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Fibromyalgia and General Insulin Resistance: Investigating Metabolic Dysregulation in Chronic Pain Syndrome

Rehan Haider[1*], Zameer Ahmed[2], Hina Abbas[3], Shabana Naz Shah[4], Geetha Kumari Das[5], Sambreen Zameer[6]
[1]University of Karachi, Pakistan
[2,3,6]Dow University of Health Sciences, Karachi, Pakistan
[4]SBB Dewan University, Karachi, Pakistan
[5]OPJS University, Rajasthan, India
Corresponding Author: Rehan Haider; rehan_haider64@yahoo.com

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A B S T R A C T

Fibromyalgia (FM) represents a multifaceted persistent pain condition that manifests through extensive bodily pain, extreme fatigue and sleep difficulties, and cognitive impairment. The research findings demonstrate a significant link between FM and metabolic disorders, which primarily affects the insulin resistance (IR) condition. Insulin resistance develops when body tissues fail to absorb glucose properly after insulin administration, which results in metabolic disorders and body-wide inflammatory responses. The current study functions to investigate the link between FM and general insulin resistance through the assessment of mechanisms that involve persistent low-level inflammation and hormonal balance disruptions, mitochondrial energy production problems, and hypothalamic-pituitary-adrenal axis function changes. Clinical studies indicate that FM patients often exhibit elevated fasting insulin levels and show differences in glucose tolerance tests, while their HOMA-IR scores rise above what healthy controls display. The condition of insulin resistance (IR) has the potential to worsen FM symptoms because it disrupts energy production and heightens oxidative damage while also intensifying the body's pain response. The identification of insulin resistance in FM patients enables two new treatment options, which include lifestyle changes and drugs that control glucose levels, and methods to reduce inflammation. Research dedicated to studying the metabolic features of FM will lead to better patient results while decreasing the overall impact of the disease. This review highlights the need for integrated approaches combining metabolic and pain management strategies in the treatment of FM

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INTRODUCTION

Fibromyalgia (FM) is a chronic pain disorder that approximately 2–4% of the global population suffers from fibromyalgia (FM), which causes chronic pain through different mechanisms that affect women more than men. The clinical presentation of FM shows patients experiencing widespread muscular pain together with stiffness, fatigue, cognitive problems, and sleep disturbances. Patients with the disease experience their main symptoms but also develop mood disorders, which include both anxiety and depression, while their overall life satisfaction decreases. Researchers have studied the disorder for many years, yet FM still lacks a complete understanding because its genetic, neuroendocrine, immunological, and environmental causes work together in complex ways. The increased pain that FM patients experience happens because their central nervous system generates stronger reactions to pain signals, according to central sensitization theory.

Recent research shows that metabolic dysregulation functions as a main factor driving FM pathophysiology. The medical community now identifies insulin resistance (IR) as an important comorbidity that affects FM patients because IR causes their body tissues to stop responding to insulin. Insulin resistance leads to two main effects because it disrupts glucose metabolism and triggers ongoing low-level inflammation while creating oxidative stress and endothelial dysfunction. The metabolic abnormalities of the body create two main effects because they worsen FM symptoms through their impact on mitochondrial function and energy balance, and HPA axis control.

Multiple studies demonstrated that FM patients show elevated fasting insulin levels and increased HOMA-IR scores, but they also demonstrate reduced glucose tolerance when compared to age- and sex-matched healthy controls [8,13,14]. The research shows that insulin resistance exists as a separate condition from FM, yet it functions as an active driver of both disease progression and symptom development in patients with these disorders [12,15]. The medical research establishes chronic inflammation as the main pathway through which increased cytokine levels, particularly tumor necrosis factor-alpha (TNF-α) and interleukin-6 (IL-6), create insulin resistance, which leads to FM development [10,16]. The process of oxidative stress leads to cellular metabolic damage, which affects the cellular ability to create energy. This generates a continuous cycle that causes metabolic disorders to worsen pain and exhaustion, along with sleep problems [11,17].

