RESEARCH
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IRRITABLE BOWEL SYNDROME AS AN EARLY DETECTOR OF INSULIN RESISTANCE AND PREDIABETES IN OVERWEIGHT ADULTS.

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Abstract
Background: Irritable bowel syndrome (IBS) is a common condition that significantly decreases the patients' quality of life. T2DM may exacerbate symptoms of IBS.
Aim: To recognize the possible role of IBS as an early detector of insulin resistance and prediabetes among overweight adult persons.
Methodology: A comparative trial that included 200 participants who were divided into 2 groups, each group included 100 individuals. Group A (IBS group) and Group B (Non-IBS group). BMI, FBG, HbA1c, liver enzymes (ALT, AST), and lipid profiles were evaluated. Clinical evaluation of IBS symptoms and Abdominal Ultrasound were performed. The Statistical analysis was conducted by SPSS. Descriptive data (e.g., frequencies and percentages) were calculated, and the x 2 test and t test were applied accordingly. A p-value less than 0.05 was considered significant.
Results: The mean baseline HbA1c level among Group A was 5.945 (t= -29.070, p<0.001), and 5.314 (t= -76.992, p<0.001), in Group B. FBG levels were 99 mg/dL. ALT and AST levels in Group A were 42.54 (t= -1.064, p=0.290) and 4.78 (t= -1.850, p=0.067), respectively, with no significant difference. In Group B, ALT and AST levels decreased significantly to 36.79 (t=-9.137, p< 0.001) and 5.46 (t= -5.608, p< 0.001), respectively. In Group A, triglycerides and ultrasound mean was 191.58 (SD=66.68) (t= 6.236, p<0.001) with significant increase, with a confidence interval (28.35, 54.81), while In Group B, they were154.41 (SD=28.85), with no statistically significant difference (t=1.529, p=0.130). The mean BMI at baseline for Group A was 29.33, significantly elevated (t=8.883, p<0.001) while in Group B it was 24.316, significantly lower than the test value (t= -2.793, p=0.006).
Conclusion: IBS can be not only as a digestive disorder but also as a potential warning sign for broader metabolic issues like insulin resistance.
Key words: IBS, metabolic syndrome, insulin resistance, prediabetes, diabetes.

1. Background

Irritable bowel syndrome (IBS) is a common condition that significantly decreases the patients' quality of life and has a negative impact on the healthcare economy. Chronic abdominal pain, irregular bowel movements that are not associated with an underlying disease, and altered bowel function (frequency and/or regularity) are its most prominent features. The main symptom of chronic abdominal pain is cramp-like discomfort that can be detected among different parts of the abdomen and is sporadically made worse and better. Constipation, diarrhea, or a combination of both might cause alterations to bowel movements. IBS comes in combined, unclassifiable, constipation-predominant, and diarrhea-predominant forms (Camilleri, 2021).

The pathogenesis includes alterations in the fecal microbiota, low grade mucosal immune activation, and disruptions of the gut-brain axis. A number of etiologies have been proposed for contributing in the pathophysiology of IBS, including dietary, immunological, inflammatory, neurological, and environmental variables (Hellström, 2019).

According to a recent epidemiological survey, 4.1% of people worldwide suffer from IBS (Sperber et al., 2021). With prevalence rates ranging from 8 to 31% in short series, the majority of reports show that IBS is more prevalent in individuals with morbid obesity than in the general population (Bouchoucha et al., 2016; Schneck et al., 2016).

Diabetes mellitus (DM) is a long-term metabolic condition identified by elevated blood sugar levels and variable levels of insulin resistance or insufficiency, resulting from defects in insulin secretion, insulin action, or both. Based on the underlying pathology, diabetes mellitus is divided into two main types: type 1 diabetes mellitus (T1DM) and type 2 diabetes mellitus (T2DM) (Gupta et al., 2024). Ninety to ninety-five percent of all occurrences of diabetes are type 2 diabetes mellitus, the most prevalent kind among adult persons. The pathogenesis of T2DM is thought to include insulin resistance

and β-cell malfunction as early and essential components. Furthermore, the upregulation of growth factors like TGFβ, pro-inflammatory cytokines like IL-1β, and other biological molecules like ROS has been linked to a rapid inflammatory process (Heydarpour et al., 2020).

There are several similarities between T2DM and IBS. These are chronic conditions that may be related to systems such as inflammation, intestinal permeability, and microbial dysbiosis. Additionally, it's possible that risk factors including obesity, stress, and physical inactivity play a role in both diseases. IBS can have a negative impact on T2DM patients' ability to control their blood sugar levels. As it involves digestive problems like diarrhea, bloating, and abdominal pain, IBS symptoms might impact a person's eating patterns and make it difficult to adhere to a diabetic diet. Stress and anxiety, two symptoms of IBS, can also negatively impact glycemic control (Ortega et al., 2020).

T2DM may exacerbate symptