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Research Article Open Access

Validation and cultural adaptation of Persian version of multidimensional health assessment questionnaire (MDHAQ) in rheumatoid arthritis patients

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Rheumatoid arthritis (RA) is a multidimensional disease. Multidimensional health assessment questionnaire (MDHAQ) is one of the latest questionnaires which provide useful information in a short time. We investigated the reliability and validity of the Persian form of MDAHAQ for the use of Iranian patients.Two groups of participants were recruited in this study. The validity test group included 110 patients, and the reliability test group included 140 patients. Translation and adaption of MDHAQ were performed by using Guillemin guideline. The reliability was tested by using test-retest and Cronbach's alpha for internal consistency. Persian version of health assessment questionnaire (HAQ) was used for assessing the criterion validity. Correlation between MDHAQ score and Disease Activity Score-28 (DAS28) and Clinical Disease Activity Index (CDAI) and Persian version of health assessment questionnaire (HAQ) was evaluated using spearman coefficient. Test-retest with intra-class correlation coefficient (ICC) gave a coefficient of 0.865 (95% CI: 0.809-0.904) for physical function and 0.786 (95% CI: 0.698-0.848) for psychological items. Cronbach's alpha was 0.885 and 0.705 for physical function and psychological dimensions respectively. Persian version of the MDHAQ had a good to strong correlation with the Persian version of the HAQ (ranging from 0.604 to 0.962) and also with CDAI (ranging from 0.616 to 0.838) and moderate correlation with DAS28 (ranging from 0.415 to 0.439).The Persian form of MDHAQ is a reliable and valid instrument for routine evaluation of RA patients in rheumatology clinic in Iranian RA patients.

Keywords: rheumatoid arthritis; multidimensional health assessment questionnaire (MDHAQ); persian version; health assessment questionnaire

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Research Article Open Access

Investigating the relationship between sonographic findings of carotid artery atherosclerosis with serum levels of salusin alpha and beta and other clinical and paraclinical findings in patients with rheumatoid arthritis

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Rheumatoid arthritis is a chronic inflammatory disease associated with cardiovascular complications and atherosclerosis. In this study we investigated the relationship between sonographic findings of carotid artery atherosclerosis with serum levels of salusin alpha and beta.The present study was a descriptive study that was conducted by examining 120 patients with rheumatoid arthritis. Clinical findings were recorded in a questionnaire and they were referred to radiology and laboratory centers for carotid artery ultrasound and measurement of thickness as well as measurement of salusin alpha and beta. Data analysis was performed using SPSS version 16 software. Our findings show that the mean carotid intima-media thickness were higher in men than in women ($P < 0.05$). Also, the duration of the disease was significantly associated with carotid lumen stenosis ($P < 0.05$). In addition, the presence of systemic involvement was significantly associated with carotid intima-media thickness ($P < 0.05$) and Salusin-beta was significantly correlated with carotid intima-media thickness and lumen stenosis ($P < 0.001$). On the other hand, the mean Salusin-alpha was significantly higher in women than in men ($P = 0.002$) and was significantly lower in patients with vasculitis than in patients without vasculitis ($P=0.005$). In addition, the mean Salusin-beta was significantly higher among patients who had experienced more than three relapses ($P=0.013$). According to the results of the present study, serum levels of salusin alpha and beta, can be effective in causing atherosclerosis and increasing the intima-media thickness of the carotid artery in patients with rheumatoid arthritis.

Keywords: rheumatoid arthritis; ultrasound; carotid artery; atherosclerosis; salusin

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Research Article **Open Access**

Investigating the relationship between anti-cyclic citrullinated peptide titer and reduction/discontinuation of oral prednisolone in patients with newly-diagnosed rheumatoid arthritis: A retrospective cohort study

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We aimed to investigate the relationship between anti-cyclic citrullinated peptide (anti-CCP) titer and the reduction/discontinuation of oral prednisolone in patients with newly diagnosed rheumatoid arthritis. In this retrospective cohort study, a total of 230 patients were enrolled and followed up. Baseline anti-CCP titer was obtained at the beginning of the diagnostic process. After the 18-month follow-up, patients in the remission phase were identified and divided, according to the pattern of use of prednisolone. Logistic regression was used to find the association between variables and reduction/discontinuation of oral prednisolone. a P-value < 0.05 was considered as statistically significant. The mean age of the population was 51.71 ± 13.08 years. Most of them (55.2%) were using methotrexate (MTX) alone. The baseline anti-CCP titers of most patients were in the normal range (53.5%). After 18 months of follow-up, 84 (36.5%) patients who reduced/discontinued the use of prednisolone were identified. There were no statistical differences between anti-CCP titer and reduction/ discontinuation of prednisolone in any type of the medication classes. The result of the logistic regression showed that patients under the treatment with MTX (as reference) had a significantly higher risk for reduction/discontinuation of prednisolone (odds ratio: 3.022, P < 0.001). No significant relationship was found between the baseline anti-CCP titers and the reduction/discontinuation of prednisolone in RA patients, after 18 months of follow-up.

