











# Evaluation of the effects of Ganoderma lucidum aqueous extract on incidental pathological findings of different tissues of mice with metastatic human breast cancer.

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# Introduction

Breast cancer is the most common type of cancer among women, which leads to death. There are different medical ways (traditional to modern) for treatment of this type of cancer, which have made a lot of progress today. Among them, we can refer to the treatment with medicinal plants. Reishi as a medicinal mushroom has been used in traditional Chinese medicine for centuries. Recently, this medicinal plant has been given special attention by Iranian researchers. The various therapeutic effects of this mushroom are related to its nutrients. One of their effects is decreasing the growth of tumor masses. It goes without saying that every medicinal plant may have side effects like other drugs, which are important to know and check. This research is based on the histopathological examination of the possible effects of Reishi on different organs in an animal model study.

# **Materials and Methods**

In this study, 13 female nude mice with an approximate weight of 20 grams were used in 4 groups. The mice were randomly divided into group 1 (including 3 mice without intervention), group 2 (including 4 tumor bearing mice without treatment), group 3 (including 3 tumor bearing mice treated with Ganoderma lucidum) and group 4 (including 3 tumor bearing mice treated with normal saline). Human metastatic breast cancer cell line (MDA-MB-231) was cultured and inoculated subcutaneously in the left flanks. The aqueous extract of Ganoderma lucidum was prepared by freeze-drying technique and stored until the start of the treatment period. After the confirmation of human metastatic breast adenocarcinoma, the treatment period started for one month. The aqueous extract was gavage to mice once a day. During the treatment period, mice were measured biometrically and at the end of the treatment period, all mice were euthanized. Based on macroscopic findings, tumor tissues, footpad and kidneys were removed for histopathological examination and fixed in 10% formalin (as fixative) and prepared for general and specific stainings. The percentage of











mitotic cells in tumor tissues compared to healthy cells was measured by Image.J software, and examination of tumor tissues, footpads and kidneys was qualitatively evaluated by light microscope. Statistical analysis of the study data was done by Graph Pad Prism software and ANOVA statistical test.

# Results

The weight and volume of tumors in the group treated with Ganoderma lucidum (G3) compared to the control groups (G2,4) had a significant decrease (P<0.05). The percentage of mitotic figures in tumor cells in the control groups showed a significant increase (P<0.05) compared to the third group. Pathological findings demonstrated kidney fibrosis and plantar cushion inflammation in the second and fourth groups compared to the first and third ones.

# Conclusion

Ganoderma extract can help to treat breast cancer by reducing the rate of mitosis in tumor tissues in a mouse model. In addition, it can be considered as a useful and safe compound in improving of life quality by reducing the footpad inflammation and also decreasing the possibility of renal fibrosis.

# **Keywords**

Breast, cancer, nude mice, MDA-MB-231













# Solitary amyloid tumor of the palate: A case report and literature review

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## Introduction

Amyloidosis is often caused by the abnormal extracellular accumulation of amyloid in organs and tissues. This condition, affecting the head and neck region, is typically localized, and may also involve the oral cavity, particularly the tongue and buccal mucosa. As a solitary manifestation, the localized amyloidosis occurring intraosseous is highly infrequent. In addition, localized amyloidosis has a great rate of recurrence.

# **Materials and Methods**

In this paper, a 50-year-old female patient with the chief complaint of pain in the anterior of the maxilla is reported. According to clinical examination, no significant pathologic lesion was seen. The radiographic image showed a radiolucent lesion around teeth four and five. The treatment of choice for the patient was an excisional biopsy.

### Results

As amyloidosis diagnosis is clinically challenging, biopsy and histologic examination of lesions are necessary in this regard.

# Conclusion

Accordingly, it is concluded that long-term follow-up is mandatory in case of localized amyloidosis because late recurrence can occur in some cases.

# Keywords

Amyloidosis hard palate rare diseases











# Investigation of the correlation between Carcinoma Associated Fibroblasts and Cancer Stem Cells in Oropharynx Squamous Cell Carcinoma related and unrelated to HPV

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# Introduction

The primary purpose of present study was to evaluate the correlation between SOX10 and CAFs in HPV-related and non HPV-related oropharyngeal squamous cell carcinoma. Relationship of recurrence, sex and mean age also were evaluated with SOX10 score and  $\alpha$ -SMA score. We also assessed relationship between time to relapse and SOX10 score and  $\alpha$ -SMA score.

## **Materials and Methods**

This study involved 31 patients to cover shedding cases for various reasons. Paraffin blocks containing tissue samples were obtained from two hospitals. Fourmicron sections were prepared from each block and tested using the SOX10 antibody. The scoring of the SOX10 biomarker and  $\alpha$ -SMA assessment results were recorded and analyzed using SPSS software. The presence or absence of HPV in the samples was determined using a methodology similar to the  $\alpha$ -SMA assessment. The study aimed to explore the relationship between the SOX10 biomarker,  $\alpha$ -SMA, and HPV presence in the samples.

# Results

There was no correlation between SOX10 score and  $\alpha$ -SMA score, while our data revealed the relationship between SOX10 score and time to relapse (p-value<0.05). we also assessed the relationship between HPV, SOX10 score and  $\alpha$ -SMA score. The results showed no relation between HPV and SOX10 score while the relationship between HPV and  $\alpha$ -SMA score was close to be significant.

## Conclusion

Lack of correlation between SOX10 score and  $\alpha$ -SMA score shows us that SOX10 expression may not have effect on presence and activity of CAFs. Additionally, based on our results we can conclude that elevated expression of SOX10 can reduce the time to relapse of disease.

# **Keywords**













carcinoma,HPV,oropharynx













# Mamary analogue secretory carcinoma; a case report of rare entity in palate

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## Introduction

Mammary analogue secretory carcinoma (MASC) is a rare, low-grade malignant salivary gland tumor. It is frequently mistaken for other neoplasms of the salivary glands especially acinic cell carcinoma. The morphological and immunohistochemical characteristics of MASC closely resemble those of breast secretory carcinoma. MASC tumors are primarily found in major salivary glands like the parotid.

# **Materials and Methods**

We identified 17 cases featuring palate involvement, even though this type of tumor is not commonly observed in palatal areas according to the published articles.

### Results

In this study, we presented a 45-year-old male who had a left side and posterior expansile palatal lesion for approximately 7 months.

# Conclusion

Clinical radiographical, histopathological and immunohistochemical analyses and treatment plan details of this patient with diagnoses of MASC are reported and the diagnostic challenges are discussed here. This report aims to increase the awareness of this diagnosis and provide a review of current reported cases for this rare entity.

# **Keywords**

MASC, Immunohistochemistry, Oral, Palate.













# Investigating the effects of Ganoderma lucidum on the apoptosis process and the amount of mitotic figures in cancer cells of nude mice with human hormone receptor positive breast cancer.

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# Introduction

Nowadays, according to the life style, the type of nutrition and other prevailing parameters, human societies are faced with various types of diseases. Cancer is one of the most important of them. Various types of this disease have affected human life. One of which specially has led to high mortality among women all over the world, is breast cancer. Although various treatments are known for this disease, due to the lack of success in many cases, it has prompted researchers to turn to the discovery of new drugs from nature. One of the medicinal plants that has significant therapeutic effects in the treatment of some types of cancer is Ganoderma lucidum as a medicinal mushroom. So far, the mechanism of effect of secondary metabolites of this mushroom on hormone receptor positive human breast cancer cells has not been investigated. This study evaluates its effects on the process of apoptosis and the level mitotic figures in the cancer cells of xenografted nude mice.

# **Materials and Methods**

Sixteen female nude mice aged 4-6 weeks were randomly divided into four equal groups. In the first group; healthy mice, in the second group; tumor-bearing mice without intervention, in the third group; tumor-bearing mice treated with Ganoderma aqueous extract and in the last group; tumor-bearing mice treated with normal saline. MCF-7 cell line was cultured in RPMI medium and 6 million cells per mouse were inoculated under the skin of the right flank. According to the freeze dryer protocol, Ganoderma aqueous extract was produced and stored in the freezer until use. At the beginning of the treatment period, 0.1 ml of drug was given to group 3 mice and 0.1 ml of normal saline to group 4 mice. Experimental animals were assessed biometrically and after euthanization at the end of the study, tumor tissues were fixed in 10% formalin for general and specific stainings for pathology investigations. After the tissue preparation stage, hematoxylin and eosin staining were used to compare tumor cells, Immunohistochemical (IHC) technique to check the amount of mitotic figures











and Terminal deoxynucleotidyl transferase dUTP Nick End Labeling (TUNEL) technique to check the amount of apoptosis induction in tumor tissue cells. Qualitative and comparative measurement of tumor cells was done with pathological images obtained by H&E technique, and the percentage of apoptosis induction in tumor cells was checked using Image.J software. The data of this study were statistically analyzed by Graph Pad Prism software and ANOVA statistical test. A significance level of less than 0.05 was considered.

# **Results**

Histopathological images of tumors showed pleomorphic tumor cells with round to oval nuclei in different sizes or prominent nucleoli, and levels of mitotic figures. The number of these cells in the second and fourth groups showed a significant increase (P<0.05) compared to the third one. Examining the Immunohistochemical slides indicated the occurrence of high mitosis in the groups two and four. The mitotic index in the third group had a significant decrease (P<0.05) compared to the control groups. The slides obtained from the TUNEL technique showed that the induction of apoptosis in the group three has a significant increase (P<0.05) compared to the second and fourth ones.

# **Conclusion**

Ganoderma aqueous extract reduces the mitotic index in tumor cells by inducing apoptosis in MCF-7 breast tumor cells. Therefore, this medicinal mushroom can be introduced as an effective compound in the treatment of patients with hormone receptor positive human breast cancer.

# **Keywords**

Breast cancer, Ganoderma, nude mice













# Levels of IL-1\beta, IL-8, and IL-10 in Bronchoalveolar Lavage Fluid of Patients with COVID-19

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# Introduction

Severe acute respiratory syndrome coronavirus 2 (SARS CoV 2) is a coronavirus that causes respiratory disease with severe lung injury designated as COVID-19. Inflammation is one of the characteristics of the disease, and therefore, we aimed to investigate the role of inflammatory cytokines in the immunopathogenesis of COVID-19 and its predictive value in diagnosing or determining the severity of the disease in laboratory-confirmed cases.

# **Materials and Methods**

In this cross-sectional study, 70 people were enrolled and allocated to two control (n=30) and case (n=40) groups. Patients with COVID-19 (PCR positive for SARS-CoV-2) comprised the case group. The bronchoalveolar lavage (BAL) fluid was obtained, and the cytokines were quantified by ELISA methods.

# Results

In both groups, the number of men was higher than women, and there was no difference between the groups in terms of sex (P=0.83). The mean IL-1 $\beta$  in the patients was more than the control group (P=0.01). The mean IL-8 and IL-10 were not statistically significant between the two groups. The mean IL-1\beta, IL-8, and IL-10 levels were not significant in terms of disease severity in patients with COVID-19.

# Conclusion

Disease severity was not related to the studied cytokine levels (IL-8, IL-1\beta, and IL-10). IL-1\beta is involved in the immunopathogenesis of COVID-19 and triggering a cytokine storm.

# **Keywords**

COVID-19, Inflammation, IL-1\u03b3, BAL fluid











# Evaluation of C4d expression and staining pattern in renal biopsy samples with focal segmental glomerulosclerosis (FSGS) and Minimal histological abnormality by immunohistochemistry method

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# Introduction

Introduction: C4d is an activation product of lectin pathway of complement. Glomerular deposition of C4d is associated with poor prognosis in different types of immune-related glomerulonephritis. The present study was conducted to investigate expression level of C4d and its staining pattern in renal biopsy of patients with focal segmental glomerulosclerosis (FSGS) and minimal histopathological abnormality by immunohistochemistry method.

# **Materials and Methods**

Materials and methods: In this retrospective cross-sectional study, renal biopsy specimen from 46 samples of minimal histopathological abnormalities, 47 samples of FSGS, and 15 samples without glomerular disease as controls, which were sent to Pathology Department of Imam Khomeini Hospital in Tehran from 2019 to 2021, were subjected to immunohistochemistry staining with C4d antibody. Demographic characteristics and information obtained from light and electron microscopy of patients were also extracted from their files. The correlation of C4d expression with other histopathological findings was statistically analyzed by SPSS software.

# **Results**

Results: C4d positive staining was observed in 97.9% of FSGS samples and 43.5% of minimal histopathological abnormality samples, which showed a statistically significant difference (P<0.001). The sensitivity and specificity of C4d expression for diagnosing FSGS were 97.9% and 56.5%, respectively. There was no significant correlation between C4d expression and any of the light and electron microscopy findings, including presence of foam cells, mesangial matrix expansion, interstitial fibrosis and tubular atrophy (IFTA), and basement membrane changes. Also, no significant correlation was observed between C4d expression and clinical symptoms of proteinuria or prolonged high level of creatinine in patients with minimal histopathological abnormality.

