The prognostic value of apoptotic marker (CD95) in adult acute leukemias

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Fas is expressed on a majority of human leukemic cells. Fas-mediated cell death is involved in drug-induced apoptosis in various cell types. Hence, failure of apoptosis could lead to chemoresistance and may therefore have an impact on clinical outcome. The aim of this study is to evaluate the prognostic value of Fas receptor expression on blast cells in adult acute leukemias. 80 adult acute leukemia patients were classified as follows: 40 (AML), 40 (ALL). 10 age-sex matched healthy controls. Patients with acute leukemia were studied at diagnosis and after treatment. Flow cytometry was used to evaluate Fas expression on blast cells from bone marrow aspirate or PB samples of the patients or on normal monocytes, granulocytes, and lymphocytes obtained from PB samples of controls. The correlation between prognostic markers and Fas expression levels on blast cells of leukemic patients at diagnosis was ascertained. After treatment, patients were followed up for periods ranging from 20 to 36 months.

Fas expression was seen to be statistically the higher (P < 0.001) on control monocytes (32.2 ± 6.95%), followed by granulocytes (23.8 ± 7.61%), whereas lymphocytes expressed the lowest levels (16.1 ± 4.01%).

Fas expression by blast cells from AML patients at diagnosis was 40.72 ± 10.3%.

Fas expression increased significantly from M1 to M5 with the weakest expression in M1 (20.28 ± 5.3%) and the strongest in M5 (52.91 ± 11.3%).

Fas expression in ALL patients was 43.87 ± 11.5%. Fas expression was positive in 14/24 (63.2%) precursor B-ALL patients and in 12/16 (84.6%) T-ALL patients. Fas expression was significantly higher (P = 0.039) in T-ALL (55.15 ± 7.8%) in comparison with precursor B-ALL (34.47 ± 5.76%).

Fas receptor expression on blast cells from ALL and AML patients could serve as an independent prognostic factor.
Frondoside A Up-Regulates the NFkB Pathway and Potentiates the Effects of Conventional Therapeutic Agents in Acute Leukemia

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Background: Acute leukemia is a very common malignancy but despite advances in treatment options, patients still die of the disease or the treatment consequences. Anti-cancer drugs derived from natural products are of interest due to the lower rate of side effects. Frondoside A, a triterpenoid glycoside from the Atlantic sea cucumber, Cucumaria frondosa, has potent anti-cancer effects in solid tumors but its effect on malignant blast cells is yet to be explored.

Methods: In this study, the effect of frondoside A on viability (CellTiter-Glo luminescence assay) and expression of apoptosis-related genes (low-density expression array) was investigated in two acute leukemia cell lines. ANOVA multivariate analysis was used for the viability results with p-value<0.05 considered significant.

Results: Frondoside A markedly potentiates the effect of conventional chemotherapeutic drugs (asparaginase, Vincristine and Prednisolone) when given in combination in the acute T-cell leukemia cell line (CCRF-CEM) and the acute monocytic leukemia cells (THP-1). Analysis of the effect of frondoside A on expression of apoptosis-related genes showed marked changes in multiple pro- and anti-apoptotic genes. Expression of some genes coding for both pro-apoptosis and anti-apoptosis proteins were increased, suggesting that a survival pathway was also activated in the frondoside A-treated cells. Interestingly, frondoside A treatment also markedly affected multiple genes in the NFkB pathway with changes being more marked in the THP-1 cell line, which is more resistant to the effects of frondoside A.

Conclusions: Activation of the NFkB pathway may explain the activation of the cell survival pathway and this observation paves the way for a new potential option for the treatment of acute leukemias. Frondoside A potentiates the anti-cancer effects of all three drugs currently used to treat acute leukemias and it may be a valuable addition to the therapeutic options in these deadly diseases.
PP03

A 12-year-old girl with skin lesions

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Background:

Blastic Plasmacytoid Dendritic Cell Neoplasm (BPDCN) is a rare aggressive hematological malignancy. It occurs mostly in adults but is rarely described in children. Here, we describe a case of BPDCN occurring in a Bahraini girl.

Case report:

A twelve-year-old girl presented with erythematous macule on the abdomen for 2 months. Similar smaller lesion was noted on her left leg for 1 year. Initial work-up at the local health center showed anemia, leukopenia and normal platelet count. Therefore, the patient was transferred to our hospital. Abdominal ultrasound showed moderate hepatosplenomegaly and abdominal lymphadenopathy. Bone marrow aspirate and biopsy showed diffuse infiltration by small-to-medium mononuclear cells with deep blue cytoplasm and occasional basophilic granules. By flow cytometry, the atypical cells showed dim CD45 with co-expression of bright CD56, CD33, CD7 and HLA-DR, while negative for all other markers. Skin biopsy was performed and showed perianexial and perivascular infiltrate of medium-sized blasts with fine chromatin, inconspicuous nucleoli and scant cytoplasm. By immunohistochemistry, the atypical cells were positive for CD45, CD2, CD43, CD56 and CD123, while negative for other markers. The diagnosis of blastic plasmacytoid dendritic cell neoplasm was given. Cytogenetic studies showed complex numerical and structural chromosomal aberrations. No TCR gene rearrangement was detected. After diagnosis, the patient was treated with high risk ALL protocol and one course of AML consolidation. She is now one year after diagnosis receiving maintenance chemotherapy without any evidence of disease.

Discussion:

BPDCN occurs rarely in children with slightly better outcome than adults. It presents mostly with skin bruise-like lesions, patches or tumor nodules. Bone marrow and lymph node involvements are common. BPDCN has to be differentiated from other leukemias especially AML with monocytic differentiation. It is best treated in children by high risk ALL protocol. Relapsed cases are treated with stem cell transplant.
Spectrum of malignant lymphoma in Bahrain: a retrospective analysis according to the 2008 World Health Organization classification

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Background and Purpose: To determine the spectrum of various types of malignant lymphoma in Bahrain according to 2008 World Health Organization (WHO) classification.

Methods: A retrospective review of all new lymphoma cases diagnosed at Salmaniya Medical Complex - the main oncology center in Bahrain - during the period between January 2010 and December 2010 was conducted. All cases were classified according to 2008 WHO classification.

Results: 221 new cases of lymphoma were diagnosed in Bahraini patients in the study period. The age at presentation ranged from 3 to 90 years with median of 48 years. Only 16 cases were in children less than 14 years of age. There were 126 males and 95 females. 80 cases (36%) had Hodgkin lymphoma (HL), 140 cases (63%) had non-Hodgkin lymphoma (NHL) and one case had composite lymphoma (HL and diffuse large B-cell lymphoma). In HL group, nodular sclerosis type was the most frequent type (49%), followed by mixed cellularity type (28%) then nodular lymphocyte predominant type (16%). In NHL group, 124 (88.5%) cases were B-cell lymphomas, while the remaining were T-cell lymphomas. Diffuse large B-cell lymphoma (DLBCL) was the most frequent type (56%), followed by follicular lymphoma (10%). Burkitt lymphoma represented only 4%. 35% of NHL were extranodal.

Conclusions: In HL, nodular sclerosis type is the most common similar to the West and recent studies from Middle East. Nodular lymphocyte predominant type represented 16% of HL. This is higher than reported in the West and most Middle East countries. Among NHL, DLBCL is the most common type similar to other Middle East countries. However, follicular lymphoma is more common in Bahrain than Burkitt lymphoma in contrast to studies from other countries in the region.
Preconditioning Neutropenia is a Key Prognostic Factor in Allogeneic Haematopoietic Cell Transplantation for High Risk Acute Myeloid Leukaemia.

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Background: Identification of prognostic indicators to predict outcomes of haematopoietic cell transplantation (HCT) is important for selection of patients most likely to benefit from the procedure. Validated systems such as the HCT-Comorbidity Index (HCT-CI) and the modified EBMT risk score provide prediction of outcomes, in particular non-relapse mortality (NRM) and survival.

Methodology: In this retrospective study we identified neutropenia prior to initiation of conditioning regimen as an additional prognostic factor in 117 adults with high-risk acute myeloid leukaemia (AML) who received HCT at a single institution from January 2005 to December 2015.

Results: With a median follow-up of 3.1 years, day 100 NRM for the whole group was 17.3% and the probability of survival at 5 years was 40.3%. Multivariate analyses yielded significant associations with improved NRM for preconditioning absolute neutrophil count (ANC) >= 1000/microL and HCT-CI < 3 (hazard ratio (HR) 0.36; 95%CI 0.1–0.9 and HR 0.39; 95%CI 0.2–0.9 respectively). The factors associated with improved survival in multivariate analysis included preconditioning neutrophil count >= 1000/microL (HR 2.9; 95%CI 1.6–5.4, P=0.01), absence of any measurable disease prior to conditioning (HR 2.1; 95%CI 1.1–4.2, P=0.03), and less than 2 disease risk defining criteria (HR 15.8; 95%CI 2.0–124.4, P=0.01).

Conclusion: Patients with ANC of 1000/microL and above prior to initiation of conditioning and those with HCT-CI below 3 had significantly better day 100 NRM. ANC of 1000/microL or above was also associated with better survival at 5 years together with disease specific factors, absence of measurable residual disease prior to initiation of condition and less than two adverse prognostic factors. Neutrophil count, a simple measurement, helps to predict outcome: this might reflect on-going disease but it is also possible that delaying transplant until ANC recovery might improve the results. Our findings advocate integration of preconditioning ANC into existing risk assessment tools.
Allogeneic Haematopoietic Stem Cell Transplantation for Primary Refractory Acute Lymphoblastic Leukaemia - a Report from the Acute Leukaemia Working Party of the EBMT

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Background: Patients with primary refractory acute lymphoblastic leukaemia (PREF ALL) who fail to achieve complete remission (CR) after two or more courses of chemotherapy have a dismal prognosis without allogeneic haematopoietic cell transplantation (HCT). There are currently no data on factors influencing their transplantation outcomes.

Methods: We retrospectively studied outcomes of transplantation for PREF ALL reported to EBMT registry. Eligibility criteria for this analysis included adult patients who underwent their first HCT for PREF ALL between 2000 and 2012. PREF disease was defined as failure to achieve a morphological CR (<5% of blasts in the bone marrow) after two or more courses of induction chemotherapy. The main endpoints of the study were survival defined as time to death from any cause, CR rate, leukemia free survival (LFS), and non-relapse mortality (NRM).

Results and discussion: Data on 86 adult patients were analysed. With a median follow-up of 106 months, the probability of survival was 36% at 2 years and 23% at 5 years. The probability of LFS was 28% and 17% and probability of NRM was 20% and 29% at 2 and 5 years respectively. For 66 patients (76%) achieving CR, 17% achieving CR, the survival at 2 and 5 years was 36% and 29%. In multivariate analysis, use of total body irradiation (TBI) was associated with improved survival. TBI and infusion of female haematopoietic cells into male recipient was associated with improved LFS. These were incorporated into a scoring system that identified three groups (two, one or no prognostic factors) with survival rates of 57%, 22% and 8% respectively.

Conclusions: Although overall these patients would clearly benefit from introduction of novel anti-leukaemic therapies, our data support the use of allogeneic HCT in selected patients with PREF ALL.
Analysis of Haematopoietic Recovery after Autologous Transplantation as Method of Quality Control for Long-term Progenitor Cell Cryopreservation.

