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Keynote Speakers

ABSTRACT 5

Epigenetic modifications in cancer: Implications for epi-drug and epigenetic editing

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ABSTRACT

Epigenetic modifications including alteration in DNA methylation, histone modification and changes in non-coding RNA gene expression are known to be involved in the pathogenesis, progression and metastasis of cancer. Due to the reversibility and the plasticity of epigenetic processes they are targeted in cancer therapy. DNA hypermethylation is associated with silencing of tumor suppressive and differentiation genes. So, DNA methyltransferase inhibitors have emerged as first epi-drugs for cancer treatment. Also, histone deacetylase inhibitors, histone methyltransferase inhibitors, histone demethylase inhibitors and inhibitors of epigenetic readers are among epigenetic modulators. In this paper, three epigenetic mechanisms will be discussed and drugs targeted these mechanisms and also epigenetic editing technologies, zinc finger proteins and transcription activator-like effector proteins, and the clustered regularly interspaced short palindromic repeats (CRISPR)-associated nuclease 9 (CRISPR/Cas9) system as a revolutionary genome-editing technology, as strategies to reverse epigenetic changes in cancer will be explained.

ABSTRACT 372

Blood Coagulation Parameters in Patients with Severe COVID-19 from Kermanshah Province of Iran

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ABSTRACT

Background: The severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) that is responsible for coronavirus disease 2019 (COVID-19) resulted in systemic inflammatory response and imbalance between homeostatic mechanisms of procoagulant and anticoagulant and is complicated with thrombotic complications. The main aim of the present study was to find the coagulation profile of intensive care unit (ICU)-admitted patients with COVID-19 from Kermanshah, Western Iran.

Methods: Coagulation parameters were analyzed using appropriate methods in 74 patients (24 aged <60 years and 50 ≥60 years) and were compared between 35 survivors and 39 non-survivors severe COVID-19 patients, admitted to the ICU.

Results: Twenty-six out of 74 patients (35.1%) required tracheal intubation (64.1% non-survivors and 2.9% survivors, p<0.001). Fifty-one out of 74 patients (around 69%) had comorbidities (hypertension, diabetes mellitus, coronary artery disease, cancer, renal transplantation, chronic obstructive pulmonary disease, and osteomyelitis). Thrombocytopenia was detected in around 30% of mostly older patients with comorbidities and in non-survivors. About 42% of patients had abnormal prothrombin time and international normalized ratio. The rates of mortality and comorbidity in patients ≥ 60 years were 73.7 and 78.4% compared to 26.3 and 21.6%, respectively in patients <60 years.

Conclusion: We detected a high rate of coagulopathy (around 42%) in severely affected patients with COVID-19. Furthermore, severe COVID-19 patients had low levels of platelets, high prothrombin time and international normalized ratio that were associated with poor prognosis. The abnormal pattern of coagulation parameters was highly associated with comorbidities and mortality. We found abnormal pattern of coagulation parameters and association of advanced age and comorbidities with high rate of mortality in severe COVID-19 patients which should be considered in management of these patients.

Keywords: COVID-19, coagulation, prothrombin time, international normalized ratio, mortality

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Poster Presentations

ABSTRACT 373

Leukocytosis and Alteration of Hemoglobin Level in Patients with Severe COVID-19: Association of Leukocytosis with Mortality

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ABSTRACT

Background: The severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) is responsible for coronavirus disease 2019 (COVID-19). In severely affected patients with COVID-19 leukocytosis was more prevalent.

Methods: The white blood cells (WBCs) count and hemoglobin (Hb) levels were studied in 74 patients with severe COVID-19 and were compared between 35 survivors and 39 non-survivors severe COVID-19 patients admitted to the intensive care unit (ICU) of Farabi hospital of Kermanshah University of Medical Sciences.

Results: Higher WBCs count was detected in patients with comorbidities (hypertension, diabetes mellitus, coronary artery disease, cancer, renal transplantation, chronic obstructive pulmonary disease, and osteomyelitis) than those without comorbidities. Comparing survivors with non-survivors indicated that 41% of non-survivors had WBCs count upper normal range. The mean Hb level in survived patients was 139.3±22.9, and in non-survived patients was 141.1±25.8 g/L (p=0.75).

Conclusion: Our study indicated a significant association between leukocytosis and the rate of mortality in patients with COVID-19. Also, our findings indicated association between mortality rate with hemoglobin level among COVID-19 patients.