## **Conclusion**







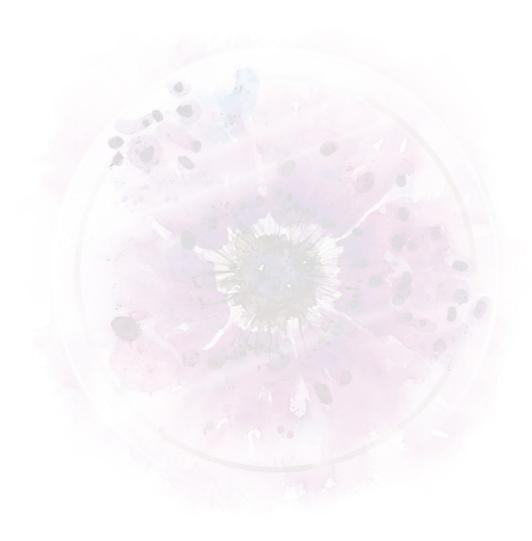




Discussion and conclusion: The expression of C4d marker had a good sensitivity and negative predictive value in the diagnosis of FSGS, but it did not effectively predict treatment response in minimal histopathological abnormality.

# Keywords

Keywords: Focal Segmental Glomerulosclerosis, C4d













# Post-COVID-19 rhinocerebral mucormycosis, a life-threatening event in the background of immunosuppressive condition: A case report

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# Introduction

In patients suffering from COVID-19, immunocompromised conditions or immunosuppressive medications such as corticosteroids may predispose them to early or delayed invasive fungal infections that invade cerebral components. This study, for the first time, describes a case of COVID-19 disease diagnosed with rhinocerebral mucormycosis through cerebrospinal fluid (CSF) analysis.

# **Materials and Methods**

A 32-year-old woman with a history of referral and hospitalization due to COVID-19 about a month ago was being treated with immunosuppressive drugs, manifested by lower extremity plegia. In the imaging assessment, intracranial hemorrhage (thalamus zone) was revealed. In cytological assessment, acute inflammations associated with fungal infection in accordance with the diagnosis of mucormycosis were definitively confirmed. Despite antifungal medication, consciousness declined one week later, and the patient developed thromboembolism and died.

# Results

# Conclusion

In patients with a COVID-19 background of immunosuppressive therapy or clinical situations related to immunosuppression such as uncontrolled diabetes, rhinocerebral mucormycosis will always be an ambush. Therefore, screening and prevention measures should be considered.

# **Keywords**

COVID-19 SARS-CoV-2 Infection mucormycosis











# Evaluating the histophatologic frequency of malignant skin tumors referred to Urmia Imam Khomeini hospital from March 2012 to March 2022

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# Introduction

Skin cancer is the most common cancer among men and the second most common among women worldwide. In Iran, it is the most common cancer in the entire population, in males, and also the second most common cancer in females. Early diagnosis and proper treatment are crucial for the management of skin tumors. Given the high prevalence of skin cancer in Iran, particularly in the West Azerbaijan province, we conducted a study to evaluate the frequency of malignant skin tumors in our center.

# **Materials and Methods**

In this retrospective cross-sectional study, histopathological reports of 923 cases of malignant skin tumors referred to the pathology department of Urmia Imam Khomeini hospital from March 2012 to March 2022 were evaluated. After statistical analysis using SPSS version 16 software, descriptive statistics such as frequency, mean, and standard deviation were used to represent the data.

# **Results**

The age mean was 64.0±18.5 years old. Most of the patients were males (63.2%). Male to female ratio was 1.7. Basal Cell Carcinoma (BCC) (57.9%) and Squamous Cell Carcinoma (SCC) (29.8%) were the most common histopathological patterns, respectively. BCC was the most common histopathological pattern in all of the studied years and among both sexes. Patients with BCC and SCC were older than those with other types of skin malignancies. All types of histopathological patterns of skin malignancies (except Melanoma and Lymphoma) were most abundant on the head and neck (melanoma more common on the limbs and lymphoma more common on the trunk).

# Conclusion

Elderly men and sun exposed areas of skin, such as the head and neck, are at a higher risk of developing skin malignancies. Therefore, it is necessary to adopt precise health, educational, and management measures to better understand the risk factors of skin malignancies in order to prevent and control them.

# **Keywords**

Malignant, skin, tumor, Histopathology













# Study of histopathological findings in liver needle biopsies referred to Urmia Imam Khomeini hospital from March 2017 to March 2022

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# Introduction

Liver is one of the main organs of the digestive system, which is vulnerable to various types of inflammatory, microbial, metabolic, and neoplastic diseases. Due to the frequent number of patients, the asymptomatic nature of chronic diseases until the end stages, and the lack of detailed studies on the prevalence of liver diseases in West Azerbaijan province in recent years, this study was designed and implemented with the aim of investigating the prevalence of liver diseases that can be evaluated with the data obtained from liver needle biopsies in our center.

# **Materials and Methods**

In this retrospective cross-sectional study, 340 liver needle biopsy histopathologic reports referred to Urmia Imam Khomeini Hospital Pathology Department from March 2017 to March 2022 were evaluated. After statistical analysis using SPSS version 16 software, descriptive data were reported in the form of descriptive statistics such as frequency, mean, and standard deviation.

# Results

The age mean of the patients was 54.8±17.1 years. Most of the patients were females (51.5%). Female to male ratio was 1.06. The most common findings in needle biopsies were neoplasms and hepatitis with 47.1% and 46.2% frequencies, respectively. Older men, with an average age of  $62.5 \pm 13.2$  years, were affected mostly by neoplasms, while hepatitis was more common in relatively younger women with an average age of  $47.5 \pm 17.3$  years. Most of neoplasms (70.6%), were metastatic. The most common primary malignancy was Hepatocellular Carcinoma (HCC), with a frequency of 18.1% among all neoplasms. Chronic hepatitis was reported as the most common type of non-neoplastic lesions, accounting for 68.2% of cases.

# Conclusion

Considering the frequency of neoplastic and non-neoplastic liver diseases' histopathology, it is recommended to study and identify the risk factors of liver diseases to help diagnosis and treatment planning for the patients.

# **Keywords**

Liver, Needle biopsy, Histopathology











# Mast cell density in gastric cancer and its relation to aggressive behavior

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## Introduction

Introduction: Stomach cancer is a serious health problem worldwide, as it is one of the most common cancers and the fourth leading cause of cancer-related death. Mast cells perform functions in the immunity system and are a type of discriminated myeloid cell. In this study, we evaluated the correlation between tryptase-positive mast cell density with prognostic histopathological findings in gastric cancer.

## **Materials and Methods**

Materials and Methods: The study was conducted as a cross-sectional study, using tissue samples from 40 patients who underwent radical gastrectomy at Sina Hospital between 2022 and 2023. After histopathological examination and determination of tumor histopathological characteristics, the samples were subjected to immunohistochemical staining using a monoclonal antibody against mast cell tryptase.

# **Results**

Results: In this study, the median density of mast cells in tumor tissue was 8/10 high power fields. There was no significant relationship between mast cell density and the number of lymph nodes involved, as well as tumor type, grade, location, and size. Furthermore, there was no significant relationship between mast cell density and tumor vascular invasion or neural invasion.

# Conclusion

Conclusion: Mast cells have vital roles in normal immune systems and pathological situations. The function of mast cells has not been completely explained in gastric cancer and needs confirmation to introduce new therapy.

# **Keywords**

Stomach cancer, mast cell













# Evaluation of the Her-2/neu value in papillary thyroid carcinoma and its relation to histopathological prognostic findings

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## Introduction

Introduction: Thyroid cancer is an important endocrine malignancy worldwide, including papillary carcinoma, which is responsible for more than 90% of thyroid malignancies. Human epidermal growth factor receptor 2 (Her-2/neu) overexpression plays a significant act in the development, progression, and invasion of various tumors through effects on the cell cycle, angiogenesis, cell movement, and apoptosis.

# **Materials and Methods**

Materials and methods: The study was conducted as a cross-sectional study, using tissue samples from 53 patients who underwent lobectomy or total thyroidectomy between 2020 and 2022. For histopathological examination and to determine the pathological features of the tumor, tumor specimens were stained for immunohistochemistry using a monoclonal antibody against Her-2/neu.

# Results

Results: In this study, Her-2/neu was expressed in 13.2% of PTC patients and not expressed in normal thyroid tissue. No significant relationship was established between Her-2/neu expression and tumor histological subtype, as well as tumor size, sex, or tumor focality. Furthermore, there was no significant association between Her-2/neu expression and vascular invasion or extrathyroidal extension of the tumor.

# Conclusion

Conclusion: No significant Her-2/neu expression was observed in the malignant thyroid tissue. These findings raise questions about the value of Her-2/neu as a potential prognostic factor or target of a specific anticancer treatment for thyroid cancer.

# **Keywords**

papillary thyroid carcinoma, Her-2/neu, prognosis.











# Computational analysis of missense variant CYP4F2\*3 (V433M) in association with human CYP4F2 dysfunction: a functional and structural impact

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# Introduction

Cytochrome P450 4F2 (CYP4F2) enzyme is a member of the CYP4 family responsible for the metabolism of fatty acids, therapeutic drugs, and signaling molecules such as arachidonic acid, tocopherols, and vitamin K. Several reports have demonstrated that the missense variant CYP4F2\*3 (V433M) causes decreased activity of CYP4F2 and inter-individual variations in warfarin dose in different ethnic groups. However, the molecular pathogenicity mechanism of missense V433M in CYP4F2 at the atomic level has not yet been completely elucidated.

# **Materials and Methods**

In the current study, we evaluated the effect of the V433M substitution on CYP4F2 using 14 different bioinformatics tools. Further molecular dynamics (MD) simulations were performed to assess the impact of the V433M mutation on the CYP4F2 protein structure, stability, and dynamics. In addition, molecular docking was used to illustrate the effect of V433M on its interaction with vitamin K1.

# **Results**

Based on our results, the CYP4F2\*3 variant was a damaging amino acid substitution with a destabilizing nature. The simulation results showed that missense V433M affects the dynamics and stability of CYP4F2 by reducing its compactness and stability, which means that it tends to change the overall structural conformation and flexibility of CYP4F2. The docking results showed that the CYP4F2\*3 variant decreased the binding affinity between vitamin K1 and CYP4F2, which reduced the activity of CYP4F2\*3 compared to native CYP4F2.

# **Conclusion**

This study determined the molecular pathogenicity mechanism of the CYP4F2\*3 variant on the human CYP4F2 protein and provided new information for understanding the structure-function relationship of CYP4F2 and other CYP4 enzymes. These findings will aid in the development of effective drugs and treatment options.







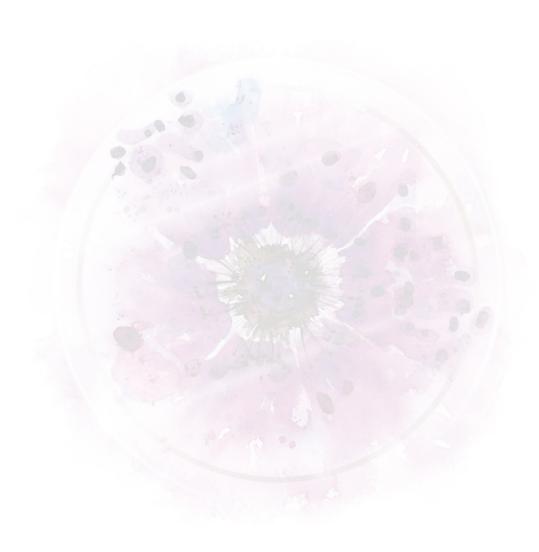






# Keywords

Damaging variant CYP4F2\*3 Warfarin In-silico















# KRAS, NRAS, BRAF, and PIK3CA mutation rates, clinicopathological association, and their prognostic value in Iranian colorectal cancer patients

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# Introduction

Mutations in KRAS, NRAS, BRAF, and PIK3CA genes are critical factors in clinical evaluation of colorectal cancer (CRC) development and progression. In Iran, however, the data regarding genetic profile of CRC patients is limited except for KRAS exon2 and BRAF V600F mutations. This study aimed to investigate the mutational spectrum and prognostic effects of these genes and explore the relationship between these mutations and clinicopathological features of CRC.

# **Materials and Methods**

To achieve these objectives, mutations in KRAS (exons 2, 3, and 4), NRAS (exons 2, 3, and 4), PIK3CA (exons 9 and 20), and BRAF (exon 15) was determined using PCR and pyrosequencing in a total of 151 patients with colorectal cancer.

## **Results**

KRAS, BRAF, NRAS, and PIK3CA mutations were identified in 41%, 5.96%, 3.97%, and 13.24% of the cases, respectively. There were some significant correlations between clinicopathological features and KRAS, PIK3CA, BRAF, and NRAS mutations. Mutations in KRAS and PIK3CA were shown to be independent risk factors for poor survival of the patients at stage I-IV (p < 0.0001 and p = 0.001, respectively). No significant impact on prognosis was observed in patients with BRAF mutations.