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Background: Haematopoietic precursor cells (HPC) are able to restore haematopoiesis after high dose chemotherapy. Their cryopreservation is crucial for successful autologous haematopoietic cell transplantation (AHCT). Although previous studies showed feasibility of long-term HPC storage, concerns remain about possible negative effects of storage on their potency.

Methodology: To study effects of long-term cryopreservation we compared time to neutrophil and platelet recovery in 50 patients receiving two AHCT for multiple myeloma at least 2 years apart between 2006 and 2016, using HPC obtained from one peripheral blood apheresis prior to the first transplant. This product was divided into equivalent fractions. One half was used for the first transplant after median storage duration of 60 days (range 17 – 165) and the other half was used after median storage of 1448 days (range 849 – 3510) at the second AHCT.

Results and discussion: Neutrophil recovery occurred at 14 days (mean, range 11 – 21) after the first and 13 days (range 10 – 20; P = 0.006) after the second AHCT. Platelets recovered at 16 days after both procedures (range 8 – 23). Considering other factors affecting haematopoietic recovery such as disease status, conditioning, HPC dose, and use of G-CSF, this single institution data demonstrated no reduction in the potency of HPC after long-term storage.

Conclusions: This data are reassuring as they indicate that long storage of haematopoietic cells does not negatively impact on neutrophil and platelets engraftment in AHCT setting provided that strict quality assurance measures are in place. Such quality measures are paramount as there is no other method capable reliably assessing cell viability in vivo after cryopreservation.

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Background: Haemorrhagic cystitis caused by BK virus (BKV) is a known complication of allogeneic haematopoietic cell transplantation (HCT) and is particularly common following HLA-haploidentical transplantation. Adoptive immunotransfer of virus-specific T-cells from the donor is a promising therapeutic approach, although production of these cells is challenging, particularly when dealing with low frequency T-cells such as BKV-specific T-cells.

Case report: Here we present a patient who developed severe BKV haemorrhagic cystitis after haploidentical HCT. This infection was resistant to standard therapy, but the patient responded well to adoptive transfer of donor cells enriched in BKV-specific T-cells using the new second-generation CliniMACS Prodigy and the Cytokine Capture System from Miltenyi Biotec. Treatment led to full resolution of the viraemia without unwanted complications.

Conclusion: Our observations suggest that use of products enriched with BKV-specific T-cells generated using this system is safe and efficient in HLA-haploidentical HCT where BKV cystitis can be a serious complication.
Acute Myeloid Leukaemia with inv(16)(p13q22) associated with hidden systemic mastocytosis: Case report and review of literature.

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Mastocytosis is a group of rare neoplastic disorders of mast cells with highly variable clinical course and prognosis. The WHO classification recognizes this clinical heterogeneity by subdividing SM patients into distinct subgroups. In this scheme, patients who have SM associated with myeloid or lymphoid neoplasm are designated as SM with associated clonal hematologic non-mast cell lineage disease (AHNMD), recently shortened to “systemic mastocytosis with an associated hematological neoplasm (SM-AHN).

Herein, we report a 30 years old male patient presented with recent history of jaundice and hepatosplenomegaly. Peripheral blood revealed anaemia, thrombocytopenia and leukocytosis of 164 x10⁹/L with 42% circulating blasts and 23% promonocytes. Initial bone marrow (BM) morphology, immunophenotyping and cytogenetics findings were consistent with the diagnosis of acute myeloid leukaemia with inv(16)(p13.1;q22) CBFB:MYH11.

BM examination post first induction showed 19% blasts and biopsy showed increased CD34 and CD117 positive cells interpreted as persistence of the leukemic process. Evaluation of BM after 2nd induction, revealed 3% blasts indicating remission. However, the aspirate showed 2% atypical mast cells and BM biopsy revealed multiple perivascular and randomly distributed focal collections of mast cells positive for tryptase, CD117, CD68 and CD25. These findings established the diagnosis of SM with AML. Re-examination of BM biopsy at diagnosis revealed multiple dense clusters of cells positive for CD117, tryptase and CD25 indicating that mastocytosis was present from the start but masked by the extensive infiltration of blasts. KIT mutation on peripheral blood was negative.

Bone marrow evaluation after completion of three consolidation courses revealed no increase inblast cells but there was persistence of mastocytosis.

In conclusion, this report indicates that the diagnosis of SM with associated haematological neoplasm may be challenging and requires a high index of suspicion and screening for mast cell disease particularly in cases of core binding factor AML is recommended.
 Measurement of the hypercoagulability state in Sudanese patients with acute myelogenous leukemia in Khartoum state

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Background and Purpose:

Leukemias are a group of disorders characterized by the accumulation of malignant white cells in the bone marrow and blood. This study aimed to measurement the hypercoagulability state in Sudanese patients with acute myelogenous leukemia in Khartoum state between November 2015 and April 2016.

Methods:

The study included 80 individuals, 40 of them were Acute Myelogenous Leukemia patients and 40 from healthy individual as control (Same age and sex with patients).

Results:

Results were as follow: the mean of fibrinogen level 282.73mg/dl in comparison to control group 270.40mg/dl, Prothrombin PT 14.05 seconds in comparison to control 12.70 seconds. Activated partial thromboplastin time APTT 34.70 seconds in comparison to control 34.30 s and thromboplastin time TT 13.943 seconds, in comparison to control 13.945 seconds.

Conclusion:

There were no obvious effects on patients with Acute Myelogenous Leukemia in most of parameters when compared with control group which show the lack of relationship between the patients with acute myelogenous leukemia and coagulability (fibrinogen; Prothrombin; activated partial thromboplastin time and thromboplastin time).
Pseudo Chediak Higashi-Like Inclusions in Acute Myeloid Leukemia

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Background and purpose: Pseudo Chediak-Higashi inclusions have been previously described in case reports in patients with AML, ALL, CMML and MDS. In AML patients, certain flowcytometry findings have been described in association with these inclusions. We report a case where pseudo Chediak-Higashi inclusions were seen in AML myeloblasts, with a phenotype and cytogenetic changes that were not previously reported.

Methods: A 67 years old female presented with lethargy and transfusion dependent anemia for 3 months. Complete blood count showed pancytopenia. Bone marrow aspiration was performed and stained using Giemsa. Cytogenetics and flowcytometry were also performed.

Results: The bone marrow aspiration showed that myeloblasts constituted 76% of non-erythroid elements. Some of the myeloblasts showed giant purplish granules with occasional vacuolation. Flowcytometry showed that the blasts were positive for CD11b, CD13, CD15, CD33, CD34, MPO, and HLA-DR. They were partially positive for CD7 and CD117. They were negative for CD2, CD5, CD10, CD19, and CD64. Chromosomal analysis revealed deletion of the long arm of chromosome 13 at (q12 q22) in 20 out of 20 metaphases examined.

The patient received low dose cytarabine and was then transferred to another facility for further management.

Conclusions: The presence of pseudo Chediak-Higashi inclusions in patients with leukemia is extremely unusual. It is not known whether this has any prognostic significance. Almost all previously reported cases showed positivity of CD2, unlike our case. The described chromosomal abnormalities were also not previous reported. We aim to report this case and share images to increase awareness of this unusual finding.
Bone marrow failure due to myelofibrosis with renal osteodystrophy & hyperparathyroidism

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Background and Purpose:

Hypoproliferative anemia due to erythropoietin hypoproduction is a common feature of chronic kidney disease (CKD). Hyperparathyroidism (HPTH) is among the possible factors contributing in anemia with CKD and recombinant erythropoietin (rEPO) hyporesponsiveness as the excess parathyroid hormone PTH could induce marrow stromal changes. Although secondary myelofibrosis and osteomyelosclerosis are known complications in renal osteodystrophy (ROD) with HPTH, their finding is uncommon. Our purpose is to emphasize on the histopathological marrow changes in ROD & HPTH and to not overlap associated myelofibrosis with neoplastic myelofibrosis.

Methodology:

A 104 bone marrow reports of a three year period at a secondary health care hospital were reviewed in a retrospective study. We found that 2.88% of those bone marrows had secondary myelofibrosis. ROD was one of the underlying pathology in this category. An extensive literatures review of bone marrow changes in ROD with HPTH is done.

Results and Discussion:

HPTH secondary to hypocalcemia in CKD is a common complication. Secondary HPTH is responsible to the most of histological changes of ROD which include presence of excess osteoid seams around bone trabeculae, tunneling into trabeculae by fibrous tissue and osteoclasts. Paratrabeucular marrow fibrosis is seen with some times complete intertrabecular fibrosis. Moderate increased marrow vascularity with calcified blood vessels and hemosiderin-laden macrophages might be present in the final stage. Therefore, ROD may progress to pancytopenia and bone marrow failure. The final stage (osteitis fibrosa cystica) is rarely seen nowadays.

Conclusion:

Rarely reported bone marrow changes of ROD & HPTH might be due to paucity of examined marrow in CKD. These histopathological changes are good target for examination in renal patients with pancytopenia and or rEPO hyporesponsive anemia as early detection with clear diagnosis may prevent further progression of hematological complications which in turn linked to patients survival rate.
A case series study of bone marrow necrosis with literature review.

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Background and Purpose:

Bone marrow necrosis (BMN) is a relatively uncommon clinicopathologic entity. It is little known regarding it in medical community although it was first described in 1941. To highlight the index of suspicion of BMN, the underlying pathology with prognosis, and the usefulness of diagnostic procedures, an extensive literature review was made.

Methods:

A case series study composed of three cases of varying degree of BMN were selected. The cases found in a retrospective study of 52 bone marrow samples examined under microscopy in hematopathology section of secondary hospital in a period of 12 months, from the first of November 2015 till the end of October 2016.

Discussion And Result:

We reported three cases of bone marrow necrosis. Two of these cases were female and one was male. One of them was a known case of sickle cell disease (SCD) in addition to chronic ITP, in remission, developed new onset bicytopenia with leukoerythroblastic picture, one with SCD with co-existence of hereditary elliptocytosis presented with pancytopenia. The third patient was a case investigated for persistent refractory anemia found to have moderate BMN with picture of anemia of chronic inflammation diagnosed eventually with mixed cellularity Hodgkin’s lymphoma. The two sicklers patients treated with supportive therapy, in addition to prednisolone given to the ITP patient. Both of them discharged with hematological recovery. The patient’s with HL referred to tertiary care hospital for chemotherapeutic treatment.

Conclusion:

Bone marrow necrosis might be caused by malignancy especially hematolymphoid malignancy, hemoglobinopathies, antiphospholipid syndrome, some drugs ingestion, anorexia and disseminated intravascular coagulation. In BMN, Fever & bone pain are the most common sign and symptom while anemia is the most associated hematological abnormality. Other cytopenia and leukoerythroblastosis with elevated lactate dehydrogenase are also common. The prognosis of BMN is variable among varying underlying pathology.
CD49d and CD26 are independent prognostic markers for disease progression in patients with chronic lymphocytic leukemia

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Objective: CLL is characterized by extremely variable clinical course. Several prognostic factors can predict disease progression and therapeutic outcomes in those patients. The aim of the present study was to evaluate the use of CD49d and CD26 as independent prognostic markers in CLL patients.