Keywords: rheumatoid arthritis; anti-cyclic citrullinated peptide antibody; prednisolone; cohort study

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Research Article **Open Access**

Association of metabolic syndrome and its components with systemic lupus erythematosus

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Systemic lupus erythematosus (SLE) patients might manifest an increased prevalence of metabolic syndrome (MetS) components like insulin resistance, obesity, and dyslipidemia. Here we aimed to assess the interconnection between MetS components and SLE and attempted to divulge the potential contribution of MetS on SLE development. We enrolled 200 cases with SLE whose diagnosis was accomplished by American College of Rheumatology (ACR) criteria. MetS diagnosed was accomplished through the International Diabetes Federation (IDF) criteria. The frequency of MetS among the SLE population was 28.5%. Systemic lupus erythematosus disease activity index (SLEDAI) was not significantly different between SLE cases with and without MetS (P = 0.352). C reactive protein level was significantly higher in the SLE cases with MetS compared to those without MetS (P = 0.0412). Body mass index, fasting blood glucose, waist circumstance (both in males and females), total cholesterol, triglyceride, and low-density lipoprotein levels were significantly higher in SLE subjects with MetS compared to those without MetS. However, in both males and females, high-density lipoprotein level was significantly lower in SLE subjects with MetS compared to those without MetS. Obesity, cardiovascular disease, type 2 diabetes mellitus, dyslipidemia and hypertension were more prevalent in MetS cases among the SLE population. Treatment with metformin (odds ratio = 0.45, 95% CI: 0.21-0.96, P = 0.0398) and atorvastatin (odds ratio = 0.46, 95% CI: 0.23-0.92, P = 0.0287) was associated significantly with a decreased risk of MetS in SLE patients. An increased prevalence of MetS in the SLE population was observed, while these patients did not have worsen disease severity. All conventional components of MetS were associated with MetS development in the SLE population.

Keywords: systemic lupus erythematosus; metabolic syndrome; prednisolone, cohort study; body mass index

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Research Article **Open Access**

The demographic & clinical and laboratory findings of systemic lupus erythematosus patients based on registration system at Autoimmune Diseases Research Center of Kashan University of Medical Sciences from 2019 until 2024

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Systemic lupus erythematosus (SLE) is a systemic autoimmune disease. Knowing clinical and laboratory findings is helpful in treatment strategies and prognosis. Therefore, present study was conducted with this aim based on SLE registry system at Autoimmune Diseases Research Center of Kashan University of Medical Sciences from 2019 to 2024. This study was conducted on SLE who were included in study based on inclusion and exclusion criteria. Patient information (demographic findings, symptoms, complications, disease severity, and clinical findings) was recorded in a pre-prepared checklist and analyzed after entering it into the version 26 software. In this study, 326 patients with SLE were investigated, 10 patients (3.1%) were male and average age was 39.2 ± 10.3 years. There was history of SLE in 9.5%. Systemic lupus erythematosus disease activity index (SLEDAI) was 7.3 ± 5.5, renal activity score was 9.5 ± 2.1. About 84.6% patients had mild to moderate disease. Fluorescent antinuclear antibody (FANA) and anti-double stranded DNA (anti-ds-DNA) were positive in 88.3% and 43.9% of patients, respectively. The most common systemic symptoms were fatigue (30.4%), weakness (19.6%), dry eye (9.8%), renal involvement (28%). Joints involvement and photosensitive rashes were observed in 77.9% and 32.5% of patients, respectively. Deep vein thrombosis, anemia of chronic diseases, thrombocytopenia and pericardial effusion were occurred in 9.6%, 3.4%, 30.5% and 9.6% of patients, respectively. Flare-up of disease occurred in 21% of patients due to discontinuation of medication. This study showed that SLE frequency was higher in women than men and the most common symptom was joint and skin manifestations. Most cases of disease flare were stop of medicine so regular follow-up and control with medication are recommended.

Keywords: systemic lupus erythematosus; registry; prednisolone; clinical manifestations; flare-up

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Case Report Open Access

Multifocal osteonecrosis in a patient with systemic lupus erythematosus and antiphospholipid syndrome associated with pyoderma gangrenosum and other complications: A case report

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Systemic lupus erythematosus (SLE) is an autoimmune disease that has various environmental and genetic causes. The symptoms of this disease are very variable and can involve any organ such as the heart, kidneys, central nervous system, joints, skin, etc. In 6-30% of cases, this disease can be associated with antiphospholipid syndrome (APS), which causes vascular thrombosis. Osteonecrosis (ON) is a condition in which bone tissue undergoes necrosis due to lack of proper blood supply. A 37-year-old woman, a known case of SLE and APS was hospitalized due to a 5 × 10 cm pyoderma gangrenosum (PG) wound and pain and swelling in her leg due to a lupus flare caused by the arbitrary discontinuation of her medications from 3 months ago. The patient had a history of various hospitalizations due to complications of SLE and APS, such as PG, miscarriage, stroke, heart failure, Libman-Sacks endocarditis, and recurrent deep vein thrombosis. After stabilizing the patient's condition, most of the patient's symptoms resolved, but the pain and swelling of the leg continued. After performing magnetic resonance imaging (MRI), multifocal osteonecrosis was observed in all parts of the patient's femur and tibia, which is a rare manifestation in SLE or APS. The wide and varied symptoms of lupus have led to the development of comprehensive criteria for it, which, however, cannot replace clinical judgment in diagnosis. SLE increases the risk of ON due to its hypercoagulable state, and 3% of lupus patients develop ON, the most common site of which is the femoral head, and MRI is the gold standard for diagnosis.