# Conclusion







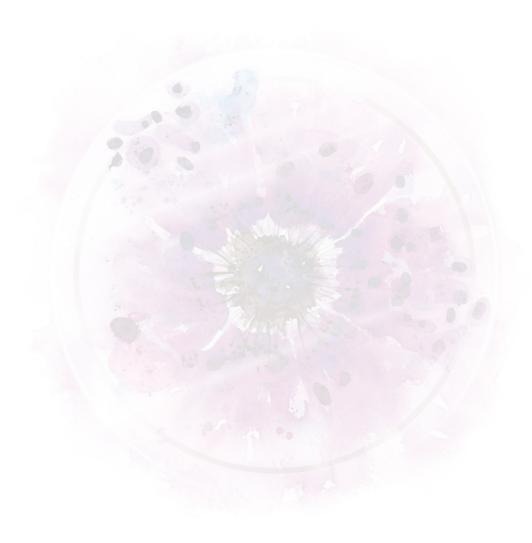




Our study revealed the prevalence of CRC biomarkers mutations in Iranian patients and emphasized the role of KRAS and PIK3CA on shorter overall survival rates in this population.

# Keywords

KRAS BRAF NRAS PIK3CA ColorectalCancer













# Evaluation of a warfarin dosing algorithm including CYP2C9, VKORC1, and CYP4F2 polymorphisms and non-genetic determinants for the Iranian population

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# Introduction

The response to warfarin, as an oral anticoagulant agent, varies widely among patients from different ethnic groups. In this study, we tried to ascertain and determine the relationship between non-genetic factors and genetic polymorphisms with warfarin therapy; we then proposed a new warfarin dosing prediction algorithm for the estimation of drug sensitivity and resistance in the Iranian population.

# **Materials and Methods**

Overall, 200 warfarin-treated patients with stable doses were recruited, the demographic and clinical characteristics were documented, and genotyping was done using a sequencing assay.

# Results

The outcomes of our investigation showed that the genetic polymorphisms of VKORC1(-1639 G > A), CYP2C9\*3, CYP2C9\*2, amiodarone use, and increasing age were found to be related to a significantly lower mean daily warfarin dose. In contrast, the CYP4F2\*3 variant and increased body surface area were linked with an increased dose of warfarin in the Iranians. Our descriptive model could describe 56.5% of the variability in response to warfarin. This population-specific dosing model performed slightly better than other previously published warfarin algorithms for our patient's series. Furthermore, our findings provided the suggestion that incorporating the CYP4F2\*3 variant into the dosing algorithm could result in a more precise calculation of warfarin dose requirements in the Iranian population.

### Conclusion

We proposed and validated a population-specific dosing algorithm based on genetic and nongenetic determinants for Iranian patients and evaluated its performance. Accordingly, by









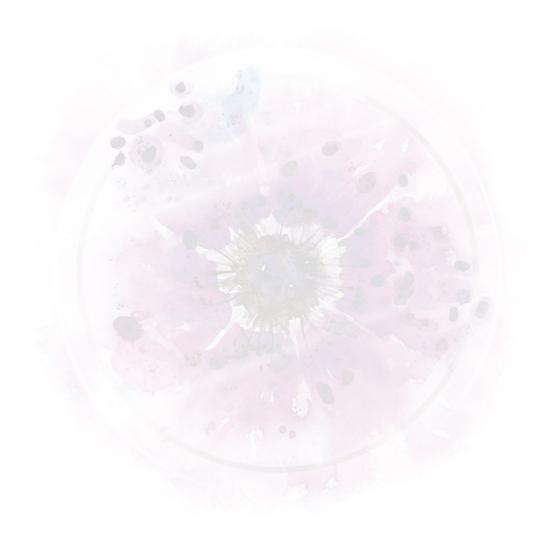




using this newly developed algorithm, prescribers could make more informed decisions regarding the treatment of Iranian patients with warfarin.

# Keywords

Warfarin non-genetic factors genetic polymorphisms















# Investigating the amount of blood transfusion and its relationship with the amount of hemoglobin before or after open heart surgery in Farshchian Heart Hospital in Hamedan.

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# Introduction

Today, cardiovascular diseases are the main cause of death worldwide, among heart diseases, coronary artery diseases have the highest proportion. One of the main methods of treating coronary artery diseases is coronary artery bypass surgery. Blood injection is an important part of these operations. The purpose of this study is to investigate the amount of blood transfusion and its relationship with the amount of hemoglobin before or after open heart surgery at Farshchian Heart Hospital in Hamedan in 2022.

# **Materials and Methods**

The current study is a cross-sectional study that was conducted on 109 patients who underwent open heart surgery in 1401. The frequency of anemic patients before surgery was calculated. The frequency of blood transfusions was also calculated. After collecting the data, SPSS version 16 software was used to analyze the variance and chi-square test.

# Results

Out of a total of 109 patients, 20% of them had anemia before surgery, 17.3% had mild anemia and 2.7% had moderate anemia, and no one had severe anemia. 60.5% of the studied subjects showed that there was a significant relationship between anemia before surgery and the amount of blood received, and there was also a statistical relationship between gender and the amount of blood received.

## Conclusion

In our study, a large percentage of people had received blood, and on the other hand, receiving blood is associated with adverse effects such as infectious events, acute kidney injury, etc. blood, including paying attention to the threshold of hemoglobin injection, using blood conservation methods during surgery and correcting anemia before surgery in patients is necessary, and with this work, the amount of blood transfusion and its complications can be significantly reduced gave

# **Keywords**

Anemia, blood transfusion, heart surgery











# Evaluation of the sensitivity and agreement of serum hydatid cyst tests for the diagnosis of lung and liver lesions in 2011-2021 in Qazvin

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# Introduction

## Introduction:

In this study, we investigated the sensitivity of hydatid serum test to diagnose lung and liver lesions in humans and and we compaired the sensitivity of the tests based on the location of the lesion (pulmonary and liver) and the number of isolated cysts

We also compare Elisa and ECL method in measuring antibody againts hydatid.

# **Materials and Methods**

# Material and method:

In this cross-sectional study, the files of patients who had hydatid cyst surgery in the hospitals covered by Qazvin University of Medical Sciences during 3 years between 2019-2021 were included in the study and the results of serum ELISA( Enzyme linked immunosorbent assay) and ECL(Electero chemiluminecance) tests for IgG of these patients were investigated and sensitivity of each test was calculated and compared. The agreement between the two tests was also checked.

## Results

## Results:

In this study, 102 patients were examined. The overall sensitivity of ELISA IgG test for hydatid cyst diagnosis was 67% (57-76%) and for ECL test was 69% (59-78%), which were not significantly different (P>0.05) and agreed. The sensitivity of ELISA IgG test for the diagnosis of pulmonary and hepatic hydatid cysts was 54% (40-67%) and 86% (72-94%), respectively, which had a significant difference (P<0.05). There was no significant difference between the sensitivity of ELISA and ECL tests with the number of cysts or gender of patient (P>0.05).











In Qaznin province ,30% of patient were lived in Qazvin city and 70% lived in rural area which the most common place was Takestan (24%) and the second common area wasMohamadieh.(20%)

# Conclusion

# Conclusion:

The results of the present study showed that hydatid cyst is a common disease in Qazvin province (102 cases in three years just in velayat hospital), the sensitivity of ELISA and ECL tests to diagnose hydatid cysts is similar, but it differs according to the location of the cyst (better in hepatic cysts) and is not related to the number of cysts or gender of patient. Although further studies in this field are recommended













# Clinicopathological Significance of PTEN Expression and Its Prognostic Effect in Colorectal Adenocarcinoma Patients

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## Introduction

Phosphatase and tensin homolog (PTEN) is a tumor suppressor gene located at chromosome 10. PTEN is a regulator of the PI3K/AKT signaling pathway that inhibits cell proliferation and promotes apoptosis. PTEN loss of function occurs in a spectrum of cancers, including colorectal adenocarcinoma. This study aimed to investigate the probable correlation of negative PTEN expression with clinicopathological features and colorectal adenocarcinoma (CRC) patients' survival.

# **Materials and Methods**

In this cross-sectional study using Immunohistochemistry stainingPTEN expression status on 151 CRC tissues was evaluated. Then the results of IHC staining was compared to those of clinicopathological features. The relationship between PTEN and KRAS mutation status was also investigated.

# Results

Of 151 CRC samples, 89 (58.9%) were negative for PTEN expression. Loss of PTEN expression was associated with KRAS mutation (P<0.0001), lymph node metastasis (P=0.002), and advanced tumor stage (P=0.016), whereas no significant association was found with other clinicopathological features. Multivariate analysis indicated that tumor site and KRAS mutation were independent prognostic CRC patients (P<0.05). The Kaplan-Meier analysis indicated a correlation between loss of PTEN expression and overall survival of patients with colorectal adenocarcinoma (P=0.01).

# Conclusion

The current study suggests that decreasing PTEN expression or its negative expression may be associated with a higher stage and poor prognosis. Combined analysis of mutated KRAS and PTEN expression could be a good predictor of disease prognosis as well as its clinical outcomes.







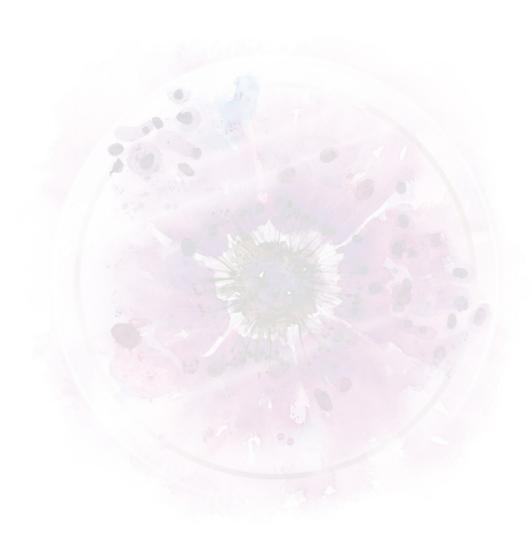






# Keywords

Adenocarcinoma Clinicopathology Colorectal cancer PTEN













# Synchronous Occurrence of Papillary Thyroid Carcinoma and Medullary Carcinoma in the Setting of Hashimoto's Thyroiditis and Multi Nodular Goiter

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# Introduction

Coexistence of follicular epithelial and bilateral parafollicular cells derivative of carcinomas in the setting of Hashimoto's thyroiditis and multinodular goiter is a very rare event. Of course, all benign and malignant thyroid lesions are more prevalent in iodine deficient areas. It seems that the context for identifying the pathways influencing thyroid carcinogenesis especially coincidence form has not yet been fully understood and needs further investigation. Here, we present a case with the synchronous occurrence of papillary thyroid carcinoma and medullary thyroid carcinoma in the setting of Hashimoto's thyroiditis and multinodular goiter.

## **Materials and Methods**

A 54-year-old woman complained of a painless mass in the anterior region of the neck. The physical examination of the patient revealed multiple nodules in her thyroid gland. In ultrasound findings, she presented with thyroid enlargement associated with multiple isoechoic and hypoechoic nodules in both lobes. Thyroid fine needle aspiration results suggested a diagnosis of medullary thyroid carcinoma in the setting of Hashimoto's thyroiditis and multinodular goiter. The frozen sections, permanent sampling, and IHC examination showed the coexistence of papillary thyroid carcinoma with bilateral medullary thyroid carcinoma in the setting of Hashimoto's disease and multinodular goiter.

# Results

# Conclusion

Studies debated about the risk factors of these pathologies including the same environmental issues or mutations in genomes and they emphasized surgeons should be aware of these lesions for diagnosis and interventional treatments. Following up the Hashimoto's thyroiditis and multinodular goiter is required for detection ofoccult malignancies, and hence the proper management and treatment should be performed.

# Keywords



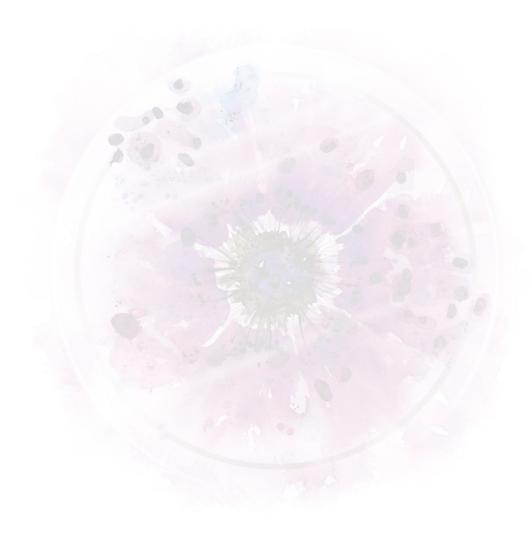








Hashimoto's-thyroiditis Medullary-carcinoma Multi-nodular-goiter Papillary-thyroid-carcinoma















# Comparative study of Liraglutide and GanAb impression in obese patients with fatty liver.

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# Introduction

The use of fast foods and machinery lifestyle in recent decades has increased the incidence of various metabolic diseases. One of the diseases that increase daily in the human population is called fatty liver. This disease is known to different grades that if it reaches the last grade, the patient is prone to liver failure and is a candidate for liver transplantation. This is the reason why practitioners prefer to diagnose and control the disease in the early stages in order to prevent it from progressing to the end stage. In addition to exercise, various drugs such as Liraglutide also play an important role in this way. Organic herbal medicines also have beneficial effects in patient improvement. This study compares the effects of GanAb and Liraglutide on the liver tissues of patients with steatosis.