Methods: The present study measured surface expression of CD49d and CD26 by three-color flow cytometry in a series of 103 previously untreated CLL patients. We evaluated the prognostic role of CD49d and CD26 to predict the risk of lymphocyte doubling, disease progression and overall survival.

Results: We confirmed that CD49d and CD26 were significant predictors of lymphocyte doubling (P < 0.001 for both markers) and disease progression (P < 0.001 for both markers) but insignificant for overall survival (P = 0.303 and 0.519 respectively). Furthermore, multivariate analysis between clinical parameters and flowcytometry markers revealed that CD49d and CD26 are independent prognostic markers for lymphocyte doubling (HR = 1.487 P =0.007 and HR = 2.248, P =0.014 respectively) and progression to a more advanced stage (HR = 3.191, P = 0.049 and HR = 7.887, P = 0.003). Also, concordant expression of both markers was found to improve their predictive power.

Discussion: Many studies reported that CD49d and CD26 combined analysis was found to improve their power to predict the risk of lymphocyte doubling and disease progression.

Conclusion: CD49d and CD26 have independent prognostic value and we suggest its use as a part of routine panel for prognostic stratification of CLL at diagnosis.
Association of MDR1 gene polymorphism (G2677T) with imatinib response in Egyptian chronic myeloid leukemia patients

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Background: Despite the excellent efficacy results of imatinib treatment in CML patients, resistance to imatinib has emerged as a significant problem. Genetic variations in genes involved in drug transportation might influence the pharmacokinetic and metabolism of imatinib. The genotype of a patient is increasingly recognized in influencing the response to the treatment.

Aim: To investigate the genotype frequencies of single nucleotide polymorphisms G2677T in CML patients undergoing imatinib treatment to determine whether different genotype pattern of these SNPs have any influence in mediating response to imatinib.

Methods: A total of 96 CML and 90 control samples were analyzed for the (MDR1) gene polymorphism (G2677T) using polymerase chain reaction-restriction fragment length polymorphism technique.

Results: Genotype distribution revealed a significant lower frequency of TT genotype in CML patients and non-significant difference in the GG, GT genotype frequencies between patients and controls. GG genotype was significantly higher in chronic phase, while GT genotype was significantly higher in Blastic crisis phase. There was a significant difference in genotype frequency of G2677T among patients showing response and resistance to imatinib in chronic phase. TT genotype was associated with complete hematological response, complete cytogenetic response, and better molecular response with a significant association. GT genotype was associated with partial hematological response and minor cytogenetic response. Optimal and suboptimal responses were observed for patients with TT genotype. Failure of drug response was associated with GT genotype; however, GG had no association with drug response. Multivariate analysis considered GT genotype as independent risk factor for resistance (P = 0.037), while TT genotype as protective factor against resistance to imatinib.

Conclusion: Determination of MDR1 polymorphisms (G2677T) might be useful in response prediction to therapy with imatinib in patients with CML.
Meningioma 1 (MN1) expression: Refined risk stratification in acute myeloid leukemia with normal cytogenetics (CN-AML)

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Background: Prognostic stratification of cytogenetic normal acute myeloid leukemia (CN-AML) is an area of active research.

Aim: The aim of this study was to determine the prognostic importance of the meningioma 1 (MN1) gene expression levels in CN-AML.

Methods: One hundred patients with CN-AML were diagnosed; MN1 expressions were analyzed using quantitative real-time polymerase chain reaction.

Results: High expressions were detected in 48 (48%) patients (expression range: 2.35–31.99, mean: 13.9±8.49) in comparison with 52 (52%) patients with low expression (expression range: 0.02–2.3, mean: 0.68±0.77). The course of the disease in patients with high MN1 expression was unfavorable. Patients with high MN1 expression was associated with significant low complete remission rate (62.5 vs. 8.4%, high vs. low MN1, P=0.001) and high mortality rate (75% vs. 46.1, P=0.03). AML patients with high MN1 expression tended to be refractory (37.5 vs. 19.2%, P=0.00) and relapse risk (54.1 vs. 23%, P=0.02). Multivariable analysis confirmed high MN1 expression as an independent risk factor for disease-free survival and overall survival.

Conclusion: MN1 over expression independently predicts bad clinical outcome in CN-AML patients.

Keywords: CN-AML, MN1, NPM1, FLT3-ITD
Association of Angiotensin-Converting Enzyme Gene Insertion/Deletion Polymorphism with Increased risk for Chronic Lymphocytic Leukaemia

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Background

Angiotensin converting enzyme (ACE) plays an important role in the stimulation bone marrow hematopoietic progenitors and umbilical cord blood cells proliferation and differentiation by converting angiotensinogen-I to its physiologically active peptide angiotensin-II which stimulates proliferation and differentiation of hematopoietic stem cells through angiotensin II type 1 receptors.

Purpose

The aim of this study was to determine angiotensin converting enzyme polymorphism insertion/deletion (ACE I/D) polymorphism in Sudanese patients with chronic lymphocytic leukemia (CLL).

Materials and methods

A total of 40 patients with chronic lymphocytic leukemia and 40 control subjects were enrolled in this study. Blood samples were collected from all patients in EDTA. Genomic DNA was extracted from all blood samples using salting out method. ACE I/D polymorphism as determined using polymerase chain reaction (PCR) method.

Results

The results showed that I/I genotype was detected in 42.5% of cases while it was completely absent among control subjects.

Conclusion

In conclusion, a significant association was found between ACE I/D polymorphism and CLL among Sudanese patients.
Proteomics prediction of treatment response in chronic myeloid leukemia patients towards personalized medicine

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Background: Chronic Myeloid Leukemia (CML), among other hematological malignancies, has witnessed development of advanced molecular diagnostics. However, there is an unmet need for development of objective markers for selection of appropriate therapeutic agents and accurate prediction of patient’s response for chronic myeloid leukemia (CML) patients. The study goal is to identify disease-specific/disease associated protein biomarkers detectable in bone marrow and peripheral blood for objective prediction of individual's best treatment options and prognostic monitoring of CML patients.

Materials and Method: Thirty one (31) bone marrow plasma (BMP) and peripheral blood plasma (PBP) samples from newly-diagnosed chronic-phase CML patients were subjected to expression-proteomics using quantitative two-dimensional gel electrophoresis (2-DE) and label-free liquid chromatography tandem mass spectrometry (LC-MS/MS).

Results: Samples were evaluated for early treatment response at 6 months and analysis of 2-DE protein fingerprints accurately predicts 13 patients that achieved major molecular response (MMR) from 12 individuals without MMR (No-MMR). The observed results were independently supported using LC-MS/MS analysis of BMP and PBP from patients that have more than 24 months followed-up. One hundred and sixty-four (164) and 138 proteins with significant differential expression profiles were identified from PBP and BMP, respectively and only 54 proteins overlap between the two datasets. The protein panels also discriminates accurately patients that stay on imatinib treatment from patients ultimately needing alternative treatment. Among the identified proteins are TYRO3, a member of TAM family of receptor tyrosine kinases (RTKs), the S100A8, and MYC and all of which have been implicated-in-CML

Conclusions: Our findings indicate that clinical proteomics analysis of a panel of protein signatures is capable of objective prediction of molecular response and therapy choice for CML patients at diagnosis as a model for personalized medicine.
How important are the genetic polymorphisms in MDR1 and BCRP genes in chronic lymphocytic leukemia and chronic myeloid leukemia?

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**Background and purpose:** There is an increasing interest to assessment of possible interaction between gene polymorphisms and risk of cancer progression. MDR1 and BCRP are involved in multidrug resistance and they can actively remove different kinds of anticancer drugs from tumor cells. The present study was aimed to evaluate the possible role of MDR1 C3435T and BCRP C421A polymorphisms as a potential risk factor for chronic lymphocytic and myeloid leukemia.

**Methodology:** This case-control study was performed on 50 B-CLL, 70 CML patients and 100 healthy subjects. Clinicopathological findings of all individuals were reported and the MDR1 C3435T and BCRP C421A polymorphisms were determined by polymerase chain reaction-restriction fragment length polymorphism method (PCR-RFLP).

**Results and discussion:** The T allele of MDR1 C3435T polymorphism was significantly higher in patients than controls. In addition, subjects carrying T allele were associated with a higher risk to develop B-CLL (OR=25.87, 95%CI= (7.96-84.15), p<0.0001) and CML (OR=3.0365, 95%CI= (1.6920 to 5.4494), p=0.0002). The CC genotype of BCRP C421A SNP was significantly higher in patients compared to controls. Furthermore, the 421 AA genotype was associated with lower risk of CML development, OR=0.2208, 95%CI= (0.1218 to 0.4003), p<0.0001. However, there was no significant allele frequencies difference for of BCRP C421A in B-CLL patients. CC421 BCRP/TT3435 MDR1 were correlated with higher risk of CML. Patients with C allele of MDR1 had poor cytogenetic response and correlations of CC421 BCRP/TT3435 MDR1 diplotype with accelerated phase of CML was significant. There are no significant differences between the genotypes and type of treatment in B-CLL patients.

**Conclusion:** The presence of MDR1 T3435C T allele of in B-CLL patients and CC421 BCRP/TT3435 MDR1 in CML cases might be proposed as potential risk factors to rapid and sever development of these leukemia and weaker response to treatment with chemotherapeutic agents.
Probable Pre-Leukaemic Molecular and Cytogenetic Aberrations in a Cohort of Sudanese Neonates: MLL gene Paradigm

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Background and Purpose:

Cancer is the most common cause of morbidity and mortality all over the world. Pediatric acute leukaemias are the most common type of childhood cancer in developed countries. The high percentage (68%) of MLL gene rearrangement supports the theory that some events that occur prenatally may play a role in the development of acute leukaemias.

This study aimed to detect the probable pre-leukaemic cytogenetic and molecular aberrations in a cohort of Sudanese neonates by using karyotyping and PCR.

Methods:

Fifty pregnant women were enrolled in the study. Family history of cancer is present in only 4% of the women. Drug history during pregnancy contained only haematins in form of Iron/Folate combination which was taken by the majority (45/50, 90%). Specifically, volunteers denied the use of hormones and anticancer drugs during pregnancy the course of the pregnancy. Few of them were reported to be hypertension and Diabetes.

Results:

There were 51 neonates, because one lady delivered twins. Male neonates were 45%, while female neonates were 55%. The mean weight of the babies was 3.1±0.9 Kg. All neonates looked healthy, and showed no aberrant anatomical abnormalities. The samples were taken from the cord blood.

Karyotyping was done to detect morphological chromosomal abnormalities and then Reverse Transcriptase – PCR was done to detect any abnormalities at the gene level related to MLL gene.

Conclusion:

We found that there is no chromosomal aberrations or gene rearrangements in a group of Sudanese neonates. Large sample size needs to be included in the future studies.
Hemoglobin Abruzzo; The altered physiology

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This is an archived case diagnosed in the Hereditary Blood Diseases Center of AL-Karama Teaching Hospital of Baghdad, Iraq.

Relevant clinical information is that it belonged to a young female, the blood film was hypochromic microcytic, the reticulocyte count with 2%, and that the sickling test and the HbH preparation were both negative.