Keywords: systemic lupus erythematosus; multifocal osteonecrosis; pyoderma gangrenosum; antiphospholipid syndrome

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Case Report **Open Access**

Systemic sclerosis leading to myelodysplastic syndrome: Case presentation and systematic review

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Systemic sclerosis (SSc) is a rare autoimmune disease that leads to fibrosis of the skin and internal organs, while myelodysplastic syndrome (MDS) is a disorder marked by ineffective blood cell production. The co-occurrence of SSc and MDS is rare, but it can occur due to the chronic inflammation and fibrosis associated with SSc, which may disrupt normal bone marrow function. This article presents a case of a 54-year-old male diagnosed with SSc for 4 years, who developed MDS characterized by refractory anemia. Despite iron therapy, his anemia persisted, leading to a bone marrow biopsy that revealed hypogranulation and hypolobulation in myeloid precursors, confirming the MDS diagnosis. A systematic review of the literature, including studies from PubMed, Web of Science, and Scopus, identified four relevant articles discussing the association between SSc and MDS. These studies highlight the rarity of this co-occurrence, but also stress the importance of recognizing hematologic malignancies in SSc patients. The findings suggest that SSc-related inflammation and fibrosis, along with immunosuppressive treatments, may contribute to the development of MDS.In conclusion, although MDS is uncommon in SSc patients, healthcare providers should be vigilant in monitoring these individuals for hematologic complications. Early detection and treatment are essential to improving outcomes in such patients.

Keywords: systemic sclerosis; myelodysplastic syndrome; anemia

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Research Article **Open Access**

Therapeutic effect of placental mesenchymal stromal cell-derived small extracellular vesicles on improvement of interstitial lung disease associated with systemic sclerosis: A single-arm clinical trial

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Mesenchymal stromal cell-derived small extracellular vesicles (MSC-SEVs) have been widely studied for their regenerative, immunomodulatory, and anti-fibrotic potentials. Interstitial lung disease associated with systemic sclerosis (SSc-ILD) is a serious pathological condition and among the main morbidities of systemic sclerosis. The aim of this study was to investigate the possible therapeutic effects of MSC-SEVs on SSc-ILD. Ten individuals previously diagnosed with SSc-ILD were included. All the cases had progressive interstitial lung disease despite receiving treatment according to the guidelines (e.g., mycophenolate mofetil and cyclophosphamide). They received five doses of intravenous placental MSC-SEVs for five consecutive days. Peripheral oxygen saturation by pulse oximetry (SaO2), six-minute walk test (6MWT), Short Form Health Survey (SF-36) questionnaire (for quality-of-life assessment), Rodnan skin score, Pittsburgh Sleep Quality Index (PSQI) questionnaire (for sleep quality), and pulmonary function tests (FEV1, FVC and FEV1/FVC) were all evaluated at the baseline and three months after the intervention. The mean age of included cases and their mean disease duration were 44.4 ± 8.4 and 12.3 ± 2.35 years, respectively. The baseline versus. post-intervention values of the investigated variables were SaO_2 (85.70 ± 13.05 vs. 92.90 ± 3.28, P=0.05), 6MWT (187 ± 114.89 vs. 229 ± 88.24, P = 0.018), FEV1/FVC (81.66 ± 5.04 vs 87.66 ± 7.14, P = 0.046), and SF-36 score (88.30 ± 5.53 vs 91.40 ± 6.50, P = 0.015). The findings on patient-relevant outcomes, particularly quality of life, SMWT, and SaO2, suggest that further randomized controlled trials would be valuable.

Keywords: systemic sclerosis; interstitial lung disease; extracellular vesicles; mesenchymal stromal cells

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Case Report **Open Access**

Clinical images of band acro-osteolysis

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A 37-year-old woman presented with hand dactylitis, fingertip pain, and swelling, along with progressive skin tightening of the upper limbs, face, and trunk over six months (panel A). She was a housekeeper with no history of Raynaud's phenomenon, psoriasis, trauma, polyvinyl chloride exposure, or family history. Examination revealed fingertip swelling and dactylitis without nail deformity. Laboratory results, including C-reactive protein, alkaline phosphatase, calcium, parathyroid hormone, and 25(OH)D3, were normal. Antinuclear antibody (ANA) profile was positive for SSA3+ and RO52+. Capillaroscopy supported scleroderma. Hand imaging showed midshaft bone resorption (band acro-osteolysis) in the 1st, 2nd, and 5th digits bilaterally and the 3rd digit of the left hand (panel B). Bone scan with 99mTc-MDP demonstrated increased uptake in both blood pool (panels C, D) and skeletal phases (panels E, F) at distal phalanges and DIP joints of the 1st, 2nd, 3rd, and 5th digits of the right hand and the 1st–3rd digits of the left hand, suggesting active inflammation. Neoplastic processes were excluded by whole-body computed tomography, mammography, and serum protein electrophoresis. Deep skin biopsy confirmed scleroderma. She was treated with prednisolone 10 mg daily and mycophenolate mofetil 500 mg twice daily. Acro-osteolysis, defined as distal phalangeal bone resorption, may affect terminal tuft, midshaft, or both (1). It occurs in 20–25% of systemic scleroderma patients. Other causes include polyvinyl chloride exposure, limited/diffuse scleroderma, renal osteodystrophy or hyperparathyroidism, idiopathic acro-osteolysis, Hajdu-Cheney syndrome, and familial forms. In scleroderma, its pathogenesis is linked to vasculopathy-induced ischemia and skin tightness