Keywords: COVID-19, SARS-CoV-2, Leukocytosis, Mortality, Hemoglobin

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Poster Pretentions

ABSTRACT 374

Sirtuin 1 C allele (rs375391) is associated with the risk of type 2 diabetes mellitus, diabetic neuropathy and diabetic retinopathy

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ABSTRACT

Background: Sirtuin 1 (SIRT1) is downregulated in patients with type 2 diabetes mellitus (T2DM) and is associated with oxidative stress. On the other hand, the TT genotype of SIRT1 (rs375391) is associated with higher mRNA expression.

Methods: We studied 300 patients with T2DM with and without complications (mean age 56.8 years) including 100 patients without complications, 100 patients with diabetic neuropathy and 100 diabetic retinopathy patients along with 98 healthy individuals (mean age 52.9 years) for SIRT1 polymorphism and oxidative stress parameters. The SIRT1 T>C variants (rs3758391) were detected using PCR-RFLP method. The oxidative stress parameters including glutathione, glutathione peroxidase, total oxidative status, total antioxidant capacity and malondialdehyde were measured using chemical methods.

Results: The frequencies of SIRT1 genotypes and alleles were significantly different comparing all diabetic patients with controls ($p<0.001$) and also comparing diabetic patients without complications, diabetic patients with neuropathy and also diabetic patients with retinopathy with controls ($p<0.001$). The frequencies of SIRT1 CC genotype were 18.7% in all diabetic patients compared to the absence of this genotype in controls. However, the levels of oxidative stress parameters were not significantly different comparing three genotypes of SIRT1 in each group.

Conclusion: Our findings indicated association of SIRT1 CC genotype with the risk of T2DM and its complications including diabetic neuropathy and diabetic retinopathy.

Keywords: Type 2 diabetes, diabetic neuropathy, diabetic retinopathy, oxidative stress, sirtuin 1 polymorphism

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Poster Pretentions

ABSTRACT 384

Variants of CXCL12 chemokine is associated with the risk of chronic lymphocytic leukemia

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ABSTRACT

Background: Chronic lymphoblastic leukemia (CLL) is one of types of blood cancer with the origin of B lymphocytes. Some genetic factors affect the diagnosis and prognosis of the disease. Regarding the role of chemokine CXCL12 in proliferation, differentiation and transfer of hematopoietic stem cells such as B lymphocytes, CXCL12 variants might be involved in the incidence and prognosis of CLL. The aim of present study was to find an association between the CXCL12 variants and haplotypes with the risk of CLL in CLL patients from Kermanshah.

Methods: Blood samples were collected from 100 CLL patients from the Taleghani hospital and Mahdieh Clinic of Kermanshah University of Medical Sciences and 100 healthy individuals. Using specific designed primers and PCR-RFLP method, the variants and haplotypes of CXCL12 were detected and statistically analyzed.

Results: The frequency of SNP rs1029153 CC was 10.1% in controls compared to 2% in patients (P=0.048). Also, the frequency of SNP rs266093 CC was 10.1% in controls and 6% in patients that was not associated with the risk of CLL (P=0.074). The SNP rs1801157 AA was detected in 11% of controls compared to 8% of patients that did not reach to a statistical significance (P=0.252).

Conclusion: Our study indicated the SNP rs1029153 was significantly associated with the risk of CLL. However, the rs266093 and the rs1801157 were not associated with the risk of CLL.

Keywords: CLL, PCR, SNP, CXCL12

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Poster Pretentions

ABSTRACT 385

Lipid profile, vitamin D level and vitamin D receptor and transporter gene variants in sickle cell disease patients form Kurdistan of Iraq

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ABSTRACT

Background: Alteration of lipid profile has been reported in sickle cell disease (SCD) patients. Also, vitamin D deficiency is associated with increased respiratory infections and muscle weakness in these patients.

Methods: In the present study 104 patients carrying sickle gene including 63 sickle cell anemia, 36 sickle/beta thalassemia, 4 sickle cell trait individuals and 1 sickle/D patient along with 110 healthy individuals from Kurdistan of Iraq – Duhok- Jin center for pediatric hemato-oncology and Qaladze Public Hospital were studied for lipid profile, 25 (OH) - vitamin D and vitamin D receptor (VDR) variants and also group-specific component (GC) variants. The mean age of controls was 15.2 years and the mean age of patients was 15.9 years. Polymorphisms were detected by PCR-RFLP method. Vitamin D concentration was determined by ELISA method, and lipid profile was determined by colorimetric method. Statistical analyses were performed by SPSS 16.0.

