Study After Hematopoietic Stem Cell Transplantation

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Objective: To develop a real time PCR based method for quantitative assessment of donor chimerism using the hydrolysis probes and SYBR green methods. To determine the genotype frequencies in 100 unrelated individuals for the 19 selected SNPs. Ã¢â‚¬Â¢ To carry out quantitative analysis of individual fractions in artificial mixtures of DNA samples by real time PCR of the Single Nucleotide Polymorphisms. To compare the sensitivity, accuracy, and cost of quantitative SNP analysis by polyacrylamide gel electrophoresis of Short tandem Repeats and real time PCR by hydrolysis probes and SYBR green methods in serial monitoring of donor chimerism in a minimum of 20 patients having undergone haematopoietic stem cell transplant.

Methods: Study Design: Descriptive cross sectional
Setting: Genetic Resource Centre (GRC) Lab Rawalpindi. Duration of study: Four years from Jan 2017 to Dec 2020. Subjects

Population sample: One hundred unrelated healthy individuals were studied for the genotype frequencies at the selected SNPs. These individuals were taken from lab staff at PRH, GRC lab, patient's attendants coming to GRC and PRH labs, PG trainees and faculty of Pathology dept.

Sibling pairs: A total of 20 sibling pairs (recipient and donor) were studied for the selected SNP genotypes to see their utility in detecting donor chimerism. Blood samples of the recipients/donors were taken before HSCT and recipient samples after HSCT as well.

Patients: Twenty patients of post Hematopoietic Stem Cell Transplant (HSCT) with various hematological disorders including aplastic anemia, thalassemia, and leukemia were studied to see the status of donor chimerism. These patients had undergone allogeneic HSCT from HLA-matched sibling donors at Pakistan Institute of Medical Science (PIMS) between Jan 2016 to Dec 2018. Blood samples of the recipients were taken one month after HSCT.

3.5 Sampling technique: Non-probability convenient sampling Sample selection:

Inclusion criteria: Unrelated healthy individuals, sibling pairs, and patients with various haematological disorders having undergone HSCT at PIMS.

Exclusion criteria: None

Results: Of the 18 SNPs tested on 100 unrelated individuals the allele frequencies of the SNPs varied from 9% to 56%. The positive allele at most of the SNP loci had a frequency between 35% and 50%. The SNPs S-1, S-3, S-6, S- 7a and S-10a were the most polymorphic (>50% frequency of the positive alleles). In the 20 sibling pairs allele frequencies of the SNPs varied from 10% to 40%. The SNPs S-1, S-3, S-4a, S-7a and S-10a were the most polymorphic (>50% frequency of the positive alleles) in the sibling pairs. The usefulness of each STR locus, defined by the number of informative loci, varied from 10% to 40%. Regarding chimerism status the real time SNP PCR by SYBR Green was able to detect significant amount of chimerism in all twenty patients undergone HSCT. Sensitivity of the real time SNP PCR assay was <1%. A comparison of the donor chimerism measured by the two methods showed that the mean percent value obtained by real time SNP PCR was 4.7% (95% CI 2.7-6.9%) less than that obtained by the STR PCR ($p < 0.001$).

Conclusion: Real time SNP PCR is technically feasible method for assessing donor chimerism status in patients undergoing haematopoietic stem cell transplant in Pakistani patients. The method is simple, quick, sensitive, and accurate.

ORAL PRESENTATION

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

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Objective: To evaluate the outcomes of allogenic bone marrow transplantation in patients with aplastic anemia

Study Design: Retrospective observational study

Study Duration and Place: Department of Clinical Hematology and BMT Gambat, Sindh, from June 2021 to December 2023

Methodology: Total 37 patients were included in final analysis. The patients were admitted to isolation rooms fitted with laminar airflow and HEPA filters. All recipients received stem cells from 10/10 antigen matched siblings. Patients received antifungal prophylaxis with Amphotericin B from start of conditioning protocol. Conditioning regiment used consisted of Fludarabine120, Cy120, ATG20.High risk patients received Cy160. Cyclosporin was used for GVHD prophylaxis to achieve target trough levels of 200 - 300 ng/ml. Patients demographics, donor characteristics, source and dose of infused stem cells, complications during and after the transplant, disease-free survival (DFS), and overall survival (OS) were recorded. SPSS version 26 was used for statistical analysis. utilizing Pearson Chi-square test, a P value <0.05 considered statistically significant.

Results: Among 37 participants, 23 were male, 14 were female with median age of 19 years (range: 5 - 41). Patients had received mean 40 RCC and 26 platelets prior to

transplantation. Ferritin level was 1650. Source of stem cells was bone marrow (BM) in 24 patients (64.9%), BM and PBSC in 13 (45.1%) patients. Mean total nucleated cell (TNC) and CD34 doses were 6.78x106/kg and 6.1x108/kg respectively. Average time for neutrophil and platelet engraftment was 12 and 17 days respectively. Immediate post-transplant complications were fungal infections (45.9%), followed by cyclosporine (CSA)-induced hypertension (21.6%). Acute graft-versus-host disease (aGVHD) was observed in 7 patients (18.9%), primarily affecting the skin (75.1%) followed by gut.

CMV reactivation occurred in 12 patients (32.4%), all of whom were administered valganciclovir. Overall and disease free survival was 73%. Leading causes of death were neutropenic sepsis, followed by graft failure. Three patients (8.1%) experienced primary graft failure, all of whom received stem cell boosts without any response. One patient exhibited poor graft function, which improved following stem cell boost.

Conclusion: Despite facing challenges like fungal infections and graft failure, the 73% overall survival and disease-free survival rates underscore the feasibility of this treatment approach in our resource-limited context. The findings underscore the significance of rigorous infection control measures and refinements in post-transplant care protocols.

