diet. Extensive research has explored the crucial role of mitochondria in energy provision and the maintenance of metabolic balance. Mitochondria in adipocytes regulate insulin sensitivity, adipocyte differentiation, and white adipose tissue browning, with mitochondrial dysfunction contributing to various metabolic disorders such as obesity and type 2 diabetes.

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SYSTEMIC JUVENILE RHEUMATOID ARTHRITIS: INCIDENCE DUE TO MIF-173C MUTATION

Introduction

Systemic juvenile rheumatoid arthritis (SJRA), also known as juvenile chronic or idiopathic arthritis, is a disease that affects approximately 11% of patients with this condition and is characterized by clinical homogeneity. Despite advances in treatment, many children with this disease still face early joint destruction, leading to the need for surgical interventions.Additionally, a significant portion of patients (48%) continue to experience symptoms even after 10 years.

Research has shown that certain genetic variations, specifically polymorphisms in the IL-6 and MIF genes, are associated with an increased susceptibility to this disorder. Macrophage migration inhibitory factor (MIF) has emerged as a novel cytokine that may play a crucial role in linking rheumatoid arthritis to atherosclerosis, highlighting the complex interplay between these diseases.

JRA is present in all over the world approximately 3 million children and young adults are sufferingfrom JRA some countries have (see table 1).

Table 1 – Percentage of systemic juvenile rheumatoid arthritis

Countries	Percentage
UK	1
US	0.5–1
INDIA	0.9
AFRICA	0.16

Juvenile rheumatoid arthritis (JRA), also known as juvenile idiopathic arthritis (JIA), is a chronic autoimmune disorder that affects children under the age of 16. It causes joint inflammation, pain, stiffness, and swelling. JRA is characterized by periods of flare-ups and remission. The exact causeof JRA is unknown, but it is believed to be related to genetic and environmental factors. Treatment for JRA may include medication, physical therapy, and lifestyle modifications to manage symptoms and improve quality of life (see Figure 1).

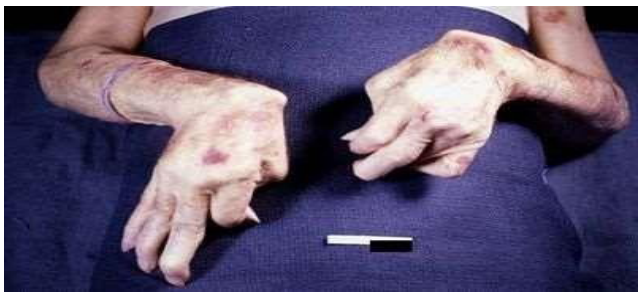

Figure 1 – The patient suffering from juvenile rheumatoid arthritis

Goal

To explore the polymorphisms in the MIF genes, that are associated with SJRA.

Material and methods of research

We conducted a search in National Center for biotechnology information and PubMed and based on our search criteria a lot of several eligible studies concerning the MIF-173C.