Keywords: acro-osteolysis; systemic sclerosis; antinuclear antibody

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Case Report Open Access

Hydrocephalus and diffuse alveolar hemorrhage in a patient with systemic lupus erythematosus and antiphospholipid syndrome: A case report

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Systemic lupus erythematosus (SLE) is an autoimmune disease that can affect many systems, such as the central nervous system (CNS), cardiovascular, musculocutaneous, renal, and respiratory systems etc. It can occur alone or in association with other autoimmune diseases, especially antiphospholipid syndrome (APS). Hydrocephalus and diffuse alveolar hemorrhage (DAH) are infrequent manifestations of SLE and APS. A 48-year-old man was hospitalized due to an occurrence of pulmonary problems, such as hemoptysis and DAH, renal problems such as increased creatinine and proteinuria (chronic kidney disease stage 4), and CNS problems such as hydrocephalus, which had not been examined for diagnosis and treatment for a long time because of his negligence. After performing magnetic resonance imaging and magnetic resonance venography and various autoimmune tests, SLE in association with APS was diagnosed in him according to the SLE/APS criteria, which responded dramatically to treatment, and the hydrocephalus and DAH improved greatly within 6 months. One of SLE's extremely rare but lethal neurological complications is hydrocephalus, whose pathophysiology has not been fully understood, and so far, only a few (fewer than 20 case reports) case series and reports are available. Also, DAH is an uncommon manifestation with a high mortality rate in SLE and is seen in less than 2% of patients. When dealing with patients with multi-organ involvement, rheumatological and autoimmune diseases should be the first diseases to be considered, and the correct diagnosis of these conditions should be accompanied by appropriate interventions. Also, these diseases may manifest themselves in different ways, and new symptoms may be added during the disease.

Keywords: hydrocephalus; diffuse alveolar hemorrhage; systemic lupus erythematosus; antiphospholipid syndrome

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Case Report Open Access

Co-occurrence of Sjogren's syndrome and hypoparathyroidism: A systematic case review

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This case report and systematic review examine the rare co-occurrence of Sjögren's syndrome (SS) and hypoparathyroidism (HP), two autoimmune disorders that can lead to complex clinical presentations. The case involves a 67-year-old female who presented with dry eyes, dry mouth, and hand paresthesia, symptoms that had been present for two to three months. Laboratory tests confirmed SS, with positive anti-SSA, anti-SSB, rheumatoid factor, and a positive Shirmer test. Additionally, the patient showed low calcium levels, high phosphate levels, and significantly low parathyroid hormone, confirming hypoparathyroidism. Imaging studies, including a computed tomography scan of the lungs, were normal, and there was no evidence of renal or pulmonary involvement. The patient was treated with calcium supplementation, calcitriol, prednisone, methotrexate, and folic acid, resulting in significant improvement in her symptoms. A systematic review of five studies from PubMed, Web of Science, and Scopus revealed that although the simultaneous occurrence of SS and HP is rare, it is documented in the literature. The review suggests that a common autoimmune mechanism, involving genetic susceptibility and autoantibody production, may contribute to both disorders. Lymphocytic infiltration of the parathyroid glands or autoantibodies targeting calcium-sensing receptors on parathyroid cells were identified as potential mechanisms leading to HP. These findings highlight the importance of early diagnosis and comprehensive management for patients with overlapping autoimmune disorders, particularly in those with symptoms of dry eyes, dry mouth, and endocrine abnormalities.

Keywords: Primary Sjogren's syndrome; extra-glandular symptoms; liver fibrosis

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Case Report Open Access

A rare presentation of Sjogren's syndrome with ascites and liver fibrosis in a young woman: A case report

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Primary Sjogren's syndrome is a systemic autoimmune disease that encompasses a wide range of manifestations, including exocrine gland involvement and extra-glandular symptoms. This case report deals with the history of a 26-year-old woman presented with ascites and peripheral edema and without any medical history or recent drug use. Initial tests demonstrated leukopenia, anemia, and thrombocytopenia, as well as normal liver and kidney function. Ascitic fluid analysis a indicated liver involvement, and imaging displayed significant fibrosis in the liver. Additional laboratory tests showed positive antinuclear antibodies (ANA), anti-Sjögren's syndrome-related antigen A (SS-A), and anti-Sjögren's syndrome-related antigen B (SS-B) antibodies. Moreover, a minor salivary gland biopsy confirmed the diagnosis of Sjogren's syndrome. The patient was treated with prednisolone, hydroxychloroquine, and mycophenolate mofetil, which led to the reduction of ascites and edema and the improvement of cytopenia. This report highlighted the importance of considering Sjogren's syndrome in patients with liver fibrosis and unexplained ascites.