ORAL PRESENTATION

Data mining of laboratory information system for establishing indirect hemoglobin A2 reference intervals in infants

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Background: Reference intervals (RIs) are important medical decision-making tools that help physicians in differentiating healthy from sick individuals. These intervals vary between age groups. Hemoglobinopathies are prevalent in Pakistan. Quantification of hemoglobin variants is pivotal in screening out hemoglobin disorders. Establishment of RIs using a direct approach is difficult, specifically in children. We chose an indirect data mining method for determination of Hemoglobin A2 RIs in infants.

Methods: Hemoglobin A2 measurements performed for all patients aged birth to 1 year between January 2013 and December 2020, were retrieved from laboratory management system of AKUH Laboratories. The study population was approximately representative of the entire geographical distribution of the country. Hemoglobin A2 was measured on Bio-Rad Variant TM II analyzer. Reference intervals were computed using an indirect KOSMIC algorithm. The KOSMIC package function on the assumption that the non-pathologic samples follow a Gaussian distribution (after Box-Cox transformation of the data), following an elaborate statistical process to isolate distribution of physiological samples from mixed dataset.

Results: A total of 88,690 specimens were analyzed for HbA2 during the study period. After the exclusion of patients with multiple specimens obtained during the study period, RIs were calculated for 22,713 infants with stratification into 5 age sub-groups. A comparison of our 2.5th and 97.5th percentile results with those of RIs from Mayo Clinic Laboratories Website showed good agreement in between age groups.

Conclusion: This study corroborates data mining as a substitute approach for establishing HbA2 RIs, particularly in resource- constrained settings. The results obtained are specific to studied population, instrument and reagent and allow understanding of the fluctuations in HbA2 synthesis with increasing age. These intervals, hence, will aid in superior clinical decision-making based on HbA2 results.

ORAL PRESENTATION

Role of miRNA26a in Acute Myeloid leukemia (AML)

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Objective:

1. To evaluate the level of miRNA26a expression in newly diagnosed cases of AML.
2. To correlate the miRNA26a levels with clinicopathological parameters.

Methods: This cross-sectional study was carried out at the pathology department at Liaquat University of Medical & Health Sciences Jamshoro and Hyderabad. Total 83 patients were included who met inclusion criteria. Study was done during a period of six months from 1-06-2022 to 30-11-2022. All newly diagnosed case of AML meeting WHO Criteria for diagnosing AML either of both genders were enrolled. Study was conducted after approval from research ethical and review committee (ERC) of Liaquat University of Medical and Health Sciences. 8 ml blood samples were taken in EDTA tube then divided into two tubes. 3 ml EDTA tube for CBC and performed on XN 1000 by Sysmex Japan, 5 ml EDTA sample were used for RNA isolation. MicroRNA was isolated using commercially available kit according to manufactures guideline. Bone marrow examination was performed in pathology department LUMHS and microRNA detections was done on PCR. The data was entered in predesigned proforma and entered into statistical package for social sciences of windows (SPSS version 26).

Results: In this study 83 patients of acute myeloid leukemia were studied; their mean age was 37.43+19.87 years. Males were in majority 80.7%, while females were 19.3%. According to the symptoms, 69.9% patients had fever, 49.4% cases had Malaise, 50.6% were with history weakness, weight loss and pian complaints were in 28.9% and 22.9% of the cases respectively. According to the AML classification, M1 was 39.8%, M2 was 44.6%, M3 was 8.4% and M4 was in 7.2% of the cases. Mean

of the microRNAs was statistically significant according to classification of AML (p=0.001). There was a negative correlation between WBC count and microRNA level (r = -0.206) and (p = 0.062), negative correlation between platelets counts and microRNA level (r = -0.115) and (p = 0.302), while study there was a strong significant negative correlation between BLAST% and microRNA level (r = -0.964) and (p = 0.0001).

Conclusion: MicroRNAs have been identified as a class of gene expression key regulators that can potentially serve as biomarkers and contribute to the pathogenesis of AML. Expression of miRNAs could be of help to physicians in the classification of AML subtypes, the determination of prognosis, and the prediction of therapeutic response in AML.

ORAL PRESENTATION

Deciphering The Puzzle: Acute Leukaemias Of Ambiguous Lineage

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Objective: The objective is to evaluate and refine diagnostic modalities for ALAL, aiming to enhance precision and accuracy in identifying this complex subtype

Methods: This is a prospective study performed at Haematology Dept, AFIP from Jan 2018 till date. All patients who were newly diagnosed as MPAL and AUL were included and followed up till date.

Results: Among the cohort of 32 recently diagnosed ALAL patients, male predominance was observed, reflected in a male-to-female ratio of 4.3:1. The median age was 27+18.2 years. Fever was most common presenting complaint . 17 cases fulfilled the definitions of MPAL and 6 cases as undifferentiated AL. Molecular and FISH study revealed 9 cases to be classified as ALAL with defining genetic abnormalities out of which 4 had BCR::ABL1 Fusion and 5 had KMT2A rearrangement. Additional molecular abnormalities included TP53 and WT1 mutations. 71% cases were immunophenotypically defined. 52.9 % cases were B/Myeloid, 29.4 % cases were T/myeloid and 10.5% cases were B/T lymphoid. 18.7 % cases were diagnosed as AUL. Cytogenetics revealed trisomy 4, del(6p), del (5q), structural abnormalities of chromosome 7 and complex karyotype. 76% cases were given ALL like induction protocol and 12.5% had additional TKIs. The median progression-free survival (PFS) was 120 days, and the median overall survival (OS) was 160 days.

Conclusion: The investigation illuminates the intricate terrain of acute leukaemia of ambiguous lineage (ALAL), delineating its diagnostic challenges and prognostic intricacies. The results underscore the heightened susceptibility of ALAL patients to inferior outcomes.

ORAL PRESENTATION

Chronic Lymphocytic Leukemia in Pakistan: Clinico-hematological profile and treatment response

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Objective: Chronic lymphocytic leukemia (CLL) is the neoplasm composed of small mature monoclonal B cells that co express CD5+ and CD23+. This can lead to lymphocytosis, leukemic infiltration of the bone marrow, lymphadenopathy, and splenomegaly. The current study aimed to evaluate the clinical-hematological parameters of CLL patients at the time of diagnosis and assess treatment response.