Results: The mean level of 25 (OH)-D in sickle patients was significantly lower (11.05 ± 6.6ng/mL) than controls (13.5± 8.37ng/mL, p=0.018). Total cholesterol, HDL-C and LDL-C in patients were significantly lower than controls. The frequency of VDR FOK1 C allele was significantly higher in case group compared to controls. However, the frequencies of TaqI and GC variants were not significantly different comparing both groups.

Conclusion: Our study indicated the presence of hypocholesterolemia, reduced LDL-C and HDL-C and vitamin D deficiency among SCD patients from Kurdistan of Iraq and different frequency of VDR FOK1 polymorphism in these individuals compared to healthy controls.

Keywords: Sickle cell anemia, sickle/beta-thalassemia, vitamin D, lipid, VDR, GC variants

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Poster Presentations

ABSTRACT 391

The Nrf2 and Keap1 variants and oxidative stress parameters are associated with Diabetic Neuropathy

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ABSTRACT

Background: Diabetic neuropathy (DN) affects at least 50% of diabetic patients and is an important factor in disease-related disabilities. Chronic hyperglycemia activates the inflammatory pathways and oxidative stress mechanisms with consequent damage to nerve tissue. The Keap1-Nrf2 pathway acts as one of the most important antioxidant pathways of the organism.

Methods: In the present study, 100 patients with DN and 100 healthy individuals were investigated. The activity of glutathione peroxidase (GPX) was measured by a Randox kit, glutathione (GSH) was measured using a fluorescent reagent (o-Phthalaldehyde), the plasma level of malondialdehyde (MDA) was detected by thiobarbituric acid method, plasma total antioxidant capacity (TAC) was measured using FRAP reagent, and total oxidative status (TOS) was measured by a chemical method. Using PCR-RFLP method, the Nrf2 (rs6721961) and Keap1 (rs11085735) variants were identified.

Results: A significant difference was observed between DN patients with controls in terms of reduced activity of GPX and glutathione level, decreased TAC, and increased MDA and TOS levels in DN patients. A higher frequency of mutant allele of Nrf2 (41%) in DR patients compared to controls was observed (27%, $p<0.001$). However, the frequency of mutant allele of Keap1 in DR patients was non-significantly lower than controls.

Conclusion: Our study indicated association between oxidative stress and DN that is reflected in the imbalance between oxidant and antioxidant system. The results also showed the decreased frequency of Keap1 mutant allele and the increased frequency of mutant allele of Nrf2 that decreases the Nrf2 expression.

Keywords: Type 2 diabetes, diabetic neuropathy, oxidative stress, Nrf2, Keap1 variants

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ABSTRACT 392

Association between Nrf2 and Keap1 variants and oxidative stress parameters with diabetic retinopathy

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ABSTRACT

Background: Diabetic retinopathy (DR), as one of the most life-threatening complications of diabetes, is a microvascular disorder that threatens vision. Oxidative stress might be involved in the pathogenesis of DR. The Keap1-Nrf2 pathway is one of the most important antioxidant pathways of the organism. During oxidative stress, Nrf2 is cleaved from the Keap1-Nrf2 complex and transported to the nucleus to induce the expression of antioxidant genes.

Methods: We studied 100 healthy individuals and 200 patients with type 2 diabetes mellitus (T2DM) including 100 T2DM patients without complications and 100 T2DM patients with retinopathy. Duration of diabetes was at least five years. Glutathione peroxidase (GPX) activity was measured by a Randox kit, glutathione was measured using a fluorescent reagent (o-Phthalaldehyde) and the plasma level of malondialdehyde (MDA) was measured by thiobarbituric acid method. PCR-RFLP method was used to determine the Nrf2 (rs6721961) and Keap1 (rs11085735) variants.

Results: Comparing plasma oxidative stress parameters between diabetic patients without complications and controls indicated a significant difference in GPX activity ($p<0.001$), and the level of MDA ($p<0.001$). In addition, in DR patients compared with controls, reduced activity of GPX and glutathione level, and increased MDA level were detected. A higher frequency of mutant allele of Nrf2 (60.5%) in DR patients compared to controls was observed (27%, $p<0.001$). However, the frequency of mutant allele of Keap1 in DR patients was significantly lower than controls.

Conclusion: Our study indicated increased oxidative stress in diabetes, both in patients without complication and those with DR compared to controls. Additionally, the frequency of mutant alleles of Nrf2 and Keap1 was increased and decreased, respectively in DR patients compared to controls.

Keywords: Type 2 diabetes, diabetic retinopathy, oxidative stress, Nrf2, Keap1, genetic variants