# **Materials and Methods**

In this study, 12 Wistar rats weighing 250-300 grams were used. The animals were efficiently divided into 4 equal groups. All mice were exposed to 12 hours of light and 12 hours of darkness. All groups have their own food ration with water ad libitum. The diet of rats in the first group was normal. Other groups used a high-fat diet. After two weeks of keeping the mice with the mentioned diets, the third group received a single daily dose of Liraglutide and the fourth group was gavage with GanAb daily in the middle of the day. The treatment period lasted one month. At the end of the study, all experimental animals were euthanized. The target tissues of all mice were preserved in 10% formalin and stained with Hematoxylin and Eosin for histopathological examination. The ratio of vacuolated hepatocytes to total hepatocytes was measured by Image. J software. The data was measured by GraphPad Prism statistical software and the significance level was considered less than 0.05.

# Results











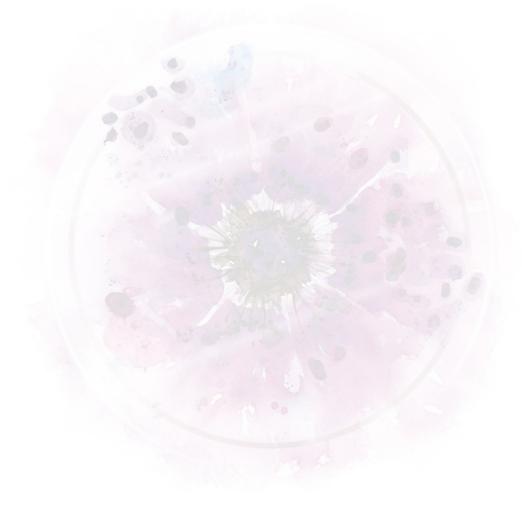
The results of this research indicated that the liver tissue of the first and fourth group rats had a normal structure. The rats in the second group were affected by grade 2 fatty liver, and the rats in the third group were affected by grade 1 fatty liver.

# Conclusion

According to pathology reports and statistical data analysis, although Liraglutide as an effective drug for treating obesity can reduce the severity of steatosis in the liver of rats with fatty liver, GanAb has more efficiency and significant effects than Liraglutide. In this way, Liraglutide was able to improve the fatty liver from grade 2 to grade 1, and GanAb was able to change the fatty liver from grade 2 to a normal state. Therefore, GanAb can be introduced as an effective and useful organic compound in the treatment of obese patients with fatty liver.

# **Keywords**

rat, fatty liver, steatosis, liraglutide













# The impact of education on the level of residents' awareness about patient blood management

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## Introduction

The patient blood management program minimizes the need for allogeneic blood and reduces unnecessary blood transfusions to improve patients' health. Familiarity of physicians with this program is necessary to improve the outcomes of patients. This study was conducted to evaluate the effect of education on the level of knowledge of medical residents about patient blood management in educational medical centers in Yazd.

# **Materials and Methods**

The study was a quasi-experimental intervention. Fifty-seven medical residents participated. A questionnaire was prepared to measure the residents' knowledge level in patient blood management before and after the educational program. The effect of training on Residents' knowledge was evaluated. The data were analyzed using t and Paired-t tests in SPSS 20 statistical software.

# **Results**

The average knowledge scores were  $9.38\pm3.77$  and  $14.01\pm3.50$  before and after education. Training had a significant effect on the knowledge score of residents (p<0.001). The lowest percentage of response before training was in evaluating and managing patients' anemia before surgery and knowledge of the use of autologous blood. The knowledge score before and after the training had no significant relationship with age, sex, field of study, history of blood prescription, and duration of medical practice.

# Conclusion

Training effectively increased the knowledge of doctors. It is suggested to hold targeted educational seminars and webinars with emphasis on the areas of anemia management before medical or surgical interventions and the use of autologous blood, publish educational content in the form of guides, and include blood transfusion medicine and the patient's blood management program in the medical education curriculum.

# **Keywords**

Knowledge Education Patient-Blood-Management













# **Evaluation of LGR5 Cancer Stem Cell Marker Expression in Breast Cancer and Its Relationship with Hormonal Profile and Clinical Pathological Features**

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# Introduction

Background: Due to the high prevalence of breast cancer and the importance of evaluating new prognostic criteria

for effective treatment of these patients, this study was performed to investigate the role of LGR5 in breast cancer and

its relationship with hormonal and clinical opathological features of the disease.

# **Materials and Methods**

This cross-sectional study

was performed on breast cancer tissue samples in the archives of the pathology department of Firoozabadi Hospital

in Tehran between 2019 and 2021. Inclusion criteria included invasive ductal carcinoma and exclusion criteria were

preoperative chemotherapy. Blocks were examined for LGR5 marker expression by IHC method using LGR5 monoclonal

antibody kits (Abcam). The expression pattern of LGR5 marker was cytoplasmic and cells presenting brown staining

in the cytoplasm were considered positive for this marker and in terms of distribution and severity of staining were

divided into three groups: mild, moderate and severe.

## Results

This study was performed on 60 patients with breast cancer with a mean age of  $55.5 \pm 9.7$ . The age range of the patients was from 33 to 70 years. The pathological











characteristics of the studied tumors are shown in Table 1. As shown in the Table 1, most of the examined patients (55%) were in grade II histopathology. The KI67 marker was positive in 45 cases (75%) and the HER2 marker was positive in 14 cases (23.3%) and 8 cases (13.3%) were triple-negative. The expression of LGR5 marker in 41 cases (68.3%) was moderate and its expression distribution in 31 cases (51.7%) was moderate (Figure 1). The of LGR5 expression in terms of molecular classification of breast cancer and tumor characteristics is shown in Table 2 that there was only a significant relationship between triple-negative type and LGR5 expression (P = 0.01) and in other cases no significant difference was observed.

# Conclusion

In conclusion, the results of the present study showed that the LGR5 marker is expressed in a remarkable percentage of breast cancer patients and its value is not high in triple-negative and had no significant relationship with tumor characteristics.

# **Keywords**

Breast cancer stem cell LGR5











# New insights into extracellular and intracellular redox status in COVID-19 patients

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# Introduction

Background: The imbalance of redox homeostasis induces hyper-inflammation in viral infections. In this study,

we explored the redox system signature in response to SARS-COV-2 infection and examined the status of these

extracellular and intracellular signatures in COVID-19 patients.

# **Materials and Methods**

The multi-level network was constructed using multi-level data of oxidative stress-related biological

processes, protein-protein interactions, transcription factors, and co-expression coefficients obtained from











GSE164805, which included gene expression profiles of peripheral blood mononuclear cells (PBMCs) from

COVID-19 patients and healthy controls. Top genes were designated based on the degree and closeness centralities.

The expression of high-ranked genes was evaluated in PBMCs and nasopharyngeal (NP) samples of 30

COVID-19 patients and 30 healthy controls. The intracellular levels of GSH and ROS/O2• 
and extracellular

oxidative stress markers were assayed in PBMCs and plasma samples by flow cytometry and ELISA. ELISA results

were applied to construct a classification model using logistic regression to differentiate COVID-19 patients from

healthy controls.

# Results

CAT, NFE2L2, SOD1, SOD2 and CYBB were 5 top genes in the network analysis. The expression of these

genes and intracellular levels of ROS/O2•  $\square$  were increased in PBMCs of COVID-19 patients while the GSH level

decreased. The expression of high-ranked genes was lower in NP samples of COVID-19 patients compared to

control group. The activity of extracellular enzymes CAT and SOD, and the total oxidant status (TOS) level were

increased in plasma samples of COVID-19 patients. Also, the 2-marker panel of CAT and TOS and 3-marker panel

showed the best performance.

# Conclusion

SARS-COV-2 disrupts the redox equilibrium in immune cells and the upper respiratory tract, leading

to exacerbated inflammation and increased replication and entrance of SARS-COV-2 into host cells. Furthermore,

utilizing markers of oxidative stress as a complementary validation to discriminate COVID-19 from healthy

controls, seems promising.

# **Keywords**

SARS-COV-2 Redox system













# Extraskeletal mesenchymal chondrosarcoma arising from soft tissues: A rare case report

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#### Introduction

Chondrosarcomas are an exceedingly rare form of cancer, impacting only a few individuals per million. Among chondrosarcomas, a small fraction belongs to the mesenchymal sub-type. Furthermore, only one-third of mesenchymal chondrosarcomas manifest in extraskeletal locations.

#### **Materials and Methods**

A 38-year-old woman was referred by a midwife after experiencing pain in the right upper quadrant of her right breast for 2 months. The mass had been palpable for 1 week before the initial assessment. According to radiological evaluations, the tumor is outside breast tissue and not connected to the bones. Hence, a biopsy of the mass is done. The biphasic morphology of the tumor during pathological evaluation, in addition to immunohistochemistry testing, confirms the diagnosis of extraskeletal mesenchymal chondrosarcoma (EMCS). Finally, the mass was surgically removed, and 6 months of chemotherapy were administered to the patient

#### **Results**

#### **Conclusion**

Given the tumor's rarity and the lack of established guidelines, diagnosing EMCS can be challenging and prone to errors. As such, meticulous sampling, along with precise pathological and imaging investigations, is imperative to accurately establish the diagnosis of these tumors.

#### **Keywords**

extraskeletal, mesenchymal chondrosarcoma











# Establishment of HLA database of plateletpheresis donors helps to select matched donors for platelet refractoriness patients

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#### Introduction

Anti-HLA alloimmunization is the most common source of immune platelet refractoriness, which occurs as a result of high polymorphism of the HLA system. A suitable and useful approach is to provide apheresis platelets from HLA-matched donors. Transfusion of HLA-matched platelets is necessary for the patient when platelet refractoriness happens. The aim of this study is to establish an HLA database of platelet pheresis donors to supply compatible platelets for people who are refractory to platelet transfusion.

#### **Materials and Methods**

In this study, HLA database of platelet donors were gained among unrelated stem cell donors. DNA was extracted from the whole blood samples of recruited donors. The allele groups of HLA-class I (HLA-A&B) were determined at low resolution level (2-digit) by polymerase chain reaction-sequence-specific primer (PCR-SSP) and Real-time PCR techniques.

#### Results

Out of the 29,500 plateletpheresis donors, a total of 1890 donors were registered as HLA-matched platelet donors. So far, a number of 900 donors were genotyped for HLA-A&B at low resolution level. A database of at least 1000 or more plateletpheresis donors with known HLA is commonly necessary to find HLA-matched donors for most patients suffering platelet refractoriness.

#### Conclusion

A registry system of HLA genotyped platelet apheresis donors is useful to improve selecting of HLA compatible donor. Expansion of HLA database by rising the number of HLA typed donors facilitates the provision of compatible platelets for platelet transfusion refractoriness patients and support long-term platelet transfusions.





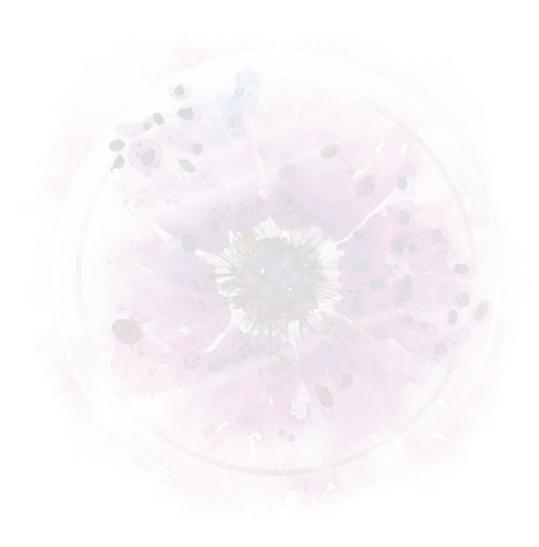






# Keywords

HLA ,platelet apheresis, database















# Misdiagnosis in maxillofacial fibro-osseous lesions. Interesting case presentation with long term follow-up

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#### Introduction

The term fibro-osseous lesion is descriptive and does not constitute a specific diagnosis. A diverse groups of processes could be caused replacement of normal bone by fibrous tissue containing a neo-mineralized product.

The major type of fibro-osseous lesions of the jaws with different etiology are as follow, fibrous dysplasia, cemento-osseous dysplasia and ossifying fibroma. All of these may exhibit similar histopathogy.