The peculiar morphology of the trace (having the base of HbA0 and HbA2 apices elevated from the X-axis from the 2.41 min to the 3.63 min of the elution time in a triangular pattern with the apex of the triangle meeting the downward slope of the HbA2 window, with a small hump identified as an unknown at the minute 3.63 of the elution) together with the relatively increased percentage of HbA2, called to my mind a quite similar chromatogram depicted in the Variant Haemoglobins: a guide to identification book of Barbara J Bain and others (figure 2.12)

Having a look at the CBC report of this patient, despite the normal Hb level of 134 g/L, the RBC saw an increase to 6.15 ×106 /L, while the MCV and MCH valued 71.4 fl, and 21.8 pg respectively with nothing remarkable with the rest of the CBC.

To the best of my knowledge, I would argue that this is a case of hemoglobin Abruzzo Heterozygote (a high affinity hemoglobin) reported from our Center.

It would be ideal to confirm the diagnosis with further studies for the nature of the structural abnormality such as DNA analysis, assessment of the hemoglobin saturation status (PaO2) with pulse oximetry and family study, mass spectrometry technique exploitation to quantify the hemoglobin percent, more easier and feasible would be the isoelectric focusing and the gel electrophoresis at alkaline and acidic PH Characteristically demonstrating a slowly moving electrophoretic mobility on cellulose acetate gel.
Co-inheritance of triple α chains with β-thalassemia trait... The unlucky contingency

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A 28-year-old-female presented with severe pallor, splenomegaly, and multiple gall stones.

Her clinical symptoms commenced about 10 months ago correlated to the implantation of orthodontic metal appliance, the patient reports no history of significance with regard to a noticeable infection

In the meanwhile, serial abdominal ultrasounds start to reveal a developing splenomegaly with concomitant formation of multiple gall stones with the ongoing hemolysis, steroids prescribed as her Indirect Antiglobulin test starts to be positive which actually helped to lengthen the period of her being transfusion-free.

Her CBC showed RBC 2.80×10¹²/L, Hb 65 g/L, HCT 24.4%, MCV 87.3 fl, MCH 23.2 pg, MCHC 26.6 g/L, RDW 29.4%, PLT 335×10⁹/L, WBC 23.8×10⁹/L, Lymphocytes 13.4×10⁹/L, and granulocytes 9.1×10⁹/L. The reticulocyte count was 22%, with the corrected reticulocyte count 13.4%. testing for G6PD enzyme activity was normal, the iron profile assessment revealed an increase in the ferritin to 588ng/ml.

The peripheral blood film showed hypochromic marked anisopoikilocytosis.

Hemoglobin HPLC chromatogram yielded a HbA2 of 4.7% consistent with the diagnosis of β-thalassemia trait.

Family study revealed that the mother was a carrier for β-thalassemia trait while the father had normal hemoglobin HPLC chromatogram, the clinical picture is believed to be of thalassemia intermedia incongruent with the Hb HPLC finding this actually drove us into a more sophisticated analysis in the form of genetics work-up, the patient managed to undergo DNA testing (employing PCR and reverse hybridization) it disclosed the compound heterozygous Mediterranean type α-thalassemia gene mutation –α 3.7 deletion associated with anti- 3.7 α chain triplicated α chain ( - α3.7 / aaa anti 3.7)

Therefore the final diagnosis decision for this case is coexistence of heterozygous β-thalassemia with compound heterozygous for 3.7 alpha gene mutation and anti 3.7α chain triplication (−α3.7/aaa anti 3.7) inherited from her father.
The phenomenon of EDTA-Dependant Pseudothrombocytopenia (EDTA-PTCP)

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A 39-week pregnant lady was referred by her obstetrician as she was decided upon to undergo a cesarean section for a history of obstructed labor in a previous pregnancy, however, the surgical team was quite confused by the her serial CBC work-ups done in the meanwhile and revealed platelet count results that did not generally exceed a maximum of 60 ×10⁹/L with blood smear reports denoting platelet clumps and were thus inconclusive.

The history, physical and systematic examination was unremarkable.

On receiving the patient, an EDTA blood sample was withdrawn CBC results using the automated analyzer showed the following; RBC 4.14×10¹²/L, Hb 117 g/L, HCT 36.1%, MCV 87.1 fl, MCH 28.3 pg, MCHC 324g/L, RDW 16.6%, PLT 21×10⁹/L, WBC 12.0×10⁹/L, Lymphocytes 4.4×10⁹/L, and granulocytes 6.6×10⁹/L.

Therefore we could not give a definite opinion about the platelet count despite the apparent satisfactory number of platelets upon examining the blood smear and the decision was made to recollect blood in a citrate tube besides an EDTA tube, as we do not have an access to vortexing to resolve the platelet clumps, and the samples were run immediately on the automated analyzer and slides were made altogether. The platelet count with the EDTA tube was 57×10⁹/L with the blood smear showing platelet clumps all over, while the CBC result with the Sodium Citrate tube were;

RBC 3.62×10¹²/L, Hb 105 g/L, HCT 31.1%, MCV 86 fl, MCH 29 pg, MCHC 338 g/L, RDW 16.6%, PLT 116×10⁹/L, WBC 7.9×10⁹/L, Lymphocytes 1.9×10⁹/L, and granulocytes 5.4×10⁹/L, and the blood film revealed good platelet count and distribution.

To overcome the dilutional effect of citrate, the calculated platelet count needs to be corrected by multiplication by 1.1 and this also applies to some other CBC parameters; RBC count, WBC count and its absolute differentials, hematocrit and hemoglobin value.
Venous Thromboembolism Risks and Prophylaxis in King Fahd Hospital, Madinah, Saudi Arabia.

Dr. Amal Albeihany, dr khalid alyami, dr ayman kharaba, dr Mohammad Al boud

1Moh, , Saudi Arabia

OBJECTIVE:

To evaluate the risk factors, physician's compliance and implementation of American College of Chest Physicians (ACCP) guidelines for venous thromboembolism (VTE) prophylaxis at our hospital.

METHODS:

A retrospective cohort study was conducted in King fahd Hospital, Madinah from July 2015 to September 2015. We used the American College of Chest Physicians (ACCP) 2012 guidelines and Caprini’s scores to assess VTE risk and to determine whether patients had received recommended prophylaxis. All hospital in-patients aged 14 years or above were assessed for risk of VTE by reviewing the hospital chart. The primary endpoint was the rate of appropriate thromboprophylaxis.

RESULTS:

414 patients were studied. The mean age was 47.74± 20.4 years, and 208 (50.2%) were female. There were 292(70.5%) patients at high risk, and 73(17.6%) at moderate risk. As Per ACCP criteria, 375 (90.5%) patients were at risk for VTE and qualified for prophylaxis. Although 227 (60.5%) received some form of prophylaxis, only 144 (38.4%) of them received ACCP-recommended VTE prophylaxis.

Conclusion

In our hospital most of the patients are at high risk for developing VTE. VTE prophylaxis guideline is not properly implemented and underutilized. Strategies should be developed and implemented to ensure patient’s safety.
Thrombocytosis; Etiology and clinical association: Analysis of 140 cases with elevated platelets

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INTRODUCTION

Thrombocytosis refers to a platelet count above the normal value in the circulating blood. Recently with the widespread use of the electronic cell counters and the subsequent availability of a platelet count as part of a routine complete blood count, thrombocytosis is more often observed as an unexpected finding.

OBJECTIVES

- To determine the frequency of common factors leading to thrombocytosis in adults.

STUDY DESIGN Cross sectional study.

SETTING

The study was conducted at the department of Hematology, King Fahad Hospital, Madinah, KSA.

SUBJECTS AND METHODS

A total of 140 patients were included in the study. Cases of thrombocytosis were taken by noting the complete blood counts performed in the haematology laboratory of King Fahad hospital by using Cell Dyn Ruby Haematology analyzer. Platelet count was repeated three times and confirmed by manual counting with peripheral blood film, which was stained by Giemsa stain. All cases of thrombocytosis were followed for investigations.

RESULTS

Mean age of the patients was 38.39±13.61 year. Out of 140 patients, 86 patients (61.4%) were male while remaining 54 patients (38.6%) were females. Factors leading to thrombocytosis were as follows: trauma 38 (27.1%), surgery 13 (9.3%), infection 46 (32.9%), malignancy 24 (17.1%), chronic inflammation 12 (8.6%), acute GI bleeding and iron deficiency anaemia 4 (2.9%). Stratification with regard to age, gender and platelet count was done.

CONCLUSION

This study concluded that the most common factors leading to thrombocytosis are trauma and infection. Thrombocytosis should be treated promptly to prevent grave complications of thrombosis and hemorrhage.

KEY WORDS Thrombocytosis, Elevated platelet count, Infection, Trauma, Malignancy
Iron shuttle chelation therapy enhances to reduce misplaced iron on secondary iron overloaded adult zebrafish

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Background

Thalassemia is the most common genetically inherited blood disorder in the world arises from defect in hemoglobin production, results in ineffective erythropoiesis and the rapid destruction of RBC in the periphery that leads to severe anemia. While transfusion therapy corrects the anemia, it gives rise to secondary iron overload. The current available iron chelation therapy has issues with toxicity and compliance. Our hypothesis is iron shuttle chelation therapy using combined iron chelators may have better effect in iron loaded adult zebrafish.

Method

To test the utility of iron chelator deferiprone (L1) and polymer based iron chelator S-DFO in vivo, zebrafish were exposed for six days to iron 1 mM Fe³⁺; ferric ammonium citrate, then iron loaded zebrafish were injected with 50 μM L1 and 500 μM S-DFO. The efficacy of treatment was assessed by measuring total tissue iron concentration using different methods; inductively coupled plasma mass spectrometry, microscopy of tissue with histochemical staining followed by transmission electron microcopy (TEM). All results expressed as mean ± standard error mean

Results

Iron treatment alone resulted in a significant increase in total iron, histochemical iron staining, also resulted in an increase in stainable iron. Treatment with iron chelators either L1 or S-DFO alone demonstrated modestly decreased total iron and iron staining. Importantly, TEM shows increase in electron dense iron particles accumulated in organelles such as mitochondria and lysosomes. L1 treatment of the iron-loaded zebrafish also showed a significant decrease in total iron concentration.

Conclusion

This study presented a clear evidence of the effectiveness zebrafish to be used as a new experimental in vivo model to study iron overload and open the door for studying the efficiency of potential new iron chelating compound other than commercially available ones.
The Role of Immunoglobulin Heavy Chain Gene Rerangment in The Diagnosis of B Non-Hodgkin’s s cell Lymphoma

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Abstract

Background: Lymphomas are a group of malignant diseases generally present as solid tumors of the lymphoid system. The major forms of malignant lymphomas (B- and T-cell) are broadly categorized into Hodgkin’s and non-Hodgkin’s types. Majority of NHL are B-cell origin. Molecular analyses, aimed not only at a more precise disease definition, but also at recognizing factors that can predict prognosis.

Aim: to reveal the usefulness of polymerase chain reaction analysis of the IgH chain gene rearrangement in the diagnosis of B-cell NHLs in Sudan.