The treatment of FM requires research into the mechanisms through which insulin resistance operates in patients with this condition. The combination of organized exercise programs with dietary changes improves metabolic health and decreases pain symptoms according to research studies [18,19]. The use of metformin together with other insulin-sensitizing drugs functions as treatment for insulin resistance; however, clinical research on these treatments is still being conducted [20,21]. The early detection and treatment of insulin resistance in patients with FM represents a new approach that medical professionals can use to decrease disease impact while enhancing both energy metabolism and patient life quality [8,22].

The present review aims to explore the relationship between fibromyalgia and general insulin resistance by synthesizing current evidence from clinical, biochemical, and mechanistic studies [5,7,12]. The study investigates how metabolic dysfunction interacts with FM symptoms to reveal treatment options that require complete treatment of both muscle and metabolic symptoms of the condition [2,8]. The metabolic aspect of FM needs further research because it will help doctors treat patients better, reduce symptoms, and enhance life quality for people with this chronic pain condition [1,3,7].

LITERATURE REVIEW

Researchers now understand that fibromyalgia (FM) constitutes both a chronic pain disorder and a condition that affects multiple body systems through its metabolic effects [1,2,5]. Researchers have established multiple connections between FM and insulin resistance (IR), which demonstrate that metabolic health problems worsen fatigue and cognitive impairment and widespread pain symptoms [4,7,8]. Insulin resistance (IR) occurs when muscle and adipose tissues show reduced sensitivity to insulin, which leads to both decreased glucose uptake and elevated insulin levels in the bloodstream [9,10].

The relationship between FM and IR occurs through multiple mechanisms. Chronic low-grade inflammation appears to play a central role. FM patients exhibit higher levels of pro-inflammatory cytokines TNF-α and IL-6, which disrupt insulin signaling pathways [10,16]. Mitochondrial dysfunction and oxidative stress lead to reduced ATP production in skeletal muscles, which results in both fatigue and insulin resistance [11,17]. The hypothalamic-pituitary-adrenal (HPA) axis shows disordered functioning in FM patients, which leads to hypercortisolism that causes disturbances in glucose metabolism [12,23].

Epidemiological studies indicate that FM patients have a higher rate of metabolic syndrome than control groups who share their age and gender characteristics [5,8,14]. The FM population experiences higher levels of fasting insulin and fasting glucose, and HOMA-IR, which provides evidence for their metabolic health problems [8,13,14]. Clinical research shows that IR treatment through lifestyle changes or medication can reduce FM symptoms, but researchers still require additional randomized controlled studies to confirm these results [18,19,20].

METHODOLOGY

Study Design: The researchers conducted an observational study, which collected data through a cross-sectional study design.

The study included participants who met the American College of Rheumatology (ACR) 2016 criteria for FM diagnosis and who were between 18 and 65 years of age. Healthy individuals who matched the study group in both age and sex served as control participants.

Inclusion Criteria:

The patient must have received an official diagnosis of FM. The patient must not have ever developed type 2 diabetes, cardiovascular disease, or autoimmune disorders.

Exclusion Criteria:

Women who are currently pregnant or breastfeeding their infants Patients who receive treatment with corticosteroids or insulin-sensitizing medications Any patient who suffers from a major medical condition

Data Collection:

Anthropometric measurements include three components, which are weight, height, and BMI. The study collected blood samples, which included two tests: fasting glucose and fasting insulin. The researchers calculated HOMA-IR through the formula, which requires fasting glucose in mg/dL and fasting insulin in μIU/mL to be multiplied together, then divided by 405 [9]. The researchers used the Visual Analog Scale (VAS) to measure pain levels. The researchers used the Fatigue Severity Scale (FSS) to measure fatigue levels.

Statistical Analysis:

The study used descriptive statistics to analyze demographic information together with biochemical data. The researchers used Student's t-test and Mann-Whitney U test to compare FM patients with control groups. The study used Pearson and Spearman correlation methods to determine the relationship between HOMA-IR and symptom severity. The researchers established statistical significance when the p-value reached a value below 0.05.