#### **Materials and Methods**

Several misdiagnosis of FOL cases received for re-evaluation from personal private office archives were chosen.

#### Results

The reasons for incorrect diagnosis referred to improper size of incisional biopsy, different phases of maturation or synchronicity of two different lesions in some cases of FOL and finally non correlation between histopathologic findings and clinical and radiological features.

#### **Conclusion**

The most important thing for preventing misdiagnosis in FOL is to communicate with clinicians and radiologists to make an exact diagnosis for leading the patient to an appropriate management.

#### **Keywords**

Fibro-osseous lesions, Misdiagnosis













# Iranian Stem Cell Donor Registry (ISCDR) Report from 2009 to 2023. National Hematopietic Stem Cell Bank

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#### Introduction

More than 80 diseases are cured using bone marrow transplantation. Iranian Stem Cell Donor Registry (ISCDR) established in February 2009 through Iranian Blood Transfusion Organization (IBTO) for recruiting, training, registering and maintaining of voluntary unrelated hematopoietic stem cell donors. The need estimated 700 unrelated BMT annually in Iran .Here we presenting achievements, challenges and goals.

#### **Materials and Methods**

Collection of Iranian Stem Cell Donor Registry data from 2009 to 2023.

#### Results

we organized 33 centers in 31 provinces and recruited 80000 voluntary unrelated hematopoietic stem cell donors of which 35000 are low resolution HLA-A,B & DR typed and had 38 BMT transplantation.

#### Conclusion

Iran need a registry size of around 2 million voluntary unrelated hematopoietic stem cell donors for annual 700 unrelated cases of BMT. One of the main challenges is setting up high throughput HLA typing technology of Donors.

#### Keywords

bone marrow transplantation, donor registry, IBTO, ISCDR.











# Development of automation in Immunohematology testing in IBTO

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#### Introduction

Hemagglutination based tube technique though still a Gold Standard, has many limitations, particularly in a blood centers having heavy workload. Human errors, lack of consistency in reading agglutination reaction, variability of red cell concentration in red cell suspension, elution of low affinity antibodies during the washing by centrifugation, are considered as part of limitations of this method. Automation in immunohematology testing results in the following benefits: Barcode system prevents sample identification errors, prevention of human errors in interpretation of results, prevention of transcription errors while documenting the results. Therefore, since 1401, the program of developing and establishing the automation of immunohematology tests has been implemented in the Iranian Blood Transfusion Organization (IBTO).

#### **Materials and Methods**

Automated platforms available for forward and reverse ABO grouping, Rh typing/weak D test, phenotyping of minor blood groups, red cell antibody screening, are performed by the following three systems and techniques: Ortho Clinical Diagnostics, is based on column agglutination technology (CAT). Diagast, uses the principle of erythrocyte magnetized technology (EMT) which avoids centrifugation and washing steps. Immucor platform is based on principle of solid phase red cell adherence assay (SPRCA).

#### Results

We have an ABO & Rh blood grouping automation system in 20 blood transfusion centers, which is equivalent to 80% of the annual donation. But by the end of 1402, this amount will be expanded to 100% of provinces and Blood donors. Rh (C c, E, e &Kell) blood grouping is performed by automation system in 6 blood transfusion centers, the provinces that have the most thalassemia patients. Antibody screening on blood donors with automation method on 1500,000 blood donors is also being implemented.

#### Conclusion

The automation systems for ABO grouping, Rh typing / weak D test, red cell antibody screening for blood donors has been implemented in the Iranian Blood Transfusion Organization. The phenotype of minor blood group on leuko-reduced blood bags for the













transfusion to the thalassemia patients and other repeated recipients also are performed by automation methods.

### Keywords

ABO& Rh typing, Automation













# Comparing Jaffe and Enzymatic Methods for Creatinine Measurement at Various Icterus Levels: Will It Affect the Priority of Liver Transplant Allocation?

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#### Introduction

The Model for End-Stage Liver Disease (MELD) scoring system is used to prioritize liver transplantations and assess the disease severity. This includes international normalized ratio (INR), creatinine, and total bilirubin. There are various methods to measure creatinine, which can cause MELD scores do not reflect the situation accurately. The goals of this research were to evaluate the impacts of various icteric levels on creatinine measurement and liver transplant allocation and to establish a reliable cut-off for bilirubin interference in creatinine measurement.

#### **Materials and Methods**

The icteric index was set up on an autoanalyzer for a simpler selection of icteric samples. A total of 400 leftover serum samples from 356 patients were selected and categorized into four groups based on their icteric indices and total bilirubin levels, including non-, mild, moderate, and severe icteric serum samples. The specimens of all four groups were analyzed for creatinine using both chemical Jaffe and enzymatic methods, and the results were compared. Concurrently, the specimens of patients candidates for liver transplantation (83 patients) were classified into 3 groups, based on their bilirubin level, and analyzed and interpreted similarly. Then, the MELD scores were calculated and compared in the three groups.

#### Results

The creatinine concentrations showed higher results using the enzymatic method than the Jaffe method, and the mean difference of creatinine increased from 0.08 in non- to 1.95 in severe icteric groups. Furthermore, in patients who were candidates for liver transplantation, the enzymatic method produced higher results for creatinine and subsequently for MELD scores. The differences between methods for both creatinine and MELD score (p-











value:.<0.0001 and 0.027) were significant when bilirubin concentration crossed the border of 4 mg/dl.

#### Conclusion

The chemical Jaffe is a readily available and considerably cost-effective method for creatinine measurement. Although it is influenced by a variety of known and unknown interfering substances, it should be applied with care when working with icteric samples, and alternative techniques like the enzymatic method should be taken into account when the bilirubin level goes over a specific limit.

#### Keywords

Jaffe enzymatic creatinine icteric interference















## The effect of direct oral anticoagulants (DOACs) on APCR assays: A unicenter experience

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#### Introduction

Nowadays, the use of new direct oral anti-coagulant medications (DOACs) is widely used for the prevention or treatment of thrombosis due to their advantages over warfarin. One of the most important advantages of DOACs compared to warfarin is the lack of need to frequent routine laboratory monitoring. Although these drugs do not affect coagulation factors as strongly as warfarin, however, due to their mechanism of action (direct inhibitory effects against coagulation factor II (Dabigatran) or factor X (Rivaroxaban, Edoxaban and Apixaban) they may interfere with thrombophilia laboratory panel tests that are based on clotting time measurement. One of these tests, which is the screening method of F V Leiden is the APC-R test. In this study, we decided to investigate the possible significant effect of DOACs on the APC-R test (false negative) in the population of patients referred to the special coagulation laboratory of IBTO for thrombophilia testing.

#### **Materials and Methods**

During a six months period from March to September 2023 any cases who requested both APC-R and factor V Leiden molecular testing were selected as study population. Clinical data including anticoagulant medications evaluated in addition to the results of APC-R and FV Leiden molecular tests. The APC-R was evaluated by reagent and instrument from Stago company with cut off more than 120 seconds as normal (no pathogenic allele for F V Leiden). FV Leiden G1961A was evaluated by real-time PC-R technique. All patients signed the informed consent form for permission of using their laboratory data for research purposes.

#### Results











In a total of 31 patients with both APCR and FV Leiden test results,7 were heterozygous (22%) and the others were carried out wild type (normal) alleles. No pathogenic homozygous FV Leiden G1961A was found. 6 patients were on DOACs treatment (one heterozygous for FV Leiden and the other five were normal). APC-R test results in all patients (normal and heterozygous) were consistent with molecular test results as gold standard method except for one patient who showed normal APC-R test result (false negative) despite heterozygosity for FV Leiden G1961A mutation. Regarding this mismatching between phenotype/genotype laboratory testing, re-sampling was done with consideration of time of sampling before the next dose of DOACs intake and the APC-R result became consistent (less than 120 s) with molecular testing

#### Conclusion

Due to the high probability of a false negative result by APC-R method for factor V Leiden mutation in patients who are on DOACs treatment, it is suggested that molecular testing only is requested in these cases and/or sampling time for APC-R test considered to be just before taking the next dose of medication.

#### **Keywords**

DOACs APC-R FVLeiden











# Multifocal EBV-associated smooth muscle tumors in a patient with cytomegalovirus infection after liver transplantation: a case report from Shiraz, Iran

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#### Introduction

Immunodeficient patients, including the recipients of solid organs, exhibit an increase in the incidence of neoplasms. Post-transplant smooth muscle tumor (PTSMT) is a distinct and infrequent entity of these groups of neoplasms. Epstein–Barr virus (EBV) is considered to be involved in the etiology of this neoplasm.

#### **Materials and Methods**

A 28-year-old man who underwent liver transplantation presented with abdominal pain and diarrhea for several months. He had a history of resistant systemic cytomegalovirus (CMV) infection after transplantation. Radiologic evaluation and colonoscopy revealed multiple liver, spleen, lung, and colon lesions. Microscopic assessment of colon and liver lesions using IHC study were in favor of spindle cell proliferation with mild atypia and a mild increase in mitotic rate without any necrosis, with features of smooth muscle tumor. Considering the transplantation history, EBER chromogenic in situ hybridization (CISH) study on paraffin blocks was requested, which demonstrated EBV RNA in tumor cell nuclei, suggesting EBV-associated smooth muscle tumor. In addition, PCR for CMV on paraffin blocks was positive. PCR for EBV and CMV viremia were negative. The dosage of immunosuppressive agents was reduced, and currently, he is being followed, with slow expansion in the size of the lesions.

#### Results

#### **Conclusion**

Although the incidence of post-transplant smooth muscle tumors (PTSMTs) is low, it should be remained in the differential diagnosis in post-transplantation patients, especially dealing with multifocal tumors. As strong stimulant for smooth muscle tumors, close follow-up and screening for EBV and CMV infection and early treatment at the time of diagnosis are recommended to avoid these virus-induced tumors.











# Keywords

EBV CMV Post-transplant-smooth-muscle-tumor EBER













# Termination of Repeat Testing in Chemical Laboratories Based on Practice Guidelines: Examining the Effect of Rule-Based Repeat Testing in a Transplantation Center

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#### Introduction

Although the automation of instruments has reduced the variability of results and errors of analysis, in some laboratories, repeating a test to confirm its accuracy is still performed for critical and noncritical results. However, the importance of repeat testing is not well established yet, and there are no clear criteria for repeating a test.

#### **Materials and Methods**

In this cross- sectional study, all repeated tests for 26 biochemical analytes (i.e., albumin, alkaline phosphatase (ALP), alanine aminotransferase (ALT), amylase, aspartate aminotransferase (AST), bilirubin total (BT), bilirubin direct (BD), blood urea nitrogen (BUN), calcium, chloride (Cl), cholesterol total (CholT), creatine kinase (CK), creatinine (Cr), glucose, gamma-glutamyl transferase (GGT), high- density lipoprotein-cholesterol (HDL-c), iron, lactate dehydrogenase (LDH), LDL-c, lipase, magnesium (Mg), phosphorus (Ph), protein total (ProtT), total iron binding capacity (TIBC), triglyceride (TG), and uric acid) were assessed in both critical and noncritical ranges over two consecutive months (routine subjective test repeats in the first month and rule-based repeats in the second month). To determine the usefulness of test repeats, differences between the initial and verified results were compared with the allowable bias, and repeat testing was considered necessary if it exceeded the allowable bias range. All causes of repeat testing, including linearity flags, delta checks, clinically significant values, and critical values, were also documented. All data, including the cause of repeats, initial and verified results, time, and costs in the two consecutive months, were transferred to Microsoft Excel for analysis. For comparison of data between the months, Student's t-test was used.

#### **Results**









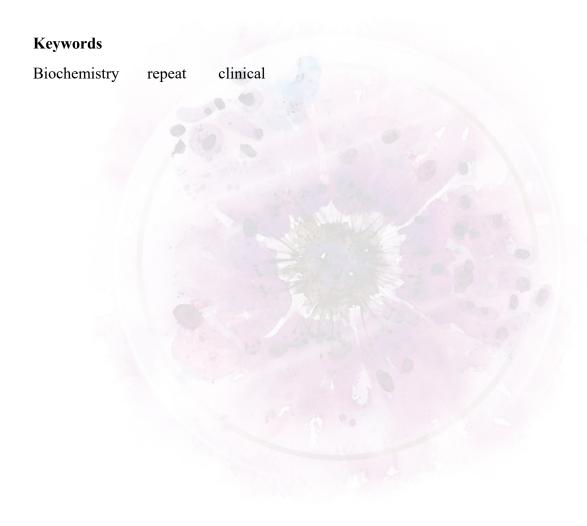




Results. A total of 7714 repeat tests were performed over two consecutive months. Although a significant decline (38%) was found in repeated tests in the second month (P < 0.001), there was no significant change in the percentage of unnecessary repeats (77% in the first month and 74% in the second month). In both consecutive months, AST and ALT were the most commonly repeated tests, and delta check was the most common cause of repeat testing. Mg, ALP, AST, and lipase showed the highest rates of necessary repeats, respectively (the least stable tests), while albumin, LDL, and CholT tests showed the highest rates of unnecessary repeats, respectively (the most stable tests). The total cost and delay in turnaround time (TAT) due to repeated testing decreased by 32% and 36%, respectively.