Methods: A retrospective study done at NIBD hospital (November2022-November2023) included 35 CLL patients who were enrolled in the study. Details regarding patient's clinical-hematological characteristics were retrieved from the medical records. The study employed SPSS version 25, and a significant result was determined with p- value<0.05.

Results: Out of 35 CLL patients, 24(68.6%) male and 11(31.4%) were female with a male-to-female ratio of 2.18:1. Mean age at presentation was 58.4 years (range: 35-89 years). Common clinical findings included lymphadenopathy (68.6%), splenomegaly (45.7%) and hepatomegaly (25.7%). The majority of patients were presented with early Rai stage: 9(25.7%) in stage 0 and 9(25.7%) in stage I. There was no significant association between clinical stage and gender. Anemia and thrombocytopenia showed highly significant associations with clinical stage at presentation (p-value=0.002 and p-value0.001, respectively). The treatment response was evaluated in 11 patients, 2(18.18%) achieved complete remission, 3(27.27%) achieved partial remission, 3(27.27%) had stable disease, and 3(27.27%) had CLL progression.

Conclusion: CLL primarily affects the elderly; interestingly it occurs earlier among the Pakistani population as compare to western population. The clinical stage was substantially associated with anemia and thrombocytopenia. The overall treatment response rate was 45.45%.

ORAL PRESENTATION

Aberrant Immunophenotypic Expression In Childhood Acute Leukemias: A Tertiary Care Hospital Experience

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Objective: The objective of this study was to determine the aberrant immunophenotype expressions in newly diagnosed pediatric acute lymphoblastic and acute myeloid leukemias.

Methods: This cross-sectional study was carried out at University of Child Health Sciences, The Children's Hospital, Lahore, from September 2022 to December 2022 after IRB approval. After taking informed consent from parents/guardians, 290 children diagnosed with acute leukemia were included in the study. Peripheral blood or bone marrow samples in EDTA vial were used for flowcytometric analysis by using FACSC anto II flowcytometer. The data was collected on a pre-designed proforma and analyzed by using IBM-SPSS V-23.

Results: Among 290 cases, Acute Lymphoblastic Leukemia (ALL) constituted 221(76.2%) cases and 69(23.7%) were Acute Myeloid Leukemia (AML). Out of the total, 32(11%) cases showed aberrant immunophenotypes. The most common aberrant antigens were reported in B-ALL and the most common aberrant expression was of CD13 (62.5%). In AML, the most common aberrant antigen seen was CD19 (55.6%) and in T-ALL the most common were CD117 and HLA-DR (26.6%).

Conclusion: The most aberrant immunophenotypic markers were seen mostly in B-ALL pediatric cases followed by AML and T-ALL. Such abnormal expressions should be kept in mind while diagnosing the children with acute leukemia as they may affect the prognosis.

ORAL PRESENTATION

Metastatic Malignancies Diagnosed On Trephine Biopsy

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Objective: Aim of our study was to highlight the diagnosis of stage IV cancers on bone marrow biopsy. At time no accessible tissue is available to document tumor of origin. The study demonstrates usefulness of bone marrow biopsy along with immunohistochemistry in the detection of bone marrow metastasis.

Methods: In this cohort study, total of 75 suspected cases of bone marrow metastasis with unknown and known origin were included. The duration of study was from January 2019 to November 2023. Patient's baseline demographics including age, gender and status of malignancy were collected and analysed.

Results: 74 patients with suspected and known solid organ malignancies were included in the study out of whom majority were female (n=40,54.1%). The mean age of female patients was 56.9±12.5 years while the mean age of male was 62.5±13.2 years. Out of 74 patients, 30 (40.5%) patients showed bone marrow involvement by metastatic infiltrate. The most common origin of metastasis was breast carcinoma in 13(43%) patients followed by prostate carcinoma in 8(26.7%) cases. The remaining cases comprised of ovarian carcinoma in 1 (3.3%), prostatic carcinoma in 1(3.3%), rhabdomyosarcoma in 1 (3.3%), gastrointestinal malignancies in 3(10%) and carcinomas of unknown origin in 3(10%).

Conclusion: Bone marrow biopsy and IHC technique provides an insight on diagnosis of malignancies of unknown origin and further typing of tumors on the basis of morphology and pattern on bone marrow trephine sections. Detection of bone marrow involvement has significant clinical implication with impact on patient's condition, prognosis and treatment.

ORAL PRESENTATION

Atypical BCR-ABL Signal Patterns Identified by FISH in Different Haematological Disorders and Its Impact on Prognosis

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Objective: Recognition of the BCR-ABL1 translocations in different leukemic patients is important for prognosis and therapies. Literature review concluded that BCR-ABL1 identified by FISH predict disease progression. Monitoring the expression of BCR-ABL1 translocations are effective means to predict disease relapse and resistance.

Methods: Fluorescence in situ hybridization (FISH) is performed on bone marrow specimens or on peripheral blood. We analyzed a total of 202 number of patients. Out of which 34 are CML, 32 are AML, 79 are precursor B-ALL, 18 are precursor T-ALL and 36 are MPNs.

Results: The patterns of BCR-ABL1 signals presented complexity and diversity. A total of 12 BCR-ABL1 signals were observed in this cohort, including 1R1G2F, 1R1G1F, 2R1G1F, 1R2G1F, 2R2G1F, 1R2G2F, 1R1G3F, 1G3F, 2G3F, 1G4F, 1R1G4F, 1R4F and 3R2G3F. Complex BCR-ABL1 signal patterns (two types of signal patterns) were observed in 16.8% of the CML patients, followed by 8.9% of the T-ALL patients, 39.1% of B-ALL, 15.9% of the AML patients and only 17.8% of MPNs patients. Out of all the patients, 70.8% patients are positive with BCR-ABL translocations. 19.3% patients have typical patterns and 10.4% have Atypical patterns, out of which 18% (n=22) shows 3R2G signal.