Keywords: Primary Sjogren's syndrome; extra-glandular symptoms; liver fibrosis

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Case Report Open Access

A novel therapeutic approach to granulomatosis with polyangiitis: pulmonary improvement with tofacitinib in a 33-year-old Female – A rare case report

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Granulomatosis with Polyangiitis (GPA) is a severe systemic vasculitis that affect predominantly small- to medium-sized blood vessels with common involvement of the lungs, kidneys, and upper respiratory tract. The pathophysiology of GPA involves dysregulated T-cell activity and overproduction of cytokines, which lead to activation of the JAK-STAT signalling pathway. Conventional treatments typically involve the use of corticosteroids, cyclophosphamide, and rituximab. This study aimed to highlight the potential role of Janus kinase (JAK) inhibitors as a novel therapeutic option in the management of autoimmune diseases. We report a 33-year-old female patient with a history of Crohn's disease and autoimmune hemolytic anaemia, who was previously managed with mesalazine and subsequently with azathioprine. She presented with respiratory symptoms (cough, chest pain, dyspnea), systemic signs (fever, fatigue, weight loss) and cutaneous manifestations (purpuric rashes and violaceous discolouration of the digits). Initial imaging revealed bilateral cavitary lung lesions, initially attributed to extraintestinal manifestations of Crohn's disease. However, further evaluation with high-resolution computed tomography, lung biopsy, and positive perinuclear antineutrophil cytoplasmic autoantibodies (P-ANCA) supported a diagnosis of GPA. The treatment was started on tofacitinib (5 mg twice daily), which resulted in marked improvement in both pulmonary symptoms and Cutaneous manifestations. This case highlights the potential therapeutic role of tofacitinib in managing GPA. It may be a possible treatment option when conventional immunosuppressive therapies are ineffective or poorly tolerated. Further clinical studies are needed to establish the efficacy and safety of JAK inhibitors in broader populations.

Keywords: granulomatosis with polyangiitis; tofacitinib; Janus kinase inhibitor; case report

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Research Article Open Access

Evaluation of association between tumor necrosis factor alpha-induced protein 3 gene polymorphism (Rs7753873) and susceptibility to Behcet's disease

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Behçet's Disease (BD) is a chronic, multisystem inflammatory disorder characterized by diverse clinical manifestations. Genetic factors play a crucial role in the susceptibility and progression of BD. The tumor necrosis factor alpha-induced protein 3 (TNFAIP3) gene polymorphism. TNFAIP3 gene is a key negative regulator of the NF-κB signaling pathway. This study aimed to investigate the association of the TNFAIP3 rs7753873 polymorphism with susceptibility to BD and its clinical features in an Iranian population.In this case-control study, 232 BD patients and 278 healthy controls were recruited. Genomic DNA was extracted from peripheral blood mononuclear cells, and genotyping of the rs7753873 polymorphism was performed using the PCR-RFLP method. The distribution of genotypes and alleles was compared between patients and controls, and their association with clinical features and disease activity was analyzed. The results showed that the frequencies of AA, AC, and CC genotypes were 79.7%, 19%, and 1.3% in BD patients, and 82.8%, 15.8% and 1.4% in controls, respectively. The A and C allele frequencies were 89.2% and 10.8% in patients, and 90.65% and 9.35% in controls. No significant differences were observed in the distribution of genotypes or alleles between the two groups ($P > 0.05$). Moreover, there was no significant association between rs7753873 genotypes or alleles and disease activity, oral or genital ulcers, joint involvement, or cardiac manifestationsThis study demonstrates that the TNFAIP3 rs7753873 polymorphism does not significantly influence BD susceptibility or phenotype in the Iranian population.

Keywords: Behçet's disease; TNFAIP3; gene polymorphism; rs7753873; autoimmune diseases

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Research Article **Open Access**

Clinical and paraclinical characteristics of IgG4-related disease: A ten-year retrospective study

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This study evaluated the demographic, clinical, and laboratory features of IgG4-related disease (IgG4-RD) patients over ten years and assessed the concordance between the 2012 Comprehensive Diagnostic Criteria (CDC) and the 2019 ACR/EULAR classification criteria. Retrospective chart review at a tertiary center (2013–2023) of 18 IgG4-RD cases defined by 2012 CDC and/or 2019 ACR/EULAR, with standardized extraction of clinical, serologic, imaging, and histopathologic data; analyses included Cohen's κ and $\chi 2$ Fisher's exact tests. The patients (N = 18) showed female predominance (66.7%) with a mean age of 44.3 years. The median diagnostic delay was 12 months. Common manifestations included salivary gland involvement (44.4%), orbital disease (22.2%), and lymphadenopathy (27.8%). Serum IgG4 levels were elevated in 83.3% of patients (median, 1373 mg/d). Histopathological findings revealed dense lymphoplasmacytic infiltration (70%) and storiform fibrosis (10%). Using the 2019 criteria, 55.6% were diagnosed with definite IgG4-RD, while the 2012 criteria classified 50% as definite and 27.8% as possible. Concordance was moderate (κ = 0.53, P = 0.01). This cohort demonstrated middle-aged female predominance with salivary-orbital involvement, contrasting male-predominant international cohorts. Despite elevated serum IgG4 in 83%, levels did not correlate with organ involvement. Moderate concordance between 2012 and 2019 criteria (κ = 0.53) highlights classification challenges. While small sample size reflects IgG4-RD rarity and limits broader generalizability, these findings underscore the need for integrated diagnostic approaches and recognition of regional clinical heterogeneity.