#### **Conclusion**

Although repeat testing has been shown to be unnecessary in most cases, having a strict policy for repeat testing appears to be more valuable than avoiding it completely. Each laboratory is advised to establish its own protocol for repeat testing based on its own practice.













# And the Oscar Goes to Peripheral Blood Film for the Detection of Lead Poisoning in a Complicated Toxic Patient: A Case Report with a Review of Laboratory Clues

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#### Introduction

Peripheral blood smear examination is an invaluable laboratory test, which provides the complete hematologic and/ or nonhematologic picture of a case. In addition to verifying the results of automated cell counters, it has the potential to identify some pathologic and morphologic changes that remain hidden using the cell counters alone.

#### **Materials and Methods**

A 40-year-old man with a three-year history of alcohol intake and marijuana abuse presented with severe lower extremities of the bone and abdominal pain. Physical examination showed high blood pressure, high pulse rate, and abdominal tenderness. He underwent extensive laboratory and imaging tests, and cholecystectomy and bone marrow studies were associated with no definite diagnosis. Right after all these invasive, expensive, and time-consuming investigations during a month, finding coarse basophilic stippling in the red blood cells in the peripheral blood smear by an expert led to the final diagnosis. Elevated blood lead level and the presence of ring sideroblasts in the bone marrow study confirmed the diagnosis of lead poisoning, and the patient responded well to chelator therapy in a short period.

#### Results

#### Conclusion

#### Conclusion

This case clearly showed the value of peripheral blood smear review and its impact on patient care. In order not to lose the cases, laboratories are recommended to design their own policy for peripheral blood smear review. The peripheral blood smear is the fastest, simplest, and













most available screening test, which can prevent many mis- diagnoses and malpractices. It provides rich morphological information, among which basophilic stippling is highly suggestive of lead poisoning.

### Keywords

Lead Poisoning smear













# Histopathologic Changes of Appendicitis Stage During the COVID-19

#### **Pandemic**

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#### Introduction

Background: We decided to compare the pathology stage of appendicitis in patients referred to Firoozabadi Medical Center before

and after the official announcement of the coronavirus outbreak in Iran because we believe that people's fears of COVID-19 are

keeping them away from hospitals and it likely causes them to come in later stages of the disease. Therefore, this study aims at

investigating the effect of the COVID-19 pandemic on the stage of appendicitis at presentation.

#### **Materials and Methods**

Methods: In this retrospective study, histopathology records of all acute appendicitis patients who underwent an emergency

appendectomy in the surgical unit in our institute between December 2019 and April 2020 were reviewed retrospectively. The study

period was designed to include 2 months before and 2 months after the officially announced onset of the COVID-19 outbreak in Iran

on February 20, 2020. All cases of complicated appendicitis (perforated appendicitis, phlegmonous appendix, itis or abscess) were

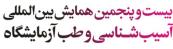
excluded. Descriptive statistics were used to describe our study variables. Furthermore, ordinal logistic regression was used to











investigate the effect of the COVID-19 pandemic and demographic variables on the stage of appendicitis at presentation. Data were

analyzed using SPSS Statistics Version 22.

#### **Results**

The study was conducted on 170 clinically diagnosed acute appendicitis patients. The odds ratio for gender was equal to

0.45 (0.23, 0.86), which means that women presented at an earlier pathological stage than men (p = 0.016). Also, patients who had

health insurance were 50% less likely to present in later pathological stages than those who did not (p = 0.024). The COVID-19

outback did not have a significant role in the pathological stage at presentation (p = 0.235).

#### Conclusion

The number of appendicitis patients was down by about 50% following the outbreak announcement in Iran.

Surprisingly, we did not find any significant changes in the distribution pattern of appendicitis pathological staging after the outbreak.

Being uninsured and male sex were found to have the most significant roles in delayed hospital presentation and higher pathological

stages in patients with acute appendicitis.

#### **Keywords**

Appendectomy, Histopathological Examination, Coronavirus Outbreak











# The role of main signaling pathways in the pathogenesis of oral lichen planus

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#### Introduction

Oral Lichen Planus (OLP) is a chronic inflammatory disorder affecting the oral mucosa, resulting in inflammation and tissue damage within the oral cavity. There is compelling evidence of a potential link between OLP and the progression of several chronic diseases in the oral cavity, including oral squamous cell carcinoma (OSCC). Therefore, a deeper understanding of the underlying mechanisms involved in OLP is of paramount importance in the search for effective treatment strategies. Factors likely to play a role in the pathogenesis of OLP include immune system activation, inflammatory cytokines, oxidative stress, and cell signaling pathways. Thus, this review explored the role of main signaling pathways in the pathogenesis of OLP.

#### **Materials and Methods**

Using the search terms "oral lichen planus," "pathogenesis," "OLP", "signaling pathways," and others, we searched PubMed, Google Scholar, and Web of Science databases for information on OLP and signaling pathways. Although some previous research summarized the involvement of the etiology of OLP, including stress, genetic predisposition, and autoimmune diseases, the scope of the research was too broad and the mechanisms, especially the signaling pathways, were not adequately explored according to our research.

#### **Results**

Several signaling pathways identified as critical players in the pathogenesis of OLP included the NF- $\kappa$ B pathway, JAK /STAT pathway, MAPK pathway, PI3K/Akt pathway, and Wnt/ $\beta$  catenin pathway. Our results indicate that understanding the association of the miRNA-mRNA-cytokine pathway is likely the main reason for the pathogenesis of OLP. The results showed that several cytokines play a role in the development of OLP. Since this disease is a T cell-mediated autoimmune disease, it is likely that dysregulation of immune-related proteins mediated by regulatory molecules such as miRNAs in mentioned signaling pathways plays an important role in the progression of OLP to malignancies.

#### Conclusion

Dysregulation of signaling pathways may contribute to the persistent inflammation, immune system dysfunction, and abnormal cell proliferation observed in OLP. Therefore, targeting these specific signaling pathways may offer therapeutic potential for the development of novel treatment approaches for OLP.





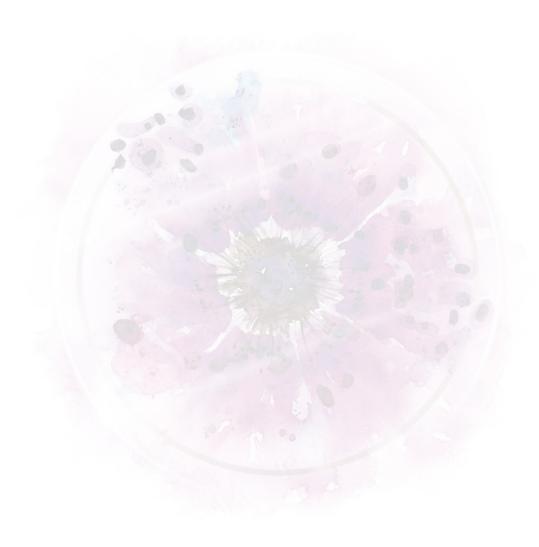






# Keywords

OLP, signaling pathways, pathogenesis















### The activity of Cord Blood Banking during 13 years in Iran National Cord Blood Bank

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#### Introduction

Nowadays, umbilical cord blood (UCB) is used as a source of hematopoietic stem cells in the treatment of malignant and non-malignant hematopoietic diseases and immunodeficiency disorders. And for this purpose, many Cord Blood Banks have been established around the world to collect and freeze cord blood units. In this study, we summarized 13-year experiences in CB processing and storage in Iran National Cord Blood Bank (INCBB).

#### **Materials and Methods**

All the procedures were done according to the last version of international standards published by Netcord/FACT organization criteria. These methods included, Donor selection, Cord blood collection, Cord blood volume reduction, TNC count, viability test, CD34+ absolute count, Screening tests and HLA typing.

#### Results

: During November 2010 to 2023, 21344 donors registered in INCBB network and within them 14347 unites were collected from 6 maternity hospitals in Tehran. All donors signed consent forms and screened based on medical history and laboratory tests. Selected units which were about 30.2% of collected units were processed according to the Netcord standards and 4340 units passed the INCBB banking and storage criteria. The mean±SD volume of units was 179.05±33.81 ml and after volume reduction, the mean±SD of TNC and viability were  $17.65 \times 108 \pm 5.9 \times 108$ , and  $90.81 \pm 6.95\%$  respectively. In the past six years, the CD34 absolute count has shown a remarkable 65.41% increase, currently reaching a level of  $2.88 \times 106 \pm 1.58 \times 106$ .

#### Conclusion

In recent years, the cord blood bank of the Blood Transfusion Organization has tried to store Umbilical Cord Blood units that have a higher cell dose and have acceptable transplant criteria. So far, 28 units of Umbilical Cord Blood stored in this center were transplanted to









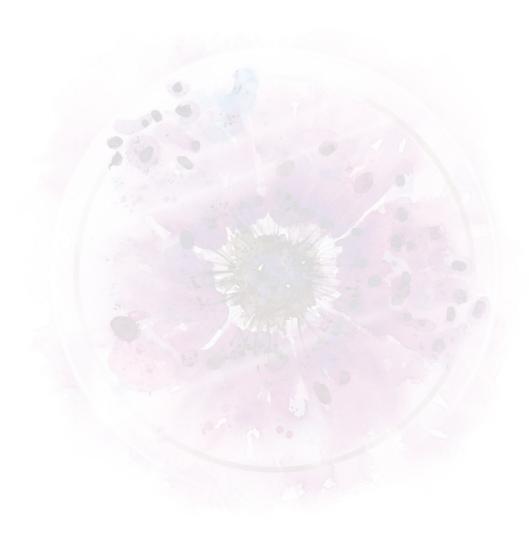




children with various Hematopoietic disorders. And currently, this center has focused on methods of improving cord blood transplantation, expansion of CB units, and optimization of methods of using Haplo-Cord transplantation.

#### Keywords

UmbilicalCordblood, Hematopoieticstemcells, hematopoietic disorders













# The role of specific miRNAs in the development of new treatments in regenerative dental medicine

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#### Introduction

Along with advances in regenerative medicine, microRNAs (miRNAs) can be used in the regeneration of dental tissues, especially tissues derived from the pulp. specific miRNAs can play a role in the induction or inhibition of odontogenic differentiation of dental pulp stem cells (DPSCs) by targeting different genes. Understanding the role of these miRNAs will help develop new treatments in regenerative medicine.

#### **Materials and Methods**

Articles were searched in PubMed, Google Scholar, and Web of Science databases using the keywords miRNAs, DPSCs, odontogenic differentiation, and regenerative dental medicine. A comprehensive search was performed by both authors.

#### **Results**

Review of the studies revealed that the expression profiles of miRNAs in DPSCs follow a specific pattern. Several studies have shown that miRNAs are important factors in promoting or suppressing DPSC differentiation. The miRNAs that promote odontoblastic differentiation include miR-27a-5p, miR-125a-3p, miR-146a-5p, miR-223, miR-675, miR-720, and miR-3065. In addition, a specific group of miRNAs, including miR-135b, miR-140-5p, miR-143, miR-143-5p, miR-215, miR-219a-1-3p, miR-295-5p, miR-488, and miR-508-5p play an important role in suppressing odontogenic differentiation.

#### Conclusion

Stimulation of DPSCs with specific miRNAs can be useful in the treatment of dental pulp diseases. Several miRNAs played important roles in promoting or inhibiting odontogenic differentiation of DPSCs by targeting various genes such as LTBP1, Fyn, NOTCH1, Smad3, DLX3, DNMT3A, and DNMT3B. Consequently, the use of miRNAs can be a revolution for the future of new regenerative treatments in endodontics.

#### Keywords

miRNAs .DPSCs .regenerative dental medicine













# MicroRNAs and signaling pathways effective in the differentiation of DPSCs and their applications in dental regenerative medicine

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#### Introduction

Human dental pulp stem cells (hDPSCs), among the promising cell sources in tissue engineering and regenerative therapies, have recently attracted increasing attention. They are used for various treatments in restorative dentistry, such as restoration of the dentin-pulp complex and periodontal tissues. Understanding the mechanisms regulating the differentiation of DPSCs is essential for their clinical application. Studies have shown that miRNAs play a role in regulating the differentiation of these cells through specific signaling pathways. However, incomplete understanding of the mechanisms regulating their differentiation has limited their clinical application.

#### **Materials and Methods**

Texts were searched in PubMed, Google Scholar, and Web of Science databases through July 2023. The keywords DPSCs, miRNA, signaling pathways, regenerative dental medicine, and tissue engineering were used in the comprehensive search for articles by two authors.