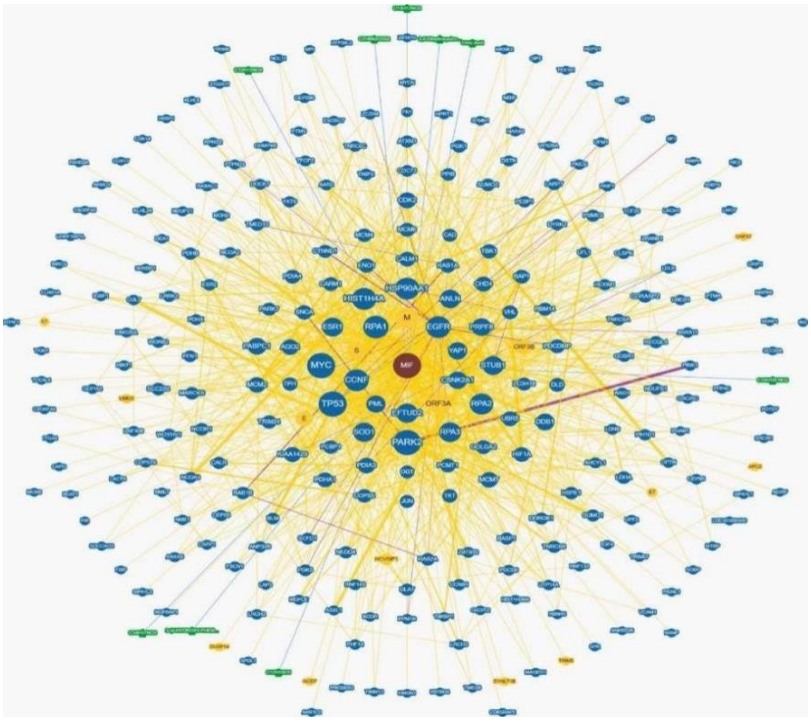

Figure 2 – Network of macrophage migration inhibitory factor (MIF)

The exons/introns of the human MIF gene span less than 0.7 kb of chromosomal DNA, 3 exons are separated by introns (189 and 95 bp). The gene for D-dopachrome tautomerase in human and mouse is identical in exon structure to MIF. Both genes have two introns that are located at equivalent positions related to a 2 fold repeat in protein structure although in similar

positions the introns are in different phases relative to the open reading frame. Other members of this super family exist in nematodes and a plant and a related gene in C. elegans share an intron position with MIF and DDT in addition to similarities in structure the genes for DDT and MIF are closely linked on human chromosome 22 and mouse chromosome 10. The MIF gene has 295 interactions on 277 interactors and there are 12 chemical interactions, AAR2, ADIRFAGO2, ANLN, ANKRD26, BAP1, BASP1, BCAT1, BCOR, BLM, BNIPL, CAD, CALRCD74, CDK2, COPS5, CLSPNDDB1, DLD, DDB1, DOCK17, E, E2F4, E7NXOSC7, FN1, FSCN1, GBE1, GCD7, GIGYF2, GOSR1, HIC2, HIF1A, HINT1, HPRT1, INS, IGBP1, JUN, KLHL8, KBTBD4, LAP3, LARP7, LDHA, LMO7, M, MAGED1, MBIP, MCM2, MIF, MPI, NME1 and some more interactions (see figure 2) [1].

Polymorphic variations in the MIF gene, specifically at the 173rd position with a G-to-C transition, were unveiled. This variation was then subjected to examination in a group of 117 individuals with SJRA and compared with 172 non-related, healthy volunteers, as documented by Donn and colleagues in 2001. It was found that possession of the MIF-103C allele corresponded with a heightened susceptibility to the illness, evidenced by a significant p-value of 0.0005. A detailed investigation of the MIF-123C allele, across 88 patients diagnosed with JRA featuring diverse clinical presentations, highlighted a universally increased risk of developing JRA, irrespective of the clinical phenotype encountered [2].

The results of the research and their discussion

SRJA involves complex interactions among various mediators, with cytokinesis playing a key role. The MIF gene, which is associated with adaptive immunity, has been implicated in the pathogenesis of numerous diseases, including rheumatoid arthritis. High levels of MIF expression in rheumatoid arthritis patients underscore its significant role in inflammation and joint destruction. The presence of macrophages is essential for the development of arthritis.

While there is currently no cure for systemic juvenile rheumatoid arthritis, early detection allows for effective management through medication, physical therapy, lifestyle modifications, and other interventions. Treatment options include NSAIDs, DMRADs like methotrexate, biological agents, corticosteroids, physical therapy, occupational therapy, and lifestyle adjustments. Among these options, DMRADs such as methotrexate are considered particularly effective for treating SJRA [3].

Conclusion

This study suggests that the MIF-173C gene polymorphism may increase the risk of rheumatoid arthritis, especially in certain seasons. The meta-analysis also indicates that gene polymorphisms may elevate this risk. While MIF polymorphisms are not consistently associated with rheumatoid arthritis, they are linked to high levels of radiologic joint damage in some cases. These findings provide valuable guidance for clinicians, caregivers, and patients when making treatment decisions. It is recommended that a shared decision – making process be employed, taking into consideration patients' values, preferences, and comorbidities. Importantly, these recommendations should not be used to restrict or deny access to therapies.

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