Keywords: IgG4-related disease; classification criteria; clinical features; serum IgG4; concordance

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Review Article **Open Access**

Psoriasis in children. Should autoinflammatory disorders be considered?

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Psoriasis in children is increasingly known as immune-complex mediated autoinflammatory and autoimmune disorders. Pediatric psoriasis shares immunopathogenic mechanisms with adult psoriasis, however, exhibits unique pathological and clinical features, including genetic predisposition and environmental triggers contributing to disease onset and progression. [1] Genetic study shows overlapping with autoinflammatory as well as autoimmune disease, indicating it is an intermediate disorder on the immunologic disease. Dysregulation of innate immunity and the IL17/23 axis activate the adaptive immune system driving Keratinocyte hyperproliferations and chronic inflammation. The innate immune system contributes to tissue inflammation, while adaptive immune responses involving T cells also play a central role. Some generalized pustular psoriasis, the most common in childhood, has a more potent role of innate immunity and autoinflammatory inflammation in comparison to other forms of psoriasis.

Keywords: psoriasis; autoinflammatory; autoimmune; interleukin 17

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Research Article **Open Access**

Effect of Jujube/Frankincense as supportive therapy to alleviate the pain with knee osteoarthritis

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Ziziphus Jujuba (Z. Jujuba) is a thorny Rhamnaceous plant found throughout Europe and Southeast Asia. It has medicinal characteristics and is employed in traditional medicine. Frankincense, also referred as Frankincense resin, is recognized for its analgesic properties. The purpose of this study was to determine the anti-nociceptive efficacy of Z. Jujuba and Frankincense to assess their effect on pain accompanied with knee osteoarthritis. In this randomized controlled clinical trial, 46 participants aged 50–70 years with knee OA were divided into test and control groups. The test group received Z. jujuba/frankincense/aloe vera (250 mg/100 mg/25 mg) tablets twice daily alongside standard treatment for one month. Pain severity was evaluated using the Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC) and Visual Analog Scale (VAS) questionnaires at baseline, one week, and one month. The test group exhibited significant reductions in pain intensity (VAS: 6.68 ± 0.44 at baseline to 3.57 ± 0.54 at one month, $P < 0.001$). WOMAC scores for pain, stiffness, and physical function also improved significantly over the intervention period compared to controls ($P < 0.05$). Pain reduced in study group compared to their respective baseline (VAS and WOMAC outcome measures). It could be recommended as complementary to routine knee osteoarthritis treatment.

Keywords: Frankincense; osteoarthritis, knee; Sipjundaebo-tang; Ziziphus Jujuba

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Research Article **Open Access**

Impact of oral black seed oil capsules on serum Tenascin-C levels in patients with knee osteoarthritis: A triple-blind randomized clinical trial

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This study investigated the effect of oral black seed oil capsules on serum Tenascin-C levels as a marker of inflammation and cartilage degradation in patients with knee osteoarthritis. Patients with knee osteoarthritis (grades 2–3) were randomized to receive either placebo or black seed oil capsules (1000 mg, containing 5.3 mg thymoquinone) twice daily for three months. Outcomes, including demographics, serum Tenascin-C, Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC), and visual analogue score (VAS) scores, were assessed pre- and post-intervention, with analysis at $P < 0.05$.40 patients were randomly allocated to intervention and placebo groups, with similar Tenascin-C levels. Four months after the intervention, the WOMAC score decreased significantly in both groups (placebo: 57.6 ± 11.8 to 54.13 ± 13; intervention: 56.2 ± 8.9 to 50.7 ± 10.1, both $P < 0.001$). The reduction in WOMAC scores was significantly greater in the intervention group compared to the placebo group (5.5 ± 5.6 vs. 3.5 ± 5.5, p=0.04). Similarly, VAS scores dropped significantly in both groups (placebo: 6.3 ± 0.8 to 5.6 ± 1.2; intervention: 6.7 ± 0.8 to 1.4 ± 1.5, both $P < 0.001$), with a more substantial reduction in the intervention group (1.3 ± 1.2 vs. 0.7 ± 1, p=0.01). However, no significant differences were observed in TNC levels in groups. The study suggests that black seed oil compounds can effectively alleviate symptoms and pain severity in knee OA patients.