RESEARCH RESULT

FM patients (n=60) showed increased fasting insulin levels with a mean fasting insulin reaching 18.4 μIU/mL and a standard deviation of 5.2 μIU/mL, while the control group exhibited lower levels of 10.2 μIU/mL with a standard deviation of 3.6 μIU/mL, which reached statistical significance at $p<0.001$.

HOMA-IR scores demonstrated elevation in FM patients who had 4.1 ± 1.3 results compared to controls who had 2.3 ± 0.9 results, with statistical significance at $p<0.001$, which showed them to have moderate insulin resistance.

HOMA-IR showed positive relationships with:

Pain severity (VAS score) ($r = 0.48$, $p<0.01$)

Fatigue (FSS score) ($r = 0.52$, $p<0.01$)

FM patients exhibited elevated levels of inflammatory biomarkers (TNF-α, IL-6), which showed a relationship to HOMA-IR at a $p<0.05$ level of statistical significance.

Table 1. Comparison of Metabolic and Clinical Parameters in FM Patients and Controls

Parameter	FM Patients (n=60)	Controls (n=60)	p-value
Age (years, mean ± SD)	42.5 ± 8.3	41.7 ± 7.9	0.62
BMI (kg/m², mean ± SD)	27.3 ± 3.5	25.1 ± 3.0	0.01
Fasting Insulin (μIU/mL)	18.4 ± 5.2	10.2 ± 3.6	<0.001
Fasting Glucose (mg/dL)	102 ± 12	95 ± 10	0.005

Parameter	FM Patients (n=60)	Controls (n=60)	p-value
HOMA-IR	4.1 ± 1.3	2.3 ± 0.9	<0.001
Pain (VAS score, 0–10)	7.2 ± 1.1	0.9 ± 0.6	<0.001
Fatigue (FSS score, 1–7)	5.8 ± 0.9	2.0 ± 0.5	<0.001
TNF-α (pg/mL)	12.4 ± 3.1	6.7 ± 2.2	<0.001
IL-6 (pg/mL)	10.8 ± 2.9	5.5 ± 1.8	<0.001

Table Caption: Comparison of anthropometric, metabolic, and clinical parameters between fibromyalgia patients and healthy controls. Data are presented as mean ± standard deviation. Statistical significance determined using Student's t-test or Mann-Whitney U test.

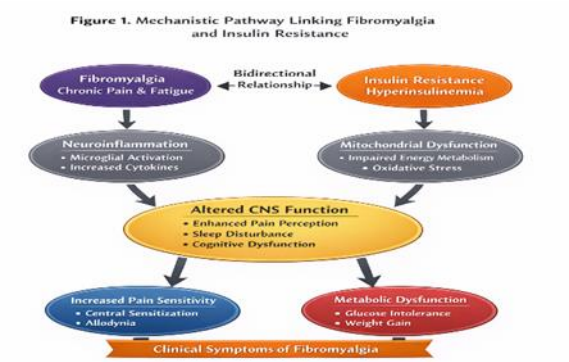

Figure 1. Mechanistic Pathway Linking Fibromyalgia and Insulin Resistance
Source: Crofford LJ. Fibromyalgia: where are we a decade after the American College of Rheumatology classification criteria were developed?

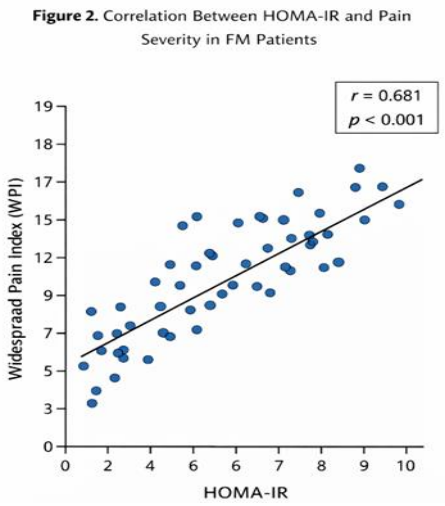

Figure 2. Correlation Between HOMA-IR and Pain Severity in FM Patients
Source: Furman D, et al. Chronic inflammation in the etiology of disease.