Methods: A total of 113 patients were prospectively enrolled in this study from January 2013 to December 2014. The patients were divided into two groups, group of them were diagnosed as B-NHL morphologically then confirmed by immunohistochemistry (81 cases). Another group of patients were suspected to have B-NHL only by morphology while immunohistochemistry was failed to confirm the diagnosis and those were reported as inconclusive (32 cases). The specimens were extracted from formalin-fixed, paraffin-embedded sections and used for IgH gene rearrangement polymerase chain reaction analyses.

Results: IgH gene rearrangement was detected in 106 cases (93.8%) using FR3 primers and in 85 cases (75.2%) using FR2 primers. Simultaneous use of FR2 and FR3 increase the detection rate of monoclonality to (99.9%). FR2 primers detect the clonality in all cases with inconclusive immunohistochemistry (100%) while FR3 primers detect the clonality in 28 cases (87.5%). Comparable to immunohistochemistry IgH gene rearrangements were detected using FR3 with insignificant difference (P.value: 0.08), while a significant differences were detected with FR2 and combined clonality (FR2 and FR3) (P.value: 0.00) and (P.value: 0.03) respectively. A significant difference was detected when examining detection of clonality using FR3 primers in relation to the site of biopsy (P.value: 0.00).

Conclusion: FR3 assay was superior to FR2 assay, although FR2 helped to increase the overall clonality rate to 99.9%.
High grade B-cell neoplasm with surface light chain restriction and TdT co-expression evolved in a case of MYC-rearranged diffuse large B-cell lymphoma. A dilemma in classification.

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B-cell and T-cell neoplasms in several instances appear to recapitulate the normal stages of B- or T-cell differentiation, and so can be classified according to their corresponding normal stage of differentiation. According to World Health Organization (WHO) Classification (2008) [1], neoplasms of the B-lymphoid cell lineage are broadly classified into precursor B-cell or a mature B-cell phenotype and this classification was also kept in the latest WHO revision [2].

We are reporting a case of male patient in his fifties presented with tonsillar swelling diagnosed as diffuse large B-cell lymphoma (DLBL), germinal center. The patient received 6 cycles of RCHOP and intrathecal methotrexate with uncomplicated course. PET/CT showed complete metabolic response. Two months later, the patient presented with severe CNS symptoms. Flow cytometry on both CSF fluid and bone marrow showed kappa-restricted monotypic B-cells population expressing CD10, CD38 with loss of CD20 and CD19 and down regulation of CD79b. Moreover, the malignant population showed TDT expression. Cytogenetics on bone marrow revealed t(8;14)(q24;q32) in context of markedly complex karyotype. Retrospectively, MYC and TDT immunostains were performed on original diagnostic tissue and came to be negative.

Moreover, FISH analysis for IGH/BCL2, MYC/IGH rearrangement was performed on original diagnostic tissue and revealed positivity for MYC/IGH with negative BCL-2 rearrangement.

We struggled in classification and understanding the origin of the emerging clone. A mechanism of “de-differentiation” of lymphoma cells into its immature precursors has been suggested and was supported by shared immunophenotypic and genetic features between the original neoplasm and the second presentation.

In conclusion, an extensive literature review did not identify a similar case of a B-cell neoplasm with such unusual immunophenotypic aberrancies (particularly TDT expression). We recommend to screen double hit and double expressor DLBL for TDT expression to draw more attention to these aggressive neoplasms and its disease characteristics.
Denovo B- Lymphoblastic Leukaemia/Lymphoma with double hit rearrangements [ t(8;22) (q24.1;q11.2) and t(14;18)(q32;q21)] presented with spinal cord compression in a young adult

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Double hit lymphoma are aggressive mature B-cell neoplasms associated with rearrangements involving MYC and BCL2. Such double-hit events are extremely rare in B-cell precursor acute lymphoblastic leukemia, especially in young adults and often associated with aggressive fatal course.

This is a report of twenty nine year-old male patient, initially presented emergency department with right mandibular mass of two months-duration associated with intermittent fever.

Laboratory work-up revealed very high at LDH 2,026.0 U/L. The patient has evident bleeding tendency, detailed coagulopathy studies revealed acquired factor XIII deficiency. Peripheral blood revealed pancytopenia with many circulating blasts (~77%). Bone marrow aspirate was infiltrated with many small sized blasts of very high nucleocytoplasmic ratio,

finely dispersed nuclear chromatin and prominent nucleoli.

The bone marrow biopsy reflected markedly hypercellularity with diffuse replacement by sheets of blasts, positive for TDT, PAX-5, CD10, c MYC, BCL-2 and CD20 with KI-67 >90%.

Flow cytometry on bone marrow revealed a precursor B-immunophenotype (CD45 (dim), CD19, CD10, Tdt and CD20). The blasts are negative for cytoplasmic and surface IgM. Cytogenetics revealed complex karyotype involving t(14;18)(q32;q21), and t(8;22)(q24;q11.2).

Karyotype: 46,XY,del(6)(q21q23),t(8;22)(q24.1;q11.2),t(14;18)(q32;q21)[20]

A diagnosis B-Lymphoblastic Leukaemia/Lymphoma with t(8;22)(q24.1;q11.2) and t(14;18)(q32;q21) was made.

The patient developed acute sudden onset paraplegia (power 0 out of 5). MRI spine showed acute cord compression which necessitated emergency radiotherapy after which chemotherapy was started on HYPER CVAD protocol. After which, MRI showed dramatic resolution of the mass.
Very few cases of B-ALL with double hit rearrangement with true precursor B-cell phenotype (positive for TdT and negative for surface light chain) have been reported. Many of these had frequent CNS involvement, complex karyotypes, highly aggressive course and short survival in less than 1 year.

Most of reported cases represents transformation of follicular lymphoma. Our patients’ young age with acute onset and absent lymphadenopathies supports denovo ALL.
Clinico-Pathologic Profile and Clinical Outcomes of Patients with Indolent Lymphoma at a Tertiary Hospital in the Philippines: A 7-Year Experience

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Background. Indolent lymphoma (IL) is a slowly growing lymphoma, generally refractory to conventional chemotherapy. There are several types of IL, which includes Follicular lymphoma, Marginal Zone lymphoma, Small Lymphocytic lymphoma, Mantle Cell lymphoma, and Waldenstrom Macroglobulinemia/Lymphoplasmacytic lymphoma. Presently, there are no known data in the Philippines on IL. This study is done to determine the clinico-pathologic profile and outcomes of Filipino patients with IL.

Methodology. This study is a retrospective chart review of outpatient department cases of IL seen at the Philippine General Hospital-Cancer Institute from January 2009 to January 2016. The following were documented: age; gender; initial complaint; presence or absence of B symptoms; sites involved; type of IL; Ann-arbor stage; prognostic indices for FL and MCL; and if bone marrow aspiration or complete whole body CT scan were done as part of initial staging. Treatment intervention and clinical outcomes were documented. Fischer's exact test at p<0.05 was used to determine the association between select parameters and outcomes.

Results. This study showed that Small Lymphocytic lymphoma was the most common IL. Most were elderly (>40 years old); male; without B symptoms; limited disease; and initial complaint related to the eye. MCL were seen in all risk groups, and positive for cyclin D1; FL were mostly grade 1, and positive for BCL2 and CD10. Majority had disease control regardless of treatment intervention. Most patients with recurrence/progression after initial treatment had limited disease and incompletely staged. There seemed to be no association between age, gender, stage, complete whole body CT scan/bone marrow aspiration with clinical outcomes, although the sample size examined was small.

Conclusion. The results of this study are mostly consistent with known literature on IL. Absence of B symptoms and limited disease may indicate a low-grade histology. Observation remained the intervention of choice for patients who were asymptomatic.
An Investigation of the Therapeutic Efficiency of daratumumab in multiple myeloma

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Despite the recent achievements in treating multiple myeloma, it is still an incurable disorder. There is a need to develop a new therapy option with novel mechanism of actions. Currently daratumumab has been studied on patients with relapsed / refractory multiple myeloma. This meta-analysis study aims to investigate the daratumumab therapeutic efficacy by reviewing the current daratumumab clinical trials either daratumumab as a single agent or in combination with other backbone regiments. This study examines the updated results of two recent daratumumab monotherapy studies and one in combination with bortezomib and dexamethasone drugs. Data about daratumumab as a single agent were measured, calculated, compared, and presented in comparable form, in order to get an updated pooled analysis of 148 patients who received daratumumab at 16mg/kg. Furthermore, CASTRO which studied daratumumab in combination with bortezomib has provided a confirmatory evidence of daratumumab efficacy by comparing patients’ outcomes with the control arm. Daratumumab has showed an outstanding antimyeloma activity in heavily pre-treated MM patients as a monotherapy. Interestingly, adding daratumumab to current backbone treatments showed better overall responses and lower proportion of disease progression or death. The underlying mechanism of that is adding daratumumab will enhance patients’ response to the previous drugs that were on. This led to the direct cytotoxicity on multiple myeloma has been enhanced and leads to prolonged responses. Daratumumab has a favourable safety profile; however, the most commonly reported side effects are infusion reactions, usually during the first or second infusion. Moreover, the therapeutic antibody (DARA) interference with blood transfusion tests has been successfully solved by the DTT reducing agent.
Langerhans Cell Histiocytosis with subsequent Juvenile Xanthogranuloma

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Development of Juvenile Xanthogranuloma (JXG) as a sequel to Langerhans Cell Histiocytosis (LCH) is a phenomenon that has been recognized lately. This rare disease sequel has been reported multiple times in the last 15 years. Here we present an 18 years old male with a brain tumor that was pathologically confirmed to be JXG, after suffering from cutaneous LCH since he was 2 years old. Review of the literature has revealed 9 cases in which JXG happened following LCH, 2 cases where they were discovered at the same time, and only one case where JXG discovered before LCH. Only in 1 of those 12 patients JXG developed in the CNS. The radiological and clinical presentation of JXG affecting the brain is non-specific, thus requiring pathological examination to reach the diagnosis. The most important tools in differentiating JXG from LCH are Electron microscopy and immunohistochemistry. EM reveals in LCH unique Birbeck granules and bean shaped grooved nucleus. On immunohistochemistry JXG expresses CD68, Factor XIIIa, and Fascin, while CD1a and S100 are negative. Whereas, CD1a and S100 are positive in LCH.
HBF Level Among HBS Disease in Omani Patients.

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a. The Background

- Sickle disease is common hematology disorder in Oman.
- Hereditary persistence of HbF (HPFH) is a good prognostic marker.
- Co-inheritance with B-thalasemia change the disease behavior.

The purpose:

- Measure HBF level to assess the incidence of hereditary persistence of HBF(HPFH) among HBS anemic patients.
- Measure HBA2 level to assess the incidence of b-thalasemia among HBS anemic patients.

b. Method:

- We retrospectively analysed 1000 HPLC which were sent to our lab.
- We selected 100 HPLC found to have HBS more than 40%.
- We quantify the level of HBF, HBA2 using the same technique.
- We measured other variables such as gender, age, HB level, and MCV level for each sample.
- All the HPLC were for adult Omani patients, not in medications that can modify HBF level, and they didn’t receive any blood transfusion in the last three months.

c. Results:

- 35 patients (35%) out of 100, and 6 patients (6%) out of 100 patients, found to have HBF more than 10% and 20% respectively.
- 35 patients (35%) out of 100 patients found to have HbA2 >4%.
- The highest HBF was 33.3%, and the lowest was 1.1%.