#### **Results**

Studies have shown that the MAPK pathway is one of the most common signaling pathways in odontogenic differentiation. It has been found to be associated with cell differentiation. In this way, certain miRNAs affect odontogenic differentiation by binding to the genes of this pathway. Other known signaling pathways in odontogenic differentiation include the PI3K/Akt pathway. Studies have mentioned a cross-talk between the PI3K/Akt pathway and Wnt/β catenin as a known signaling involved in odontogenic differentiation. In addition, the role of TGF-β signaling pathway in the differentiation of dental papilla cells has been reported.

#### **Conclusion**

DPSCs are the focus of interest in the field of regenerative therapies because they are easily accessible, can be isolated by noninvasive methods, and have the potential to differentiate into various cell lineages. But limited knowledge of the mechanisms that regulate their differentiation has made their clinical application challenging. Therefore, understanding the regulatory mechanisms underlying the differentiation of DPSCs is essential for their therapeutic application. The discovery of miRNAs and their mechanisms of action via various signaling pathways in the differentiation of stem cells, which are key components in









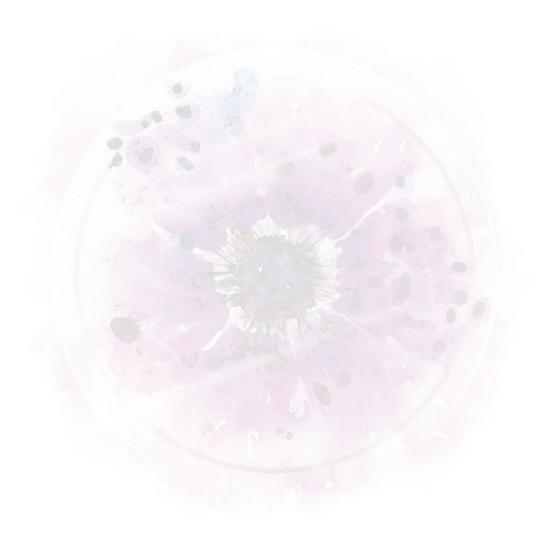




the field of regenerative therapies, plays a very important role in the progress and development of dental tissue engineering. Our study showed that among the signaling pathways involved in odontogenic differentiation of DPSCs, MAPK, and PI3K-Akt are known to be the most important signaling pathways.

### Keywords

DPSCs, miRNAs, signaling pathways













# The Association Between Mortality due to COVID-19 and Coagulative Parameters: A Systematic Review and Meta-Analysis Study

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#### Introduction

Aims and Objectives: This systematic review and meta-analysis study aimed at evaluating the association between mortality due to COVID-19 with coagulative factors.

#### **Materials and Methods**

Methods: A systematic search was conducted on electronic databases from the beginning of the pandemic until July 2023 to identify relevant studies on COVID-19 patients and their laboratory findings related to coagulation markers and mortality outcome. Eligibility criteria were defined based on the PICO framework, and data extraction was performed by two authors independently using a standardized sheet. Statistical analysis was accomplished using the random effects model, and heterogeneity among studies was assessed using the I2 test. R and RStudio were used for statistical analysis and visualization.

#### **Results**

Results: Our systematic literature search yielded 5,994 studies, with 35 studies meeting the inclusion criteria for our meta-analysis. The mean platelet count was significantly lower in deceased COVID-19 patients compared to survivors (-21.08), while aPTT and fibrinogen levels did not show significant differences. The pooled mean difference of D-Dimer, INR, and PT were significantly higher in deceased patients (2.23, 0.08, and 0.76, respectively). These findings suggest that platelet count, D-Dimer, INR, and PT may serve as potential indicators of mortality in COVID-19 patients.

#### **Conclusion**

Conclusion: The results of our systematic review and meta-analysis revealed a significant reduction in the pooled platelet count among deceased individuals when compared to survivors. However, no significant distinctions were observed in the pooled mean activated partial thromboplastin time (aPTT) and fibrinogen levels between the deceased and survivor groups. On the other hand, there were noticeable variations in the pooled estimated mean of International Normalized Ratio (INR), prothrombin time (PT), and D-Dimer levels, with significantly higher values in the deceased group compared to those who survived.

#### **Keywords**

COVID-19, mortality, coagulation, laboratory findings











# Depth of invasion and extranodal extension": The influential factors to predict survival rate of oral tongue squamous cell carcinoma patients

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#### Introduction

Background and objectives: Cancer staging is an important step in diagnosis and is closely related to determination of patients' prognosis and designing the appropriate treatment strategy. Squamous cell carcinoma (SCC) of the tongue is a malignant tumor that comprises 90% of the oral cavity tumors. American Joint Committee on Cancer has published the latest version of staging system for tongue SCC; but it is important to know whether this change in staging and addition of depth of invasion (DOI) and the extranodal extension (ENE) to the pT have any influence on patients' prognosis. Therefore, the present study was designed to compare the survival of patients with tongue SCC, staged based on this new system with the old staging system.

#### **Materials and Methods**

Materials and methods: In this descriptive-analytical study, the pathology records of patients with tongue SCC who underwent surgery at Pathology Department of Cancer Institute Hospital (IKHC), 2017-2021, were collected by referring to the hospital information system archive of the hospital. Patients' age, sex, tumor size, DOI, lymph node involvement, ENE, tumor stage and grade, focality, vascular and perineural invasion, and involvement of surgical margins were recorded. Also, information about recurrence, metastasis, type of treatment, and death until data collection were collected. Then the rate of change of T, N and stage were calculated based on AJCC 7 and 8 protocols and its association with survival were analyzed using SPSS v.21.

#### Results

Results: Of 204 patients, 53.4% were men; 70.1% were older than 45 years old. Recurrence rate was 18.12% and mortality rate was 12.17%. The majority of patients who died had recurrence (75%), while only 11.9% of patients who survived had recurrence (P<0.001). Significant changes in staging system 2021 resulted in upstaging of 64 patients (31.4%) in total stage, 91 patients (44.6%) in T, and 30 patients (14.7%) in N (P<0.001). Kaplan Meier analysis showed that mean survival of patients was not different between patients upstaged as T and stage based on 2016 and 2021 staging system (P>0.05); while patients with upstaged N had a shorter mean survival (32.43±5.13 vs. 50.38±1.46; P=0.001).











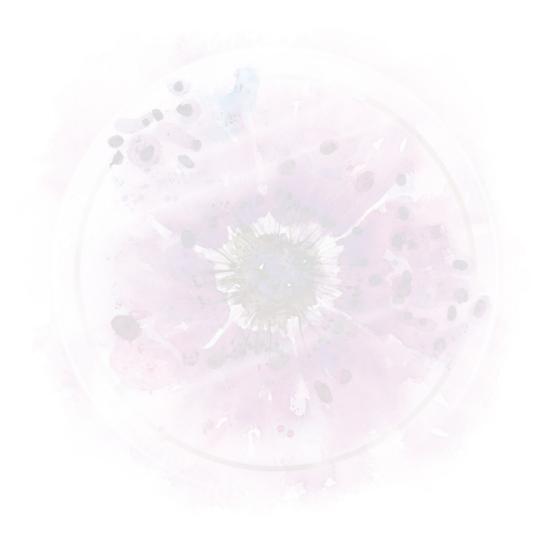


#### Conclusion

Conclusion: This study showed the importance of pathology reports based on the latest edition of the AJCC and the accuracy in examining factors such as DOI and ENE, and the need to pay attention to these factors in choosing the appropriate treatment methods by the oncologist.

#### Keywords

Carcinoma, Squamous Cell; Survival; Staging













# Platelet secretion defects in Hermansky -Pudlak syndrome: A case report

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#### Introduction

Hermansky-Pudlak syndrome (HPS) is a subtype of platelet storage pool deficiency (SPD), specifically  $\delta$ -SPD. This disorder is associated with a bleeding diathesis and a prolonged bleeding time. The platelet function tests, generally demonstrate diminished or entirely absent second wave of aggregation in response to ADP, collagen, or epinephrine. Electron microscopy is necessary to observe absent dense granule contents and to exclude other causes of secretion defects.

#### **Materials and Methods**

A 12-year-old male with repeated and prolonged episodes of epistaxis. He had a history of easy bruising, increased bleeding with minor cuts, and surgical procedures that needed multiple transfusions of platelets and packed red blood cells. The total ISTH-BAT bleeding score was eight. Physical examination demonstrated oculocutaneous albinism and nystagmus. There is no family history of albinism or significant bleeding symptoms in the family. The patient referred to the IBTO special coagulation laboratory for laboratory assessments of bleeding disorders.

#### Laboratory Data:

The platelet count was normal (353 × 103/ $\mu$ L). The aPTT and PT were normal. The coagulation factors VIII, IX, XI and XII, vWF antigen and ristocetin cofactor activity (VWF:RcO) were all normal. Platelet function studies demonstrated the absence of a secondary wave of aggregation in response to collagen (2.0 & 5.0  $\mu$ g/ml), and epinephrine (10.0  $\mu$ M). There was no ATP release with ADP (10  $\mu$ M), collagen (2.0  $\mu$ g/ml), and AA 1.5 Mm agonists in lummiaggregometry. The response to two doses of ristocetin (0.7 & and 1.5  $\mu$ g/mL) was normal. Whole-mount electron microscopy revealed no dense granule in the platelets.











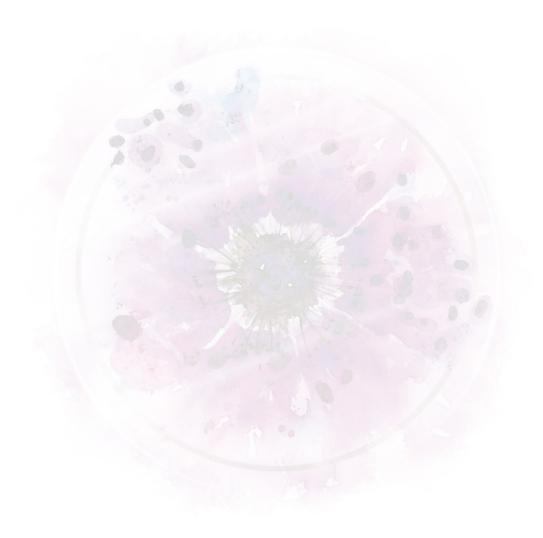
#### **Results**

#### Conclusion

HPS is a rare congenital bleeding disorder. The diagnosis is mainly made with clinical findings of syndromic presentation associated with bleeding diathesis. HPS should be considered in any patient with ophthalmic nystagmus and evidence of albinism. The combination of clinical presentation and laboratory findings confirms the diagnosis.

### Keywords

bleeding disorder platelet secretion disorders













# Epidemiological features trend of gastric cancer (GC) in Shahid Beheshti Hospital, Babol during 2000 to 2019

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#### Introduction

In Iran, high incidence and mortality rates of gastric cancer have been reported, especially in Mazandaran province. Understanding the epidemiology and process of gastric cancer can play a very important role in planning. This study was conducted with the aim of investigating the occurrence and changes trend of gastric cancer in north of Iran in Babol city due to the uncertainty of its trend in this region.

#### **Materials and Methods**

The present study is considered as a descriptive cross-sectional research that was conducted on patients with gastric cancer during 2000 to 2019 whose endoscopy or gastrectomy samples were registered in the Cancer Research Center at Babol University of medical Sciences. The pathology files of patients in Shahid Beheshti educational and therapeutic hospital who were diagnosed with gastric cancer after endoscopy or gastrectomy were extracted. Then, the necessary data was recorded in the checklist. Data were analyzed in SPSS V.26 software using T-Test and Chi-Square statistical tests.

#### Results

In this study, 637 patients were identified during the study period. According to the results, most of the patients were male (78.2%) and the predominant pathology observed was intestinal type (88.7%). The results show that male patients were significantly older at the time of diagnosis (P=0.002) and had a higher rate of cardiac tumors than female patients (P=0.034). The examination results of the gastric cancer trend over time show that diffuse-type pathology and poor differentiated tumor have increased significantly over time (P<0.001 and P=0.002, respectively), while no significant change was observed in the distribution of gender, age, and tumor location (P<0.05).

#### Conclusion

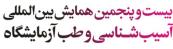
According to the findings of the present study, gastric cancer is three times more likely to be diagnosed in males than females and tumors with diffuse, lower stage, and poor











differentiation have increased in the 20-year period, but no trend was observed in the average age of disease diagnosis, gender ratio and tumor location.

### Keywords

gastric neoplasm, epidemiology, incidence













# Salivary gland tumors, A 7 year's study of histologic typed, sites, and sex distribution in hospitals affiliated to Shiraz University of Medical Sciences 2014 to 2020

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#### Introduction

Salivary gland tumors are one of the most important diseases of the head and neck region. So, recognition of their histological types, locations and gender will guide for better selection of diagnostic procedure and proper treatment protocol. The aim of this study is determination of the Prevalence of salivary gland tumors in hospitals affiliated to Shiraz University of Medical Sciences during the years 2014 to 2020.

#### **Materials and Methods**

In this cross-sectional study in Shiraz University of Medical Sciences affiliated hospitals, all the patients with salivary gland tumors who presented to Khalili and Ghadir hospitals during 2014 to 2020 are material of this study. The hospitals are located in the Shiraz, Iran, which is completely ethnically Iranian.