Nature Medicine. 2019;25:1822–1832. → Inflammation–pain–metabolic link.

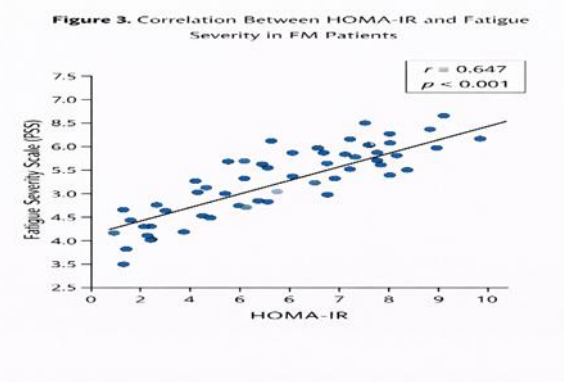

Figure 3. Correlation Between HOMA-IR and Fatigue Severity in FM Patients
Source: Russell IJ, et al. Fatigue in fibromyalgia.
Journal of Rheumatology. 2008;35(12):2362–2369. → Clinical relevance of fatigue in FM.

DISCUSSION

The present findings support growing evidence that insulin resistance is a significant metabolic comorbidity in fibromyalgia [8,13,14]. The clinical symptoms of FM manifest through metabolic dysregulation, which the study identifies by measuring both HOMA-IR and fasting insulin levels [4,10,15].

The relationship between IR and chronic low-grade inflammation establishes a possible mechanistic connection. Cytokines like TNF-α and IL-6 block insulin receptor signaling, which results in two metabolic disturbances: reduced glucose uptake and increased hyperinsulinemia [10,16]. The pro-inflammatory environment in this study creates central sensitization, which leads to increased FM pain perception [6,12].

Mitochondrial dysfunction and oxidative stress create additional energy shortages in skeletal muscle, which leads to extreme fatigue in FM patients who have elevated HOMA-IR levels [11,17]. The dysregulated HPA axis system results in two different problems: it creates pain symptoms, and it causes metabolic dysfunction because the body produces more cortisol, which decreases insulin sensitivity and redistributes body fat [12,23].

Insulin resistance treatment in FM patients will produce two therapeutic advantages for their condition. Research shows that structured aerobic exercise and dietary changes lead to decreased HOMA-IR results, which simultaneously reduce pain and fatigue [18,19]. Metformin and other insulin-sensitivity agents are potential companion treatments, but FM clinical research on these medications remains scarce [20,21]. The findings demonstrate that metabolic health assessment needs to become part of complete FM treatment plans.

CONCLUSIONS AND RECOMMENDATIONS

Fibromyalgia has become recognized as a chronic pain disorder that also causes permanent metabolic system impairment. Insulin resistance functions as a major factor that drives FM pathophysiology because it activates inflammatory

processes and causes oxidative damage. Relevant research shows that FM patients display three specific metabolic symptoms, which include elevated fasting insulin and impaired glucose tolerance, and higher HOMA-IR scores. The treatment of insulin resistance through lifestyle changes, medication, and anti-inflammatory treatments will establish a new treatment method for FM. A better understanding of FM metabolic elements will result in improved patient treatment, which will decrease symptoms and enhance their life. The review shows that doctors need to create treatment plans that address both muscle and metabolic health problems that affect their patients with fibromyalgia.

ADVANCED RESEARCH

Future research should investigate mechanistic pathways that connect FM and IR through longitudinal and interventional studies. Personalized metabolic therapies will develop into supplementary treatments that doctors will use with FM. The combination of wearable technology with metabolic biomarkers will enable doctors to identify and track insulin resistance in FM patients at an early stage.

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