Conclusion:

- HBF more than 10% is common among HBS anemic patient (who have HBS>40%), this could indicate hereditary persistence of HbF (HPFH).
- HB A2 more than 4 % is common among HBS anemic patient (who have HBS>40%), which could indicate the co-inheritance with B-thalassemia.

- final analysis are pending.
Frequency and types of anaemia among female students in Sakaka city

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Introduction: Aljouf is one of the biggest areas of Saudi Arabia, but little is known about the frequency and causes of anaemia in this population. This prospective cross-sectional study was aimed to detect the frequency and types of anaemia in healthy female university students at the Faculty of Applied Medical Sciences of Aljouf University.

Materials and methods: This study was carried out among one hundred and ninety eight female university students in Sakaka city, Aljouf region between October and December 2015. Five ml of venous blood samples were collected from each participant into an EDTA container for full blood count (FBC), using a haematogyanalyzer and a plain container for ferritin levels, using a chemistry analyzer.

Results: Approximately one third of our study population, sixty four participants (32%) were found to be anaemic. Of anaemic cases, the frequency of mild microcytic (10–11.7 g/dL), moderate microcytic (8–10 g/dL) and severe microcytic (Hb<8 g/dL) and normocytic anaemia (Hb<11.8 g/dL) was 24.4%, 3%, 1.5% and 2.5% respectively. All these groups were diagnosed with iron deficiency anaemia (IDA) rather than other anaemia with microcytic picture, as their mean ferritin level was significantly lower, 6.9ng/ml (p value< 0.01) than the control group -96.3 ng/ml. Macrocytic anaemia was observed in only one participant with high MCV level and normal ferritin level, [MCV level=97fl and Hb =10g/dl and ferritin level = 120.5 ng/ml].

Conclusion: The high frequency of IDA rather than other anaemias in the current study may be due to the nutritional habits and lifestyle of female university students in Sakaka city. Therefore, proper nutritional and educational programs are suggested as ways of avoiding the complications and risk of IDA in the future within university female students of Aljouf region, Saudi Arabia.
Sickle cell anaemia in a Saudi population of Aljouf region, rheological and haematological analysis

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Aljouf is a big region in northern area of Saudi Arabia, but little is known about the sickle cell anaemia (SCA) in this population. This prospective cross-sectional study was aimed to detect the whole blood viscosity, complete blood count (CBC) and Hb F levels in patients with SCA versus healthy individuals of Aljouf region.

This study was carried out among thirty two participants (12 patients with SCD and 20 healthy individuals) of Sakaka and Al Qurayatt cities, Aljouf region between August 2015 to March 2016. Five ml of venous blood samples were collected from each participant into EDTA container for full blood count (FBC), venous blood was collected into EDTA blood containers from each subject for whole blood viscosity, Full blood count (FBC) and Hb variants.

Whole blood viscosity (WBV) in sickle patients was significantly (p<0.05) lower, 5.6 cst (±0.4) among patients with SCA than in healthy individuals, 7.6 cst (±0.6). PCV and Hb were significantly lower (p<0.001) in sickle patients than in control samples. RDW, PLt and WBC were significantly higher in patients with SCA compared to the control group (p<0.03, 0.02 and 0.01 respectively). Hb F level was significantly higher (p<0.05), 13.6 ±3.2 (mean ± SD) in patients with SCD compared to the healthy individuals, 2.3 ±1.2% (mean ± SD). The median (range in years) age of participants with HbAA (18 – 24), whereas it was (4 – 10) in HbSS. Patients with Hb SS were significantly younger than the control samples (p<0.01).

SCA in the studied areas can be accompanied by mild clinical symptoms, with Hb F detected in high levels and WBV measured in low levels. Therefore, Arab Indian haplotype is expected to be more common in Aljouf area.

Key words: sickle cell anaemia, blood viscosity, erythrocyte deformability, full blood count and Hb F level.
Haematological Reference Value Profile for Healthy Individuals from the Aljouf region of Saudi Arabia

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Many factors influence haematological values such as sex, age, ethnic origin, geographic location, season, and genetic disease. The aim of this study was to detect the haematological reference value profile for healthy adults from the Aljouf region of Saudi Arabia.

The project was carried out on 2040 healthy individuals, 1152 male and 888 female, with ages ranging from (17 – 28 Yrs.). A group of participants were recruited from the higher secondary schools, university students and premarital centres of Aljouf cities. Haematological reference value profile, haemoglobin (Hb) concentration, red blood cell count (RBC), RBC indices, white blood cell count (WBC), differential WBC and platelet (PLt) count were measured. Moreover, a peripheral blood film was prepared in order to detect abnormalities of RBC and all samples were examined for liver function tests (LFT) and renal function test (RFT) performed, along with a lipid profile.

Hb concentration, haematocrit (Hct) and RBCs were found to be significantly higher in males than in females (p value< 0.01). On the contrary, platelet ranges were significantly lower in male as compared to female (p value< 0.01). No significant differences in the study population were determined in the other haematological parameters, p value> 0.05.

Our findings reflect that healthy adults from the Aljouf region have some haematological parameters differing quantitatively from Caucasians. The haematological reference value profile reported here can be used as normal reference values for Saudi people of the Aljouf region to help in diagnosis and consequently treatment individuals with haematological disorders.
Individuals with sickle cell trait (SCT), the heterozygous state of sickle hemoglobin β-globin gene (HbAS), are generally reassured that their health will not be affected by their carrier status. Renal disease, especially hematuria, is one of the most common and severe complications experienced by patients with sickle cell disease (SCD); but a complete understanding of the relationship between SCT and the development of chronic kidney disease (CKD) is still lacking. In this short review, we present an overview of SCT and renal complications in SCT, and discuss and identify SCT as a risk factor resulting from an interplay between genetic and environmental influences. Although SCT itself may not be a disease in itself, there is evidence suggesting clinical conditions related to SCT. Additionally, we highlight the rationale for further studies into this area, which could affect the global public health recommendations on any associated health risks.
PP38

Screening of G6PD Deficiency among Sudanese Patients with Diabetes Mellitus

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Screening of G6PD Deficiency among Sudanese Patients with Diabetes Mellitus

Abstract

Background

Glucose-6-Phosphate Dehydrogenase (G6PD) deficiency is one of the most common human genetic abnormalities. Little information is known about the relationship between G6PD deficiency and diabetes mellitus. This study was conducted to determine the occurrence of G6PD deficiency and anaemia among Sudanese diabetic patients.

Materials and Methods

A descriptive cross-sectional study was conducted from April to July 2007. A total of 50 diabetic patients were enrolled in this study. Three ml of venous blood was collected from each patient and poured into ethylene diamene tetra acetic acid anticoagulant container. Haemoglobin concentration and packed cell volume were measured for each subject as screening tests for anaemia. Methaemoglobin reduction test was done for screening of G6PD deficiency.

Results

The results of this study showed that the mean of Hb concentration among G6PD deficient patient was 9.7 g/dl while it was 13.3 g/dl among non-deficient patients and this difference was statistically significant (P.Value :0.00.). The present study found that the deficiency of G6PD enzyme was common among non-insulin dependent diabetes mellitus patients (22) than in insulin dependent diabetes mellitus patients (8%).

Conclusion

In summary deficiency of G6PD was reported in one third of Sudanese patients with diabetes mellitus.
HWA: A Needful Nomenclature for A Masked Hematology Disorder

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Introduction: Anemia is a condition in which the number of red blood cells and the hemoglobin are insufficient to meet the body’s physiologic needs. The term hypoferritinemia means low iron storage in the ferritin form [1]. Hypoferritinemia without anemia (HWA) is a hematological disorder causing clinical manifestations as general weakness; easy fatigability, depressed mode and hair loss, but with normal complete blood count parameters (CBC) [2].

Aim: To highlight the importance of HWA and to distinguish it with the nomenclature “HWA” to make it popular among general practitioners and hematologist because of its easy to be missed due to of the normal (CBC) test and normal morphology, while the patient has a long standing suffering.

Method: A retrospective study, conducted on 6993 (4,370 females and 2,623 males) from Amiri Hospital database, it included low serum ferritin patients from 2010 until 2016, the patients aged from 15 – 88 years old. The following parameters were used to detect HWA disorder: serum ferritin, RBC, Hb, Hct, MCV, and MCH.

Results: HWA is found in 130 (50 males and 80 females) patients which represent 0.018% of the hypoferritinemia cases, in ratio 1.7 to 1 females to male.

Conclusion: HWA is a masked chronic hematology disorder. It is deferent from iron deficiency anemia in having normal CBC and normal blood smear morphological features. HWA and IDA can be compared with low vitamin D and osteoporosis, as in both of low vitamin D and osteoporosis vitamin D is low but they are considered as different disease entities because of low BMD in osteoporosis [3]. The nomenclature HWA is justefide and mandatory in hematology terminology.
Study of the Mean Platelet Volume as a Marker of Pulmonary Hypertension in Thalassemic Patients

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Background: The majority of thalassemic patients on chronic blood transfusion develop pulmonary arterial hypertension (PAH) that is affected with the onset of the disease, duration of treatment and splenectomy.

Aim of Study: We focus on our recent study to investigate mean platelet volume (MPV) in thalassemic patients either with or without PAH.

Patients and Methods: Our study was performed in pediatric hematology department and outpatient clinic in Zagazig University Hospital –Egypt, during period from June 2015 to February 2016. The study enrolled 96 thalassemic individual who were divided into 2 groups: Group 1 "pulmonary hypertension group": involved 48 thalassemic individual with PAH and group 2 "control group": involved 48 thalassemic individual without PAH. All those patients were subjected to full history taking, complete physical examination, routine laboratory investigations and echocardiography.

Results and Discussion: In this study, both studied groups revealed highly significant difference in MPV but no significant difference in platelet count. The studied groups showed that there is highly significant differences in sPAP [systolic pulmonary artery pressure] and mPAP [mean pulmonary artery pressure] in thalassemic patients with or without PAH. MPV had not any statistically significant association with demographic characteristics of thalassemic patients including sex, consanguinity, carrier parents and other diseased siblings. While, MPV and clinical characteristics of thalassemic patients showed highly statistical significant association with splenectomy. The Correlation analysis of all study variables & MPV revealed highly significant positive correlation with platelet count in both PAH group and control group; there is also highly significant negative correlation with sPAP in PAH group, and significant negative correlation with mPAP, age, and duration of treatment in group 1.

Conclusion: In conclusion, our study revealed significantly decrease MPV in thalassemic patients but the decrease was more significant in thalassemic patients with PAH than in those without PAH.
Soluble Cd36 as a Determinant of Disease Severity among Patients with Sickle Cell Anaemia in Nigeria

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BACKGROUND This descriptive, cross-sectional study was aimed at determining the relationship between soluble CD36 (a cell adhesion marker), levels of %Hb F, haematological parameters and disease severity in adults with SCA in Kano, Nigeria.