Keywords: knee osteoarthritis; Tenascin-C; black seed oil; thymoquinone

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Research Article **Open Access**

The potential of neutrophil-to-lymphocyte ratio, monocyte-to-lymphocyte ratio, and platelet-to-lymphocyte ratio in diagnosis of osteoporosis

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Osteoporosis is a chronic and progressive disorder with dysregulated immune responses. The neutrophil-to-lymphocyte ratio (NLR), monocyte-to-lymphocyte ratio (MLR), and the platelet-to-lymphocyte ratio (PLR) have been reported as predictors of osteoporosis. Here, we intended to assess potential of NLR, MLR, and PLR as a diagnostic marker to predict osteoporosis. Furthermore, the association between bone mineral density (BMD) and these ratios were investigated in the cases with osteoporosis. Here, 315 subjects with osteoporosis, 305 subjects with osteopenia, and 350 cases as healthy controls were included. The BMD of the subjects was measured in the hip and L1-L4 spine using the Stratos device via dual-energy X-ray absorptiometry method. The frequency of immune cells was determined in the whole blood cells. Patients with osteoporosis had higher levels of the NLR, MLR and PLR. The Z-score and T-score of hip and Z-score and T-score of spine were significantly lower in the cases with osteoporosis compared to osteopenia and healthy controls. There was an inverse correlation between NLR, MLR, and PLR with the Z-score and T-score of hip and Z-score and T-score of spine in patients with osteopenia. Area under curve for NLR was 0.67 (95%CI: 0.524 to 0.816, P = 0.0345), for MLR was 0.71 (95%CI: 0.568 to 0.851, P = 0.009), and for PLR was 0.79 (95%CI: 0.664 to 0.921, P= 0.0003) to distinguish between osteoporosis and osteopenia. NLR, MLR, and PLR may serve as tools to diagnose osteoporosis.

Keywords: neutrophil-to-lymphocyte ratio; monocyte-to-lymphocyte ratio; platelet-to-lymphocyte ratio; osteoporosis

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Research Article **Open Access**

Evaluation of the prevalence of vitamin D deficiency & insufficiency in medical students in 2024

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Vitamin D deficiency is an important global health problem and there aren't similar studies in medical students, we decided to investigate the prevalence of vitamin D deficiency & insufficiency and its associated factors in medical trainees and interns at Kashan University of Medical Sciences during 2024. In this cross-sectional-analytic study, 295 medical students were included. After obtaining the code of ethics from the Medical Ethics Committee and obtaining informed consent from all medical students the study was conducted. Demographic information of the students (age, gender, body mass index (BMI), consumption of dairy products in diet and exposure to sunlight) were entered in the checklist. Then, 5 cc of venous blood was taken and the serum was separated and stored at -20°C until the test. Then, serum vitamin D levels were measured by ELISA method. In this study from 295 medical students were enrolled 159 (53.9%) were male and 136 (46.1%) were female. 57.3% of the students were interns. According to the results of this study, 28.8% had insufficient vitamin D levels, 16.9% had vitamin D deficiency, and a total of 45.7% had vitamin D levels below 30 ng/dl. This study show that, low vitamin D levels were significantly associated with gender, BMI, family history of vitamin D deficiency, sun exposure, and dairy consumption. Given the relatively high frequency of low vitamin D levels in medical students, periodic screening programs, targeted prescription of supplements, and lifestyle modification education (emphasizing nutrition and safe sun exposure) should be on the agenda of medical universities.

Keywords: vitamin D; vitamin D deficiency; vitamin D insufficiency; adequate exposure to sunlight; proper nutrition

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Research Article **Open Access**

Association between vitamin D receptor BsmI (rs1544410) gene polymorphism and serum vitamin D, serum calcium and osteoporosis risk in women over 40 years

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We aimed to investigate the relationships between the vitamin D receptor (VDR) BsmI (rs1544410) gene polymorphism, vitamin D and calcium levels, and the risk of osteoporosis in women aged 40 years and older. This case-control investigation enrolled participants (30 cases and 30 age-matched controls) and classified into normal and osteoporotic groups using a dual-energy X-ray absorptiometry scan. Vitamin D and calcium levels were obtained from peripheral blood samples. Polymerase chain reaction-restriction fragment length polymorphism (PCR-RFLP) was performed to detect the BsmI polymorphism. Differences between groups were analyzed using an analysis of variance (ANOVA) test. The lumbar and femoral T-scores, and calcium levels, were significantly lower in the cases compared to the controls ($P < 0.005$). Among postmenopausal women, the lumbar T-scores significantly differed between cases with VDR polymorphisms ($P = 0.003$) and controls ($P = 0.001$). Among premenopausal women, there was only a significant difference in VDR polymorphisms in the control group ($P = 0.006$). Calcium and vitamin D levels were significantly different between the VDR polymorphisms in cases and control groups, but only among postmenopausal women ($P < 0.005$). No significant differences were observed between the VDR polymorphism in terms of femoral T-scores, neither in the cases nor the controls ($P > 0.005$). We found no differences in VDR polymorphism between individuals with and without osteoporosis. The lumbar T-scores, calcium, and vitamin D levels were significantly different between the VDR polymorphisms in the case and control groups among postmenopausal women.