#### **Results**

Among 451patients, 71.4% (322 cases) had benign tumors and 28.6% (129 cases) had malignant tumors. The age range was from 10-95years and 56% of patients were male. The mean age of patients was 49.8. Individuals with benign tumors had significantly lower age at the time of diagnosis, in comparison to the malignant cases (46.2 years vs. 58.6 years, p < 0.001). WT (95.9%), lipoma,and SCC had a male predominance,while PA had a female predominance. Regarding the site of the tumors, parotid gland was the most common site (89.2%). Regarding the two most prevalent malignant tumors, these statistics stands for total male dominancy, with 25 cases (18.8%) for Mucoepidermoid carcinoma and 14 cases(10.5%)for Acinic cell Carcinoma.Our analysis of the most prevalent benign tumors revealed that at the time of diagnosis the mean ages of cases with Pleomorphic Adenoma and Warthin tumor were significantly lower and higher than the average age of patients with benign tumors, respectively(p < 0.001).

#### Conclusion

In summary, our findings indicate that parotid gland account for the majority of SGTs. Pleomorphic adenoma and Mucoepidermoid carcinoma were the most frequent benign and malignant SGT, respectively. Malignant tumors had a higher age of onset than benign ones. Certain histopathologic types had a strong gender predilection (WT). In conclusion, we demonstrate that ethno-geographic variation results in fairly diverse distribution of SGTs







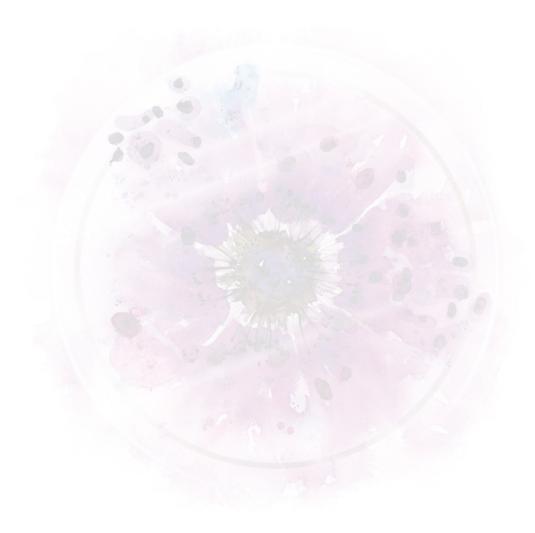




across tumor sites and histopathologic types. Further research into clinical and survival aspects of these pathologies are needed to elucidate the clinical factor and impact.

### Keywords

Salivaryglandtumors histologictyped Iranianpeople ParotidNeoplasms















## Co-existence of Hodgkin lymphoma and primary mediastinal large B-cell lymphoma

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#### Introduction

Besides introducing gray zone lymphoma as a distinct entity in WHO classification, synchronous diagnosis of a primary mediastinal B-cell lymphoma (PMBL) in patients suffering from Chronic Hodgkin's lymphoma (CHL) has been mentioned in recent literature. Frankly, either synchronous or metachronous occurrences of HL could be diagnosed in a single patient. Here we present a similar case, eighteen-year-old male who has synchronize HL and PMBL.

#### **Materials and Methods**

An eighteen-year-old male had an isolated cervical lymph node enlargement associated with a mediastinal mass about one year ago. The cervical lymph node was excised and diagnosed as classic Hodgkin lymphoma and he received appropriate treatment. One year later he developed mediastinal widening due to the enlargement of the pre-mentioned mediastinal mass. Now in his mediastinal lesion excised sample, diffusely distributed intermediate-size neoplastic cells were identified. These cells were composed of round to oval vesicular nuclei with clear cytoplasm. Some Reed-Sternberg-like cells are also seen. The neoplastic B-cells stained with CD30 and CD23. Conversely, CD5, CD15, and Pan CK were negative. Histo morphologic and IHC staining were all in agreement with the diagnosis of PMBL.

#### Results

#### Conclusion

The biological relativeness of CHL and PMBL is well known and the possibility of their transformation is well established. Synchronous PMBL with CHL has been stated in literature in young patients mainly females who were initially worked up for CHL. Its incidence is 0.9% with a worse outcome. However, studies have not shown any clonal relationship between them.

Conclusion: Although CHL could co-exist with PMBL and even transform into it, it seems they derive from two separate B-cell clones.

#### **Keywords**

Hodgkin lymphoma Mediastinal large B-cell











## Diagnostic approach to type 2B von Willebrand disease in seven affected family members

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#### Introduction

von Willebrand disease (VWD) is the most common hereditary bleeding disorder. VWD is divided into three types including Type 1, Type 2, and Type 3. Type 2 is divided into four subtypes 2A, 2B, 2M, and 2N based on clinical symptoms and different pathogenesis. Type 2B is a rare subtype and is characterized by gain-of-function mutation in VWF gene. Its diagnosis is crucial for treatment decisions since DDAVP medication is contraindicated in these patients. Near all mutations located in exon 28 of the VWF A1 domain. The increased affinity of VWF to glycoprotein Ib (GPIb-α) of platelets leads to thrombocytopenia. Definitive diagnosis of Type 2B is very challenging due to the heterogeneity of the disease and considerable technical complexity of laboratory tests.

#### **Materials and Methods**

In this study, seven family members who were suspected for type 2 VWD and referred to the IBTO special coagulation laboratory for definite diagnosis were investigated. Routine coagulation tests including prothrombin time (PT), activated partial thromboplastin time (aPTT), FVIII coagulant activity (FVIII:C), VWF antigen (VWF:Ag), VWF activity (VWF:IbM) and ristocetin induced platelet aggregation (RIPA) were performed for the patients. Molecular study of exon 28 VWF gene by Sanger sequencing method was done for evaluation of possible.

#### Results:

We presented the diagnostic approach to the 7 patients(4F/3M) from a family (first- or second-degree related ) suspected of type VWD 2B admitted to the IBTO special coagulation lab. The age range of the patients were 1-46 years old. As preliminary coagulation tests PT (median: 14.8, range: 13.1-16), aPTT(median: 40, range: 34.2-49.7) and Platelet count (median:  $156x [10] ^3\mu/1$  range:  $85x [10] ^3-299 [x10] ^3$ ) were done. The primary











VWD diagnostic test results were as FVIII:C(median: 32, range: 26-52), VWF:Ag (median: 25, range: 19–43) VWF:IbM (median: 8, range: 5–25). The ratio of VWF:IbM/VWF:Ag (median: 0.26, range: 0.2–0.7) was done for the first line screen for type 2 diagnosis and then low-dose RIPA test as a specific diagnostic test for type 2B was (0.6 mg/ml final concentration) (%)(median: 83, range: 66–100) which is compatible for a gain-to-function of VWF-platelet GPIb. At the end for discrimination between type 2B VWD from platelet type VWD

(so-called pseudo VWD ) VWF exon 28 sequencing was done and revealed Heterozygous mutation V1316M and P1266Q amino acid substitutions in this family and confirmed type 2B VWD.

#### **Results**

#### Conclusion

#### Conclusion

A step by step guideline-based approach in a specialized coagulation lab is needed for the correct diagnosis of type 2 B VWD as one of the subtypes needs different treatment approach.

#### **Keywords**

Exon 28 Type 2B VWD











## Ovarian Angiosarcoma in the Background of mature cystic Teratoma in a Pregnant Woman

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#### Introduction

Angiosarcoma is rarely detected in ovaries while it is much more common in deeper soft tissue. About one-quarter of all angiosarcomas originate from mature teratomas, even though the foremost malignant transformation of mature teratoma is squamous cell carcinoma. Here we represent one of the unusual presentations of an ovarian angiosarcoma.

#### **Materials and Methods**

A pregnant woman, G3L1Ab1 30 years of age and gestational age of 36W and 2d was presented to our hospital with fetal heart rate deceleration. Urgent delivery was done by Cesarean section and her placenta was sent for histopathology examination. Besides, the left side ruptured ovarian cystic lesion accompanied the placenta. Representative assessed sections of the placenta showed maternal malperfusion changes. On the other hand, microscopic examination of the ovarian cyst showed hemorrhage and anastomosing vascular channels lined by atypical endothelial cells arranged in an infiltrating pattern in a background of mature teratoma. Some Sertoli and Leydig cells were also in between which were decorated with inhibin and calretinin in immunohistochemical study. The aforementioned neoplastic cells stained positive for WT1 (cytoplasmic), CD31 and FLI1 although CD34 was negative. Finally, the diagnosis of ovarian angiosarcoma was made.

#### **Results**

#### Conclusion

Ovarian angiosarcoma presentation in pregnancy is rare and its diagnosis requires thorough observation and a comprehensive immunohistochemistry panel as in our case which CD34 was negative. Sex cord-stromal cells can be entrapped in the tumor making the diagnosis more challenging or the tumor can be misdiagnosed as a poorly differentiated Sertoli Leydig cell tumor.

#### **Keywords**

Angiosarcoma Mature cystic Teratoma Pregnancy













## Type 2N von Willebrand Disease: Accurate Diagnosis and Its Challenges

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#### Introduction

Quantitative or qualitative defects of the von Willebrand Factor (vWF) can lead to von Willebrand Disease (vWD), which is the most common inherited bleeding disorder worldwide. Type 2N vWD is an uncommon autosomal recessive disease in which vWF's binding capacity to FVIII is decreased. Due to the pathophysiology of Type 2N vWD, clinical manifestation and primary laboratory findings of affected individuals are similar to patients with mild to moderate hemophilia A. For optimal treatment and accurate genetic counseling, it is crucial to differentiate these disorders from each other. This review describes ways to diagnose type 2N vWD and differentiate it from hemophilia A based on the most recent guidelines from ISTH.

#### **Materials and Methods**

Considering the importance of accurate diagnosis of type 2N vWD due to the different inheritance pattern and treatment from hemophilia, the current review aims to investigate the latest and most accurate diagnostic methods by referring to more than 50 related articles in PubMed, Medline, Scopus, and Google Scholar database.

#### Results

Clinical manifestation and primary laboratory findings in type 2N vWD may resemble mild to moderate hemophilia A. In affected patients with type 2N vWD, FVIII:C levels range from 1 to 40 U/dl with normal or slightly reduced vWF antigen (vWF:Ag) levels, which leads to a low FVIII:C/vWF:Ag ratio (<1). Similarly in hemophilia A, FVIII:C levels can be measured from 1 to 30 U/dL with low FVIII:C/vWF:Ag ratio. Based on the most recent guidelines published by AHS, ISTH, NHF, and WFH use of either vWF:FVIIIB assay or genetic testing for suspected patients as definite methods of diagnosis is recommended. However, the vWF:FVIIIB assay alone will not be as informative as genetic testing. Thus, the panel suggests that the tests can be complementary in the diagnostic work-up of patients.

#### Conclusion













According to published articles, type 2N vWD is an uncommon autosomal recessive disease that resembles mild to moderate hemophilia A. Thus, it is essential to differentiate these conditions from each other using vWF:FVIIIB assay and genetic testing as definite methods of diagnosis. Moreover, it seems necessary for reference coagulation laboratories to set up these methods to further prevent misdiagnosis of type 2N vWD.

#### Keywords

von Willebrand Disease Hemophilia A















# Investigating the status of blood usage and wastage in Shohada Kargar Hospital, Yazd, Iran

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#### Introduction

Blood components are increasingly used worldwide, and their wastage is a challenge that must be managed. Most blood supplies are used during pregnancy complications, gynecology, trauma, surgery, hemato-oncological diseases, transfusion-dependent hemoglobinopathies, and chronic diseases. Shohada-e-Kargar Hospital is one of the topmost blood consumers in Yazd province, so in this study, we decided to study the trend of blood consumption and wastage in this hospital from 2016 to 2020.

#### **Materials and Methods**

The study was cross-sectional. Using the checklist prepared based on predetermined variables; we referred to the relevant databases in Shahada Kargar Hospital. The required information included the number of blood products requested, issued, discarded, and the type of products that were collected. The data was analyzed using SPSS version 23 and the chiscore test.

#### Results

The total number of requested blood components was 15,338 units. Total blood components demand, issued, and used decreased during the study period (p<0.001). The highest number of blood component requests was related to surgical wards (8520 units). The most requested product was Red Blood Cells (11800 units). The lowest requested blood component was Cryoprecipitate (542 units). A total of 399 blood components (3% of all blood components) were wasted. The ratio of crossmatch to blood transfusion was equal to 1.034.

#### **Conclusion**

The results showed that the demand and use of the blood components had a decreasing trend throughout the years of the study. The ratio of cross-match to blood transfusion was acceptable. It is suggested to use blood optimally and only request it when necessary where there is no substitute for blood to lower costs and preserve blood reserves, thus preventing shortages of blood and improving the outcome of patients.

#### **Keywords**

Blood wastage usage Blood component