METHODS One hundred and forty subjects with SCA in steady state were purposively selected and compared with 70 apparently healthy controls. Ten millilitres of venous blood was obtained to determine CBC (using Auto haematology analyzer), %Hb F (estimated by modified Betke’s method) and sCD36, using Human Soluble CD36 Elisa Kit (ADIPO Bioscience Inc., USA). Severity was assessed by El-Hazmi’s scoring system. Student t-test and Pearson’s correlation were used as statistical test and P-value < 0.05 was used to define statistical significance.

RESULTS The median sCD36 was significantly higher (P<0.01) in subjects with SCA (22.3 ng/ml) than in the controls (14.8 ng/ml). A direct correlation was observed between sCD36 and WBC count (r=0.7410; P<0.001), an inverse correlation was observed between sCD36 and %Hb F (r= -0.5406; P<0.001) and a direct correlation was observed between sCD36 and severity score (r=0.5808; P<0.001) in the subjects. No such relationship was observed among the parameters in the control group. Complications like ACS, stroke, retinopathy and AVN of the femoral head were observed to be associated with high sCD36 levels. A multiple logistic regression modeling revealed that WBC count predicted the most significant odds (OR = 3.87; P < 0.001) for sCD36 positivity.

CONCLUSION The level of sCD36 is a marker of disease severity and may predict the occurrence of vascular-related complications of adults with SCA; and WBC alone may be used as a surrogate marker of sCD36 level.

Key words: sCD36, Disease severity, Sickle Cell Anaemia, Nigeria
Two Autoimmune Diseases in Haemoglobin H Disease: A Case Report of a Rare Entity

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The incidence of AIHA in patients with rheumatoid arthritis has not been shown to exceed that in general population. The prevalence of rheumatoid arthritis in patients with AIHA approximates that in the general population. On the basis of these data, it is extremely difficult to establish a relationship between rheumatoid arthritis, AIHA and haemoglobin H disease. A 36-year-old Saudi female was found to have rheumatoid arthritis (RA) in November 2006. Her rheumatoid factor (RF) initially was positive; 128 IU/mL. Treatment with disease-modifying antirheumatoid drugs (DMARDs) including hydroxychlorquine and predisolone was started and showed improvement. In 2011, the patient had frequent ER visits with hemolytic crisis. She was admitted to our hospital because of palpitations, generalized body pain, dizziness, headache, pallor and dyspnea due to severe anemia. Results of laboratory studies were haemoglobin 4.2 g/dL; reticulocyte count 0.7% and haptoglobin 71.1. The direct and indirect Coombs’ tests were positive. Diagnosis of autoimmune hemolytic anemia (AIHA) and haemoglobin H disease was made in the base of the laboratory findings. Abdominal ultrasound was also done showing enlarged liver reaching the right iliac crest, enlarged spleen measured about 19 cm. The patient we have described had the unusual presentation of rheumatoid arthritis with AIHA and haemoglobin H disease. The latter which is an extremely rare association and no cases have been reported yet. We believe the three remain distinct entities.
Importance of Mean Cell volume of reticulocyte (MCVr) in diagnosing vitamin B12 deficiency in blood donors at sub-clinical level.

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a.BACKGROUND AND PURPOSE:

Deficiency of Vitamin B12 can cause pancytopenia, dementia, neuropathy, sub-acute combined degeneration of spinal cord, infertility particularly in males, malabsorption, neuro-psychiatric disorders. hyper-homocysteinemia may also which may cause a predisposition to ischemic heart disease and cerebrovascular accidents. late diagnosis of the deficiency can lead to irreversible damage vital systems. various studies have highlighted diagnostic value of Mean Cell Volume of Reticulocyte(MCVr), and it offer an accurate and cost effective way of diagnosing Vitamin B12 deficiency. a cross-sectional study design was used for determining diagnostic accuracy of MCVr.

b.METHODS:

The study was carried out in consecutive blood donors satisfying inclusion criteria. These samples were tested for MCVr( expressed in fl) on Abbott CELL-DYN Sapphire. The gold standard test used was serum vitamin B12( expressed in pmol/l) measured by using the Roche Diagnostic kit (Mannheim, Germany) in E170 analyzer. Index test used was MCVr. Vitamin B12 test results were used to define true negatives, false negatives, true positives, and false positives. Performance of different MCVr values versus serum vitamin B12 was measured using sensitivity, specificity, positive predictive value and negative predictive value and most appropriate cut-off value of MCVr was considered on basis of highest specificity at sensitivity of at least 82.9%. Receiver operating characteristic curve (R.O.C) was also drawn between MCVr and serum Vitamin B12 values.

c.RESULT:

153 donors were eligible for study out of 184. MCVr cut-off greater than or equal to 98.5 fl gave sensitivity of 82.9% and specificity of 81.2%, The Area under the curve of R.O.C was found to be 0.847 (Standard error 0.03, confidence interval 0.781 to 0.913)

d.CONCLUSION:
The MCVr can be used to diagnose Vitamin B12 deficiency in blood donors. Blood donors with MCVr value greater than or equal to 98.5 fl can be diagnosed as vitamin B12 deficient.
Knowledge and Attitudes Towards Voluntary Blood Donation Among Adults in Sharjah, UAE

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Background and Purpose: The UAE has a rapidly growing population with an increasing need for blood supply. Blood donation is encouraged by providing portable blood donation centers in many areas. However, there is still a shortage of blood. The aim of this study was to evaluate the level of knowledge and the attitudes towards voluntary blood donation in the city of Sharjah, UAE.

Methods: A descriptive cross-sectional study was carried in public areas of Sharjah using convenience non-random sampling method. 357 participants filled out the self-administered, pilot-tested questionnaire constructed based on material acquired from previous similar studies. The questionnaire included 28 questions. Data was analyzed using SPSS. Chi Square, T-tests and Pearson correlation were used when applicable.

Results: 40.6% of the participants donated blood before, 61.4% of them were males. The Knowledge Percentage Mean Score (PMS) of the participants was 55.40±14.36. A significant relationship has been found between donation status and knowledge PMS (p=0.001). Knowledge PMS affects males’ donation status more than females’ (p<0.0001 vs p=0.338). The knowledge PMS for donors was 58.56±14.31, while non-donors 53.24±14.01. Some of the factors influencing the donation status included gender (p<0.0005), age (p=0.002) and educational level (p=0.007). The attitude and knowledge PMS had a significant relationship (p=0.003), Pearson correlation <0.2. 83.8% of participants had an overall positive attitude.

Conclusions: The UAE population less than adequate knowledge about blood donation and suboptimal donation practices, but the attitude was generally positive. More female donors need to be recruited. Correcting the misconceptions and stressing the need for blood seems to be the most important step for increasing blood donation in the UAE.
Seroprevalence of Human Parvovirus B19 in packed red cell units received by anemic pediatric patients in Beni-Suef University hospital Egypt

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Background and purpose: Human parvovirus B19 (HPV-B19) is a small non-enveloped DNA virus. Although it generally causes self-limiting conditions in healthy people, B19V infection may have a different outcome in patients with inherited hemolytic anemias or bone marrow suppression, triggering a life-threatening drop of hemoglobin values leading to profound anemia and sometimes aplastic crisis. The aim of our study is to detect prevalence of Parvovirus B19 in the donated blood units from healthy donors in Beni-Suef university blood bank in a trial to reveal the importance of its screening as one of transfusion transmissible viruses. In a trial to detect whether the recipients of these units are at risk of developing clinically significant Parvovirus B19 infection.

Patients and methods: The study was conducted on 91 packed red cell units in Blood Bank of Beni-Suef University Hospital throughout 6 months period from January 2016 to July 2016 which were screened for IgM antibodies against Parvovirus B19 using Enzyme linked immunosorbent assay (ELISA) test. In addition to eight weeks follow up for Hemoglobin level and clinical manifestations of PVB19 infection for 91 pediatric patients with thalassemia and sickle cell anaemia who received the PRCs.

Results: A total of 8 (8.8%) of the transfused packed red cell units were positive for Parvovirus B19 IgM, while 67 (73.6%) were negative and 16 (17.6%) were at the grey zone. Age and sex had no statistically significant effect on HPV-B19 seropositivity (p>0.05). None of the patients showed clinical manifestations indicative of post-transfusion infection or drop in hemoglobin level.

Conclusion: The seroprevalence of human parvovirus B19 IgM among blood donor population in our study was high, and poses an adverse transfusion risk especially in high-risk group of patients. Although the clinical follow up for these patients didn’t reveal clinical relevance.
To assess the effectiveness of predonation water drinking on vasovagal reaction rates among north Indian blood donors

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Background and purpose: Novice blood donors are at increased risk for unpleasant blood donation related symptoms (e.g. dizziness, weakness and lightheadedness) and experience of such symptoms can contribute to a decreased likelihood of repeat donation. Recent clinical studies found that water ingestion produces hemodynamic effects that may be sufficient to reduce risk of syncope and related reactions during blood donation.

The purpose of study was to assess effectiveness of predonation water drinking strategy on vasovagal reaction rates.

Methodology: The study was conducted after taking approval from research and ethics committee of the institute. Standard donor acceptance criteria were followed to select donors. A total 6478 healthy blood donors were assessed. Of 6478 participants, 3239 blood donors received and 3239 donors did not received water. Both first time and repeat donors were included in study. A random numbers table was used to assign these donors in groups receiving or not receiving 500 ml of water. A 500-ml plastic bottle at room temperature was given to donor at the time of registration.

Results: The primary outcome variable was a dichotomous variable of yes or no for syncopal attack. A secondary outcome was severity of events, which was recorded as an ordinal variable of mild, moderate or severe. The rate of donor reaction was 1.2% in donors given predonation water drink versus 2.8% in donors not given a predonation water drink. Ingestion of 500 ml of water before whole blood donation had significantly decreased vasovagal reactions 1.2 % vs. 2.8% (OR 0.48 vs. OR 2.10).

Conclusion: 500 mL water drink significantly decreased vasovagal donor reaction rate in otherwise healthy blood donors. Finally, experience gained with this study was that the ingestion of water by donors did not interfere with donor processing and was judged by collection staff as an easy protocol to implement.
Comparison of two different preparation protocols for platelet concentrates from a developing nation

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Background and Purpose: Now a days there is need of a platelet product that is more efficacious i.e. good quality with less storage changes, minimal risk of transfusion transmitted infection, low cost and adequate corrected count increment (CCI) after transfusion. There has been an ongoing debate about superiority of one PC type over the other and there are very few studies from this part of the world to address this issue. In this study two types of platelet concentrates (PC), platelet rich plasma (PRP-PC) and buffy coat (BC-PC) were analyzed for quality parameters.

Methods: A total of 60 PCs were included in the study and sampling done on day 1 and 5. The quality assessment was done for: Volume, Swirling, Platelet count per bag, White Blood Cells (WBC) count per bag, pH changes, Sterility, Mean Platelet Volume (MPV), Platelet Distribution Width (PDW). Independent sample t test was used for comparison.

Results: Mean volume, pH and platelet count of BC-PC and of PRP-PC were not significantly different. The mean WBC count, mean PDW and MPV between the two were different and statistically significant. All PCs showed swirling at any given point of time of storage and all were sterile.