Keywords: BsmI gene polymorphism; vitamin D receptor; osteoporosis; post-menopause women

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Research Article **Open Access**

The prevalence of orthostatic hypotension, orthostatic intolerance and postural orthostatic tachycardia syndrome in Ehlers-Danlos hypermobility syndrome in children and adolescents

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Ehlers-Danlos hypermobility syndrome (hEDS) is a hereditary connective tissue disorder frequently associated with autonomic dysfunction. Orthostatic hypotension (OH), orthostatic intolerance (OI), and postural orthostatic tachycardia syndrome (POTS) are among the most common autonomic manifestations. To determine the prevalence of OH, OI, and POTS in children and adolescents with hEDS. A cross-sectional study was conducted among pediatric patients (aged 10–19 years) with confirmed hEDS. Participants underwent standardized clinical and autonomic assessments. Statistical analyses were performed using SPSS. A total of 65 children and adolescents with hEDS were evaluated (mean age 14.3 ± 2.1 years; 61.5% female). OI was observed in 76.3%, OH in 31.6%, and POTS in 28.9% of participants. Females were significantly more affected than males ($P < 0.05$). Age did not significantly influence prevalence. Comorbidities such as chronic pain and gastrointestinal symptoms were frequently reported among those with autonomic dysfunction. Autonomic dysfunction is highly prevalent in pediatric hEDS. Routine screening for orthostatic disorders should be incorporated into clinical practice.

Keywords: Ehlers-Danlos syndrome; hypermobility; orthostatic hypotension; orthostatic intolerance; postural orthostatic tachycardia syndrome; dysautonomia; pediatrics

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Review Article **Open Access**

Internal dosimetry of ^{166}Ho-Chitosan complex in radio-synovectomy

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Radio-synovectomy (RSV) is a non-surgical therapeutic procedure designed to treat chronic inflammatory issues**,** such as rheumatoid arthritis and hemophilic arthropathy, through the intra-articular injection of radiopharmaceuticals into the affected joint. Among the recommended radionuclides used in RSV, Holmium-166 (^{166}Ho) has got much attention due to suitable decay properties such as short half-life, high beta energy, gamma-ray emission with suitable energy for nuclear imaging. ^{166}Ho-chitosan as a therapeutic agent has shown good clinical outcomes in RSV. Internal dosimetry is an important part that focuses on evaluating the absorbed doses of radiation delivered by radiopharmaceuticals within the body. This process is essential for optimizing therapeutic outcomes while minimizing risks to healthy tissues. This paper aims to estimate the absorbed doses of ^{166}Ho-Chitosan in human organs.To calculate Self and Cross Doses, S values for the standard model were determined using MCNP. Then, using the MIRD, the absorbed dose in the target organ and vital organs, was obtained. The absorbed dose values calculated in ORNL phantom per MBq of activity accumulated in the synovial joint are: Synovial tissue: 2.60×10^{-4}, femur: 1.39×10^{-11}, heart: 1.05×10^{-13}, and kidney: 1.58×10^{-12} mGy/MBq. As can be seen, the absorbed dose in the target tissue (synovial) is significantly higher than non-targets. This study demonstrates that RSV using ^{166}Ho is a safe and effective method for treating synovitis. The radiation is well-concentrated within the target while the dose received by the surrounding healthy tissues was negligible and the non-target organs remained within the safe range.

Keywords: radio-synovectomy; holmium-166; dosimetry

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Research Article **Open Access**

The prevalence and contributing risk factors of coronavirus disease 2019 infection in patients with metabolic syndrome

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Components of metabolic syndrome (MetS) was reported to contribute to severe and worse outcomes of coronavirus disease 2019 (COVID-19). We evaluated the association of MetS and its components with susceptibility to COVID-19. In this study, 1000 subjects with MetS which diagnosed via the International Diabetes Federation (IDF) criterion were recruited and. Real-time PCR was exerted to detect SARS-CoV-2 in the nasopharyngeal swabs. Among the MetS patients, 206 (20.6%) cases were detected to have COVID-19. Smoking (OR = 5.04, 95%CI = 3.53-7.21, P < 0.0001) and cardiovascular disease (OR = 1.62, 95%CI = 1.09–2.40, P = 0.015) were associated with increased chance of COVID-19 in the MetS patients. Body mass index was significantly higher (P = 0.0001) in MetS cases with COVID-19. Obesity was associated with increased susceptibility to COVID-19 in MetS patients (OR = 2.00, 95%CI = 1.47–2.74, P < 0.0001). Total cholesterol, triglyceride, low density lipoprotein were significantly higher in the MetS cases with COVID-19 than those without COVID-19. Dyslipidemia was associated with increased chance of COVID-19 (OR = 1.50, 95%CI = 1.10–2.05, P = 0.0104). Fasting blood sugar level was significantly higher in the MetS cases with COVID-19. Type 2 diabetes mellitus was associated with increased risk of COVID-19 in MetS patients (OR = 1.43, 95%CI = 1.01-2.00, P = 0.0384). Hypertension was associated with increased chance of COVID-19 in the MetS patients (OR = 1.44, 95%CI = 1.05–1.98, P = 0.0234). In conclusions, MetS and its components, like obesity, diabetes, dyslipidemia, cardiovascular complications were associated with increased chance of COVID-19 infection development and probably with aggravated symptoms.

Keywords: coronavirus disease 2019 infection; metabolic syndrome; susceptibility

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