Conclusion: Atypical BCR-ABL1 signal patterns shows poor prognosis in BCR-ABL1 positive leukemia. Monitoring BCR-ABL1 signal patterns might be an effective means to provide prognostic guidance and treatment choices for these patients.

ORAL PRESENTATION

Prognostic Impact Of Wilms Tumor 1 Mutation In Acute Myeloid Leukemia Patients

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Objective: The objective of this study was to identify WT-1 gene mutation in patients with Acute Myeloid Leukemia (AML) and investigate its impact on the response to induction therapy and overall prognosis.

Methods: This prospective cohort study was conducted at Haematology Department, Armed Forces Institute of Pathology Jan to Dec 2023. A total of 98 newly diagnosed cytogenetically normal AML patients were included in this study. Clinical data including age, gender, presenting symptoms and examination findings were noted. Hematological parameters such as complete blood counts, peripheral blood smear findings, bone marrow aspirate and trephine findings were documented. Real time fluorescent qualitative PCR using specific primers for WT-1 mutation was performed on ABI-7500 real time PCR system. Baseline demographic, hematologic parameters, comorbidities, treatment details, response rates, were collected by chart review after appropriate ethical approval. Complete remission required bone marrow blasts <5%, absolute neutrophil count > 1x109/L, and platelet count >100x109/L.

Results: A total of 98 AML patients were included, of which 12 (12%) harbored WT1 mutations. At diagnosis, WT1 mutant group showed significantly mean total leukocyte count (TLC) (29 x 109/L vs 19 x 109/L, p=0.03) and mean blast percentage in the bone marrow (76% vs 65%, p=0.04) compared to the WT1 wildtype group (n=86). No significant differences were observed in baseline hemoglobin levels (8.5 g/dL vs 8.3 g/dL, p=0.62) or platelet counts (52 x 109/L vs 44 x 109/L, p=0.41) between the two groups.

After standard induction chemotherapy, WT1 mutant AML patients had an inferior response rate compared to wildtype patients (complete remission 41% vs 59%, p=0.12). Induction mortality rates were also numerically higher in WT1 mutants (17% vs 10%, p=0.28). Taken together, these findings highlight the adverse prognostic impact of WT1 mutations in AML patients (n=98) - with higher leukocytosis, increased disease burden, and a trend towards worse initial response to chemotherapy compared to WT1 wildtype cases.

Conclusion: WT1 mutation is an important molecular event in AML, and has been shown to be associated with a relatively prognosis. This research could lead to the development of more effective risk stratification and treatment strategies for AML patients with WT1 mutation.

ORAL PRESENTATION

Treatment Outcome Of Chronic Myelomonocytic Leukemia; A Single Centre Experience From Pakistan

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Objective: Chronic myelomonocytic leukemia (CMML) is characterized by monocytosis and dysplasia of myeloid progenitor cells. The clinical and laboratory data on CMML diagnosis and therapy in our region is scarce. The study was conducted to observe the outcome of CMML patients according to CMML types, karyotype, and treatment.

Methods: A cross sectional study was conducted at National Institute of Blood Diseases and Bone Marrow Transplantation, Karachi Pakistan from 2018-2022. Baseline investigations, clinical parameters and treatment was recorded. Bone marrow biopsy samples were evaluated and cytogenetic analysis was performed on bone marrow cultures using standard procedures. Descriptive statistics were reported by using SPSS version 23.0.

Results: A total of 29 CMML patients were analyzed. Median age was 63(28-85) years with male predominance (62%). MPN subtype was found to be more prevalent 25(86%) and 22(76%) patients had normal karyotype. Overall Cytarabine was given in 8(28%) patents with MPN type, azacitidine to 2(7%) with MDS type and decitabine was offered to 13(52%) patients with MPN type and only a single MDS type patient received decitabine. Fourteen (44%) patients were died out of which 12(86%) had MPN type. In risk stratified groups, post treatment infections & transfusion dependency were evaluated with no significant association observed. Significant post treatment infections were observed in MPN (p-value =0.042).

Conclusion: In CMML it was observed that although there was no significant association among the treatment groups yet decitabine was given in majority of MPN type subgroup and post treatment infections were prevalent.

ORAL PRESENTATION

Pattern of immune reconstitution post allogeneic stem cell transplant: data from a resource constraint country

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Objective: To assess the pattern of immune reconstitution and its possible association with pre-, post-transplant variables.

Methods: This prospective observational study was conducted at The Armed Forces Bone Marrow Transplant Centre/ National Institute of Bone Marrow Transplant (AFMBTC /NIBMT) Rawalpindi, Pakistan from May 2022 to December 2022. All patients (both genders, irrespective of age) undergoing matched related donor allogenic hematopoietic stem cell transplant were included in the study. While patients undergoing Haplo-identical or Autologous bone marrow transplant were excluded from the study. Data was analyzed using SPSS version 25.0.

Results: The study included 43 patients, there were 67% male and 33% female patients (male-to-female ratio, 2:1), and median age was 11.19 ± 9.4 years. Out of total patients 23% had malignant conditions while 77% had non- malignant diseases. Majority were matched sibling donors followed by fully matched parents as donor. The mean TNC and CD34 dose infused to the patients was 5.1±1.2and 5± 2.2 respectively. Cellular and humoral reconstitution at 6 months after transplant was used to assess immune reconstitution. In cellular reconstitution, the mean of WBC was 7.1 ± 2.5 x 109/L (min- max: 2.3 -12.5 x 109/L), lymphocyte count was 22.6 ±11X 109/L (min- max: 2.1- 50 109/L), CD3 cell was 66.7 ±15.2X 109/L (min- max: 34 – 90 X 109/L), CD4 cell was 19.8 ±8.7X 109/L (min- max: 4 - 42X 109/L), CD8 cell was 39.7 ±14X 109/L (min- max: 14 - 67X 109/L), CD19 cell was 16.1 ±11.9X 109/L (min- max: 1 – 52 X 109/L), NK cell was 9.3 ±5.8X 109/L (min- max: 1 - 26X 109/L) and the ratio of CD4 to CD8 was 0.57 ±0.4 X 109/L (min- max: 0.06 - 1.6). In humoral

reconstitution, the mean of IgA was 1.7 ±0.8g/l (min- max: 0 - 4), IgG was 11.8 ±4.8g/l (min- max: 1 - 21) and Ig M was 1.58 ±2.5 g/l (min- max: 0 - 18). We found significant association of pre-transplant condition regimen and GVHD prophylaxis with low CD4 count. Low CD19 was significantly associated with Source of Stem Cells, patient-donor gender disparity and GVHD treatment. The patient-donor relationship was found to be associated with low IgA, IgG, and IgM levels. We only discovered a significant association of patient gender with IgA levels.

Conclusion: In conclusion, our data suggest that at post-transplant 6 month there was an adequate immune reconstitute. Therefore, post-transplant 6 month in Allo-HSCT could be considered for immunization and stopping anti-viral prophylaxis.

ORAL PRESENTATION

Melphalan-Based Autologous Haematopoietic Stem Cell Transplantation For Multiple Myeloma In A South-asian Population

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Objective: To determine the effect on overall survival (OS) and progression-free survival (PFS) of patients undergoing Auto- HSCT with two different doses of melphalan condition i.e., 140 mg/m2 versus 200 mg/m2 in a South Asian population.

Methods: Eighty five patients underwent Auto-HSCT starting from 01 Jul 2011 to 30 Jun 2023 in the Department of Clinical Hematology and Bone Marrow Transplant, Shifa International Hospital, Islamabad who were diagnosed with multiple myeloma and underwent Auto-HSCT. Requisite data was obtained from electronic medical records, and physical medical records. All patients were followed-up till 30 Nov 2023.

Results: Fifty nine (69.4%) patients were male, with a mean age of 50.87 Ã‚Â± 8.75 years at the time of Auto-HSCT. The Mel-140 group had an overall survival of 76.0% and 48.9% at two and five years post-transplant, respectively, while the same was 76.6% and 63.3%, respectively, in the Mel-200 group. The Mel-140 group had a progression- free survival at two years of 62.2%, and 30.6% at five years, while it was 76.9% and 48.7% in the Mel-200 group, respectively. There was no difference between the groups with regards to the frequency and severity of adverse effects, or the occurrence of transplant-related mortality.

Conclusion: Mel-200 is similar to Mel-140 in terms of adverse effects and transplanted-related mortality, with superior outcomes in terms of long-term overall survival and progression-free survival.

ORAL PRESENTATION

Allogeneic Stem Cell Transplant in Primary HLH
A single center experience

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Objective: To determine the outcomes of allogeneic stem cell transplant in children with primary Hemophagocytic Lymphocytosis (HLH).

Methods: This is a single-center retrospective analysis of all patients diagnosed as primary HLH who underwent allogeneic stem cell transplant at Armed Forces Bone Marrow Transplant Center (AFBMTC) Rawalpindi, Pakistan from April 2014 to August 2023. After taking approval from the Institutional Review Board of the hospital, patients record were searched and relevant data including demographics, disease characteristics, transplant details, and follow up was collected. The diagnosis of HLH was made as per Histiocyte Society criteria with defined genetic mutations where available and clinical and bio-markers for the rest of the cases 7. All patients received initial chemotherapy as per HLH 2004 protocol before transplant. All the patients underwent related donor transplants (fully matched or haploidentical). Six antigens (HLA-A, -B, -DRB1) or eight antigens (HLA-A, -B, -DRB1, -DQB) DNA-based HLA typing was done at low/intermediate resolution. All patients received TBI-free conditioning chemotherapy, either reduced intensity (RIC), Treosulfan-based reduced toxicity, or myeloablative (MAC) conditioning. Post-transplant, blood counts were monitored daily to document neutrophil and platelet engraftment. Donor chimerism was done at 1, 3, and 6 months and 1-year post-transplant. Cyclosporin and Mycophenolate Mofetil (MMF) was used for GvHD prophylaxis. Short-course Methotrexate (3 doses, with Folinic acid rescue) was added for MAC conditioning. MMF was stopped on day +30 and Cyclosporin was continued, with trough levels monitoring (target trough levels 200-250mg/dl),

for 3 months and then tapered off over the next 3 months.
Overall survival (OS) and disease-free survival (DFS) were the primary outcome measures. Secondary outcome measures included transplant-related mortality (TRM), donor chimerism, and acute GvHD. The data were stratified in relation to disease subtype, donor type, duration between diagnosis and BMT, donor chimerism at 3 months and HLA-disparity. Kaplan-Meier survival estimates were plotted and the Log-rank test of significance was applied using SPSS v26.0, considering p value < 0.05 as significant.

Results: A total of 28 patients were included in the final analysis. The median age of patients at the time of transplant was 2 years (4 months - 14 years). Twenty patients (71.4%) were male and the rest (n=8, 28.6%) were female. There were 8 (28.6%) cases of GS2 and 20 (71.4%) had familial HLH. In 2 patients underlying genetic mutation was identified (STX11 and PRF1), 10 patients had history of death of a sibling with HLH while 8 patients had no family history. The median duration between diagnosis and transplant was 7.5 months (2 months - 2 years).

In all patients, the source of stem cells was bone marrow harvest (BMH), with additional peripheral blood stem cells (PBSC) collection in 2 patients. All the donors were family donors (sibling=19, 68%, parent=9, 32%). The donor was fully matched in 68% (n=19) cases while 32% (n=9) were haploidentical. Of the haploidentical donors 5 were parents and 4 siblings. Conditioning chemotherapy was RIC in 89% (n=25) and MAC in 11% (n=3). The mean CD34 dose was 8.7 x 106/kg (SD ± 7.76), and the mean total nucleated cells (TNC) dose was 6.36 x 108/kg (SD ± 2.86).

All patients except 2 achieved neutrophil engraftment at a median of day +14 (range 10-28) post-transplant. In the 2 cases, 1 had primary graft failure and died on Day +26, while the other died on Day +7, before engraftment status could be assessed. Platelet engraftment occurred in 24 out of 28 (86%) patients at a median of day +25 (range 16-45). Acute GvHD (grade I-IV) was reported in 39% (n=11) of patients; 8 had isolated skin GvHD, 2 had skin, liver, and gut GvHD, while 1 developed skin and gut GvHD. Febrile neutropenia was the most common complication in the peri-transplant period, affecting 27 patients (96%), followed by mucositis (n=12, 43%), CSA- induced hypertension (n=8, 28.6%), gut toxicity (n=7, 25%), CMV reactivation

(n=5, 18%) and veno-occlusive disease (n=3, 10%). Chimerism data at 3 months post-transplant was available for 24 patients, out of which 71% (n=17) had complete chimerism, 25% (n=6) had mixed chimerism, and 1 patient had secondary graft failure. On further follow-up, two of those with mixed chimerism progressed to secondary graft failure: 1 had disease relapse and is currently receiving re-induction while the other is stable with no evidence of recurrence.

With a median follow-up of 1 year (7 days - 12.7 years), OS was 68% (n=19) and DFS 64.4% (n=18). Among the 9 patients who died, 2 had secondary graft failure followed by infections

Conclusion: Primary HLH is uniformly fatal if left untreated. Allogeneic stem cell transplant after disease control with dexamethasone and etoposide combination chemotherapy is a viable curative option with a durable response. Larger, prospective studies are required to establish optimal conditioning regimens and explore the role of alternative donor transplantation

ORAL PRESENTATION

Immune Reconstitution Post Allogeneic Bone Marrow Transplant

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Objective: To evaluate immune reconstitution following allogeneic hematopoietic stem cell transplantation.

Methods: Retrospective Cohort study

Results: In our study ALC recovery was observed in 93.87% of all the patients on D+180 that increased to 100% on D+365. The average being 2609.06 ¼L (SD=1271.223) and 2970.96 ¼L (SD=1077.470) on D+180 and D+365 respectively. On D+180, the CD3+CD8+ achieved the highest recovery rate (100%), followed by CD16+CD56+ (96%), CD19+ (84%) and CD3+CD4+ in 2% only. The CD3+CD4+ recovery on Day +365 was 14%.CD3+CD4+ recovery was seen in patients with age <8 years, non-malignant diseases and was associated with lower incidence of GVHD. The recovery rates of immunoglobulin levels IgG, IgM and IgA on D+180 were 92%, 90% and 84% and after 1 year 98%, 90% and 96% respectively. We also found out patients receiving high CD34+ dose (>5x 106/kg) had significantly shorter median time compared to those who received low dose (12 days vs. 14 days [P=0.04]). No difference seen between the high dose and low dose groups in cumulative incidence of acute or chronic GVHD.

Conclusion: IR was affected by various factors after allo-BMT and ALC and immunoglobulin level recovery were understandable predictors of post-BMT outcomes.

ORAL PRESENTATION

Treatment outcome of Hematopoietic Stem Cell Transplant in Fanconi Anemia; Single Centre Experience from A low- and middle-income country.

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Objective: Fanconi Anaemia (FA) is a multisystem rare hereditary disorder characterised by progressive bone marrow failure, congenital malformations and predisposition to malignancy including MDS, AML and epithelial cancers. HSCT has emerged as a potential cure for bone marrow failure and haematological malignancies. Reduction in cyclophosphamide dose and irradiation in the conditioning regimen has improved the Overall survival (OS) from 80% to 95% in FA patients.

Methods: This retrospective study analysed the data of 41 cases of FA including27 (65.9%) males undergoing HSCT at AFBMTC from February 2009 to December 2023. All Fanconi anaemia cases, undergoing HSCT with fully HLA- matched family donors were included. A non-myeloablative conditioning regimen consisting of Flu120/Cy30/ATG20was used for all cases.

Results: The mean age at the time of HSCT was 9.6Ã‚Â±3.1years. Bone marrow was the source of stem cells used in 33(80.5%) cases. Cyclosporine-induced hypertension was the most common complication documented in 36(87.8%) cases followed by neutropenic fever in 35 (85.4%). Acute GVHD and chronic GVHD were documented in 14(34.1%) and 11(26.8%) cases respectively. Treatment-related Mortality at day 100 was 7(17.07%). Total mortality of the cohort was 11 (26.82%). In univariate analysis, age at HSCT, sex, mucositis. aGVHD and chronic GVHD had no statistically significant association with OS and DFS. After a mean follow-up of 64.19Ã‚Â± 46.11 months, OS and DFS rates were 30 (73.2%) and 29 (70.0%) respectively.

Conclusion: HSCT is the only curative option for Fanconi anaemia-related haematological disorder. In resource-limited settings, an overall survival of more than 70% is very promising. Primary and Secondary graft failure remains a major challenge in HSCT of Fanconi Anaemia

GUEST SPEAKER

Incorporating Immunotherapy upfront in the management of B-cell ALL

Dr Talha Badar
Assistant Professor of Oncology, Mayo Clinic, USA

The complete remission (CR) rates have improved with multi-agent chemotherapy in adult B-cell acute lymphoblastic leukaemia (ALL); however, remissions are not long lasting with frequent relapses. Secondly, multi-agent chemotherapy regimens not well tolerated in elderly ALL with higher morbidity and mortality. Several immunotherapy-based combinations including rituximab (anti-CD20 monoclonal antibody [mAb]), Inotuzumab Ozogamicin (anti-CD22 antibody drug conjugate) and blinatumomab (CD3/CD19 bispecific antibody construct) have demonstrated superior efficacy compared to conventional chemotherapies alone inductions. Blinatumomab which has demonstrated to improve measurable residual disease (MRD) negativity in B-cell ALL, is most promising and most advanced in development as an upfront immunotherapy combination in B-cell ALL. In this review I will be highlighting the evolution of immunotherapy-based treatment approaches in management of treatment naïve B-cell ALL.

GUEST SPEAKER

Dilemma of Treating Intermediate Risk AML in Resource Constrained settings

Prof Dr Muhammad Ayaz Mir
Head of Haematology Department
Shifa International Hospital, Islamabad, Pakistan

Intermediate Risk AML has had a fluid definition for years being the grey zone of AML. It can no longer be diagnosed without NGS. Targeted therapies are available or in trials for many subtypes. Prospective trials are hard to do due to a dynamic target. High TRM should prohibit blanket transplant consolidation approach due to marginal benefit. A scoring system like MDS would be a better clinical tool.

GUEST SPEAKER

Indications for Allogeneic HSCT in ALL in 2023

Prof Dr Shabeeha K. Rana
Consultant Haematologist, American hospital, Dubai, UAE

ALL is a hematologic malignancy, characterized by rapid proliferation of immature lymphoblasts. This expansion causes compromise of blood components and bone marrow function. Since 2012, significant changes to aspects of the treatment landscapes for adult ALL have occurred, including greater experience with pediatric inspired chemotherapy regimens, expanding application of assessments for measurable residual disease (MRD), and emergence of novel targeted and immune therapeutics. These modalities have substantially improved overall survival (OS) rates. Despite these advancements, a subset of patients with high-risk features or those who experience a relapse after initial treatment continue to face poor outcomes, with 5-year survival rates approximately at 50%. For this group of patients, allogeneic HSCT often represents the only potentially curative option. HSCT is a long-established standard of care for these patients with long-term favorable OS outcomes. However, its role in the treatment paradigm of ALL remains a topic of ongoing discussion. HSCT leverages the immunologic graft-versus leukemia effect to eradicate residual leukemic cells, offering the promise of long-term disease control. Even so, HSCT is a complex procedure with significant associated risks, including graft versus-host disease (GvHD), infections, and transplant-related mortality (TRM), which have traditionally limited its universal application.

This abstract shed light on the current use and indications of allogeneic stem cell transplantation for acute lymphoblastic leukemia, in particular reference to Philadelphia chromosome related disease in view of current evidence and clinical applications.

GUEST SPEAKER

Transplant Strategies in Aplastic Anaemia in Resource Limited Countries

Prof Dr Parvez Ahmed
Hematologist & Director Bone Marrow Transplant Program at QIH Islamabad, Medical Director Pathwel Center of Hematology and BMT, Rawalpindi, HOD, Department of Hematology & BMT Gambat and Visiting BMT consultant PKLI Lahore.

Aplastic anemia (AA) has a relatively higher incidence in Asian countries and is seen more often in younger age groups compared with the western populations. Despite better disease understanding and progress in management options, it is a potentially fatal disease especially in resource limited countries due to suboptimal health care facilities. In addition to supportive care specific treatment options consists of immunosuppressive therapy (IST) using horse antithymocyte globulin (hATG) plus cyclosporin with or without eltrombopag and allogeneic bone marrow transplant (allo BMT). Majority of the patients present late with severe disease, have bacterial and fungal infections and are highly sensitized due to multiple blood transfusions. These factors coupled with limited accessibility to health care facilities make the management of AA challenging. IST; associated with up to 70-80% response in advanced countries, is not the best treatment options in majority of the cases due to non-availability of hATG and suboptimal blood component support. Moreover patients succumb to severe cytopenias that does allow enough time for marrow recovery following IST. Upfront allogeneic BMT using matched related donor (MRD) or matched unrelated donor (MUD) is the best treatment option for majority of the patients. Allo-HCT should be the first line treatment in patients ≤50 years of age with SAA/VSAA if MRD is available. Recent advancements in haploidentical transplants has seen encouraging results which means that most of the younger patients without MRD or MUD will be able to get bone marrow transplant. Bone marrow transplant centers in most of the developing world lack

advanced facilities like high resolution HLA typing, pre-storage leukodepletion, infectious disease diagnosis, certain essential drugs, molecular hematology laboratories, TBI based conditioning protocols and optimally trained human resource. For optimal BMT outcomes all these factors are to be deliberated during planning transplants in resource-limited setting.

GUEST SPEAKER

Choosing Whom and How to Transplant in Beta Thalassaemia Major

Prof Dr Tariq Ghafoor
Prof of Paediatric Oncology and Director
Armed Forces Bone Marrow Transplant Centre,
Rawalpindi, Pakistan

Beta Thalassaemia is the most common genetic diseases caused by reduced or absent synthesis of the beta-globin chains resulting in ineffective erythropoiesis and haemolysis, which lead to severe anaemia. Conservative treatment consisting of life long regular blood transfusion and iron chelation has improved survival into the fourth or fifth decade of life in the western world. Bone marrow transplant is the only curative treatment. Conditioning protocol consisting of Flu120, Bu16, Cy160, TG 4.5 to 7.5 has OS 82.0% and DFS 80.9%. Serum Ferritin < 1000 ng/mL, hepatomegaly less than 2 cm has better OS.

GUEST SPEAKER

Management of Advanced Hodgkin Lymphoma in the Era of Novel Agents

Dr Sairah Ahmed
Associate Professor & Director CART Program
University of Texas MD Andersen Cancer Center, Houston, USA

Dr. Sairah Ahmed will discuss the treatment of advanced cHL with standard frontline chemotherapy in addition to chemotherapy combinations with CD30-directed antibody-drug conjugate brentuximab vedotin and PD-1 blockade.

GUEST SPEAKER

Managing Multiple Myeloma in 2024

Prof Dr Saad Z. Usmani
Chief of Myeloma Service and Professor
Weill Medical College, Cornell University, USA

Multiple myeloma (MM) is the second most common blood cancer and the most common plasma cell disorder in the world. The outcome and management strategies for this disease have evolved significantly in the last two decades. For multiple myeloma, the incorporation of immunomodulatory drugs, proteasome inhibitors, monoclonal antibodies, and autologous stem transplants have led to a 4-fold improvement in survival outcomes. New immunotherapies using bispecific antibodies and chimeric antigen receptor T cell therapies have proven their efficacy and safety in the relapsed setting. These T-cell redirecting strategies are now being studied in clinical trials in earlier relapse and newly diagnosed settings. The current presentation will provide a summary of management strategies for MM in the year 2024 and future research directions.

GUEST SPEAKER

CLL: A Brief Overview of Landmark Trials Shaping Current Management.

Prof Dr Khurram Bilal Tariq
Haematologist and Medical Oncologist
Selby B Jones Regional Cancer Center, Boone, USA

This brief talk will take us through the various landmark clinical trials that have played a crucial role in revolutionizing the management of CLL. We will build our talk around the NCCN guidelines and focus only on the standard of care, FDA approved treatment options with a focus on BTK inhibitors and Bcl-2 inhibitors. The talk will also focus on clinical pearls necessary for clinical practice

GUEST SPEAKER

Refining The Art Of Tackling Graft Versus Host Disease

Prof Dr Syed Waqas Imam Bokhari
Consultant Clinical Haematologist
Shaukat Khanum Memorial Cancer Hospital, Lahore, Pakistan

Although Graft versus leukemia effect is the main mechanism of allogeneic HCT providing a long-term anti-leukemia effect, graft versus host disease goes hand in hand with it and remains a major factor affecting morbidity and mortality. The science behind preventing and managing GVHD has progressed significantly over past few years leading to effective measures in prophylaxis pre and post transplantation as well as introduction of new therapies in management of acute and chronic GVHD. It is imperative that these anti GVHD measures are taken timely and appropriately. These include careful donor selection, source of stem cells, effective GVHD prophylactic regimen (including cyclophosphamide post-transplant, ATG, combinations of calcineurin inhibitors, Methotrexate and newer immunosuppressive agents such as Abatacept), and incorporation of newer drugs such as Ruxolitinib and Belumosudil for management of steroid refractory GVHD. This presentation in aimed at reviewing latest research and guidelines in order to refine how we go about tackling GVHD. Immunosuppressive agents such as Abatacept), and incorporation of newer drugs such as Ruxolitinib and Belumosudil for management of steroid refractory GVHD. This presentation in aimed at reviewing latest research.

GUEST SPEAKER

Advances in GVHD

Dr. Shahrukh Hashmi
Chair Haematology and Oncology
Mayo Clinic, Sheikh Shakbout Medical City, Abu Dhabi, UAE

In 2024, the overall epidemiology of GVHD has not significantly changed, however, significant advances in the treatment of GVHD have occurred. We have seen innovative research presented at international meetings which include clinical trials in the treatment of chronic GVHD, topical treatments for GVHD, fecal microbial therapies for treatment of acute GVHD, and lastly better modeling for prediction of GVHD. Though no blockbuster drug is in the horizon that can cure GVHD in majority of the patients, alleviation of symptoms of GVHD is a win for patients and caregivers. We are hopeful that in the future, we will be able to prevent GVHD, rather than struggling to treat it.

GUEST SPEAKER

BMT setting: Infections and Infection Control

Kishwar Sultana
Bone Marrow Transplant Coordinator
Armed Forces Bone Marrow Transplant Centre,
Rawalpindi - Pakistan

Infection in HSCT recipient is associated with high morbidity and mortality, so infection prevention is a major goal for successful outcome of transplant patients, infection control measures are important in all health care setting but they are vital in BMT setup, key is to follow basic guidelines for prevention of infection.

GUEST SPEAKER

Management Of Complications Associated With Central Venous Catheter.

Najia Gul
Bone Marrow Transplant Nurse
Armed Forces Bone Marrow Transplant Centre,
Rawalpindi - Pakistan

Objective: To assess the safety and complications of central venous catheters (CVC) in patients undergoing chemotherapy and stem cell transplantation (SCT) for various haematological disorders at Armed Forces Bone Marrow Transplant Centre Rawalpindi, Pakistan.

Materials And Methods: Patients having CVC placement from January 2002 to Aug 2013 for intensive chemotherapy and SCT were included in this study. Polyurethane, Hickman or PICC line was placed under local or general anaesthesia depending upon patient's age and condition. The line was removed on completion of treatment, proven CVC infection or any serious complication.

Results: A total of 805 CVCs were placed during study period. Indications for CVC placement were SCT (n=258), intensive chemotherapy (n=369) and miscellaneous reasons (n=178) like antimicrobials delivery, apheresis, administration of anti-thymocyte globulin (ATG) and parenteral nutrition. Median age of the patients was 21 years (range 2 – 72). Mean duration of CV catheterization was 29 days (range 1 – 151). Types of catheter used included Polyurethane (n=773), Hickman (n=29), PICC (n=2) and Porta Cath (n=1). Subclavian vein was most common site for CVC placement (n=706), followed by internal Jugular vein (n=96). Right side of the body was used for 634 placements, while 171 placements were made on left side. Five hundred forty five procedures were done under local anaesthesia whereas general anaesthesia was used in 259 cases. Number of attempts made for successful placement was one in 560 cases, two in 185, three in 45 cases and four in 15 cases. In seventeen cases the CVC required re-adjustment due to mal-positioning and

removal in 242 cases for suspected line infection or other complications. Various complications observed were systemic infection (n=143), positional flow (n=52), leakage (n=32), catheter colonization (n=29), bleeding (n=21), complete blockage (n=20), accidental removal (n=10), malpositioning (n=5), and pneumothorax (n=3). Second catheter was placed in 56 cases. In rest of the cases the line was removed on completion of treatment. Two hundred and twelve patients with CVC experienced neutropenic fever. Clinically significant isolates from blood culture were Staphylococcus (n=49), Pseudomonas (n=24), E coli (n=23) and Klebsiella (n=14). CVC tip culture tested positive in 29 cases, with predominant organism being Staphylococcus (n=19).

Conclusion: Placement of CVC is a safe procedure in transplant and intensive chemotherapy setting. Although associated with significant rate of complications, yet its usefulness far outweighs associated risks.

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