Lower WBC count in BC-PC units can be attributed to efficient soft spin in BC method. The reason of increase of PDW in PCs may be because of the fact that storage leads to platelet activation. In general variation in MPV is dependent on pH. MPV increases as a result of swelling of platelets.

Conclusion: In our experience BCP-PC may be preferred in place of PRP-PC in most of the clinical situations without compromising the quality. Limitations of our study include lesser sample size, lack of in-vivo measurements like corrected count increment and metabolic changes.
The DICEP regimen effectively reverses the poor outcome for lymphoma patients with suboptimal response or failure post 1st salvage treatment

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Background/purpose: The management of Hodgkin’s (HL) and non-Hodgkin lymphomas (NHL) patients (pts), with refractoriness to 1st salvage treatment (salv1), is a major challenge, since their outcome is considered extremely poor.

Methods: We herein evaluated the safety and efficacy of the DICEP regimen [Dose Intesified Cyclophoshamide (1750mg/m2), Etoposide (350mg/m2) and Cisplatin (35mg/m2), days:1-3], in 27(HL=11, NHL=16) pts, with either suboptimal response (<50%, n=21) or disease progression (n=6), after at least 2 cycles of salv1 regimen. Moreover, we evaluated pts' long term outcome post autologous stem cell transplantation (ASCT).

Results: DICEP was well tolerated, nevertheless as expected, all pts experienced hematological toxicity (Grade:3-4 WHO). Twenty-two developed febrile neutropenia, not requiring admission to intensive care unit. No other toxicities (grade≥3) were observed. The mobilization/collection was successful and a median of 7,9(1,5-33,5) x106/kg CD34+ cells were collected. In the 13/19 patients able for re-assessment a further disease reduction was achieved [CR:7, very good response(>75%): 4, minor response(≤50%): 2]. Three pts had stable disease while 3 experienced progression. Overall 23/27 pts autografted after a median of 44(22-70) days post DICEP; 4 with progressive (n=3) or stable (n=1) disease did not undergo ASCT. For all the pts, the 5-yr overall survival (OS) was 70% (HL=71%, NHL=66%) while the 4-yr progression free survival (PFS) post DICEP (±ASCT) was 62% (HL=60%, NHL=64%), p=ns. Especially for the 23 autografted pts, the 5-yr OS and PFS were 80% and 70% for the HL-pts and 65% and 72% for the NHL-pts respectively ( p=ns)

Conclusion: Our data demonstrate that DICEP is an effective regimen with acceptable toxicity without negative impact on the CD34+cells collection. The post DICEP achieved response rates in combination with the very encouraging PFS rates post ASCT, in this unfavorable group of patients, support the rationale for using DICEP as salv1 regimen in selected pts.
What is the optimal conditioning regimen for patients with chemosensitive Hodgkin’s lymphoma undergoing autologous stem cell transplantation? A retrospective comparison of single-agent high-dose melphalan and BEAM.

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Background/aim: Though is the most widely used, still remains questionable whether BEAM is really the optimal conditioning regimen for autologous stem cell transplantation (ASCT) for lymphoma-patients. High-dose Melphalan (HDM:200mg/m2) has been used as preparative regimen, however, so far, there are limited experience and data comparing BEAM with HDM.

Methods: We retrospectively analyzed and compared the outcomes in terms of efficacy and toxicity from 34 Hodgkin-Lymphoma patients, autografted in two different institutions, using either HDM(n=17) or BEAM(n=17). The chi-square and T-test and Kaplan-Maier method were used for the statistical analyses.

Results: The patient-groups were similar regarding age (45 vs.36ys p= ns), sex (8 vs.7 females) and disease status before ASCT (6 vs.8 in CR and 11 vs.9 in VGPR). The BEAM-group patients had been treated prior to ASCT with 3(2-8) cycles, while the HDM-group patients with 4(2-6) cycles of salvage regimens. The median number of the CD34+ infused-cells were 9,2x106/kg for the BEAM-group and 5,7x106/kg for the HDM-group (p=0,06).

All patients successfully engrafted, the median day for neutrophils>1000/mm3 was 16 vs.12 (p<0.001) and for platelets>25000/mm3 10 vs.14 (p=0.05) for the BEAM- and HDM-group, respectively. The 4-ys overall and progression free survival were similar, 67% and 63% respectively. No treatment related mortality was noticed in the BEAM-group, while in the HDM-group 1/17 died due to MERS-CoV pneumonia. No other toxicities (WHO≥3) were observed with both regimens.

Interestingly, the median hospitalization period for the HDM-group (including regimen administration) was 17(14-48) days, while the required hospitalization period for the BEAM-group was 22(16-31) days.

Conclusions: our study though retrospective and with a small series of patients, showed that HDM as compared to the standard BEAM regimen, has similar efficacy and acceptable regimen–related toxicity, while the significant shorter periods in terms of neutrophils-recovery and hospitalization, may contribute to a better cost effectiveness for the HDM-regimen.
Outpatient-based autologous stem cell transplantation for patients with Multiple Myeloma (MM): feasible, safe and cost effective approach

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Background/purpose: Given the improvements in the supportive care during the peri-transplant period, autologous stem cell transplantation (ASCT) became feasible in an outpatient-basis, especially if the conditioning regimen does not require continuous 24-hours infusion, offering benefits in terms of shorter hospitalization, minimal exposure to hospital pathogens, and cost effectiveness.

Methods: We herein describe the outcome of 8 outpatient-ASCTs which were performed in MM patients with a median age of 40(36-55)ys. The eligibility criteria for the ASCT-outpatient program included psychosocial evaluation, patient’s compliance assessment, 24-hours caregiver availability and signed informed consent. The pre-transplant supportive care, conditioning regimen and graft infusion were given in an allocated room in Hematology/SCT department. The antimicrobial, antifungal and antiviral prophylaxis were administered according to the standard guidelines. Patients were evaluated daily or every other day in the outpatient-clinic. The criteria for admission were fever>38oC, intractable nausea/vomiting or diarrhea, mucositis needing total parenteral nutrition and any other toxicity grade>3 (WHO)

Results: The conditioning regimen was Melphalan:200mg/m2 (n=3) or 140mg/m2 (n=5). The median day for ANCs>500/mm3 was 15(11-18) and for PLTs>25000 was 12(0-21). Four patients were admitted post autograft, one for poor food/fluid uptake due to mucositis plus intractable mucositis/nausea and three for febrile neutropenia. No other toxicities (WHO>3) were observed. All patients are alive 1,5(1-22) months post autograft. The hospitalization period for the 8 ASCTs was 23 days (median:3) which favorably compares with the average of 14 days hospitalization for a “conventional” ASCT.

Conclusions: Our data confirm that the outpatient-ASCT is a feasible and safe approach provided that a caregiver is available and there is closely evaluation and adequate supportive care. Taking into account the nosocomial complications and the potential high cost of the prolonged hospitalization, it is easily concluded that the outpatient-ASCT offers lower risk of infections and significant cost saving compared to the usual inpatient-ASCT approach.
PP51

Efficacy and safety of Brentuximab vedotin in combination with Bendamustine as salvage therapy and potential “bridge” to stem cell transplantation for patients with refractory Hodgkin lymphoma.

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Background/purpose: Patients with primary refractory/relapsed Hodgkin Lymphoma (HL) who failed to 1st salvage therapy have an extremely poor outcome even after autologous stem cell transplantation (autoSCT) and therefore there is an unmet need for more effective and less toxic salvage approaches.

Methods/Patients: We evaluated the efficacy and safety of the Brentuximab vedotin (Bv) and Bendamustin (B) combination (BvB) in 10 pts aged of 23(17-34) ys, with refractory HL after at least one salvage-chemotherapy. Two patients had previously undergone autoSCT. The disease stage was II, III and IV in 5, 3 and 2 patients respectively, while 3 pts had also B-symptoms. The BvB regimen was administered on outpatient basis (i.v. infusion: Brentuximab 1.8 mg/kg on day-1 and Bendamustine 90 mg/m2 on days 1 and 2) in 3-week cycles.

Results: After a median of 2(2-5) cycles, 7/10 (70%) pts achieved sufficient response [5/10 (50%) achieved complete remission according to PET/CT criteria]. In 3/10 the disease progressed. No toxicity WHO≥3 was observed. All the 6 responders underwent allo- or autoSCT after a median of 2,5(2-5) months post BvB therapy; 2/6 responders (previously autografted) underwent alloSCT. Two responders were successfully mobilized after the BvB regimen (collected CD34+cells: 7,7 and 4,1x 106/kg) while in two the graft was collected prior to BvB treatment. One patient refractory to BvB, autografted successfully after a 3rd salvage treatment. All the eight transplanted patients are alive 10(1-16) months post SCT. The 2 non-autografted (no-responders) patients finally succumbed to progressed HL.

Conclusion: Our data support the evidence that the BvB treatment is an efficacious and safe approach and merits further investigation to clarify its exact role as a potential “salvage-bridge” to a successful autoSCT for patients with refractory HL.
PP52

Bortezomib-Lenalidomide-Dexametasone versus Bortezomib-Cyclophosphamide-Dexametasone for newly diagnosed multiple Myeloma patients eligible for autologous stem cell transplantation: a single center experience

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Background/purpose Bortezomib-dexamethasone plus Lenalidomide(VRD) or Cyclophosphamide(VCD), are currently widely used regimens for Multiple Myeloma(MM) patients, however, comparative studies between VRD vs.VCD are extremely limited.

Methods/patients: We retrospectively studied 19 newly diagnosed MM pts who underwent early-ASCT after VRD (n=10) or VCD (n=9) treatment. Patients-groups were similar regarding age at diagnosis (52 vs.54 ys), diagnosis-ASCT interval (5,8 vs.5,7 mos) and maintenance treatment post-ASCT (8 vs.6 pts). According to the revised international staging system the VRD-group patients were classified as stage I:1, stage II:7, stage III:2, while the VCD-group patients as stage I:3, stage II:5, stage III:1, p=ns.

Results: After a median of 4 cycles of treatment (VRD: 4-6 and VCD:2-6, p=ns) finally, in the VRD-group 4 patient achieved complete remission (CR), 5 very good partial remission (VGPRL: ≥75% reduction of M-band) and 1 partial remission (PR: 50-75% reduction of M-band) while from the VCD-group, 3 patients achieved CR, VGPR:2 and PR:3 (p=ns). The liver, renal, neuro- and myelo-toxicity were minimal and no patient discontinued the treatment. The 5-ys overall survival (OS) was 100% vs.75% for the VRD and VCD-group respectively (p=ns) and was not influenced by disease stage at diagnosis, disease status pre-ASCT and maintenance treatment post-ASCT. The 4-ys progression free survival (PFS) was significantly superior after VRD regimen (75% vs.36%, p=0.05) and after CR/VGPR achievement before ASCT (PFS: 50%) while no pts with PR pre-ASCT remained progression free 2 ys post ASCT (p=0.001). In multivariate analysis only the CR/VGPR attainment before ASCT affected favorably the long term PFS.

Conclusion Our results are in line with larger series of patients studies. Interestingly, the low disease burden pre-ASCT favored the prolonged PFS. Since VRD regimen resulted in more CR/VGPR achievements, it is reasonable to conclude that VRD could be chosen as 1st treatment choice for newly diagnosed MM patients candidates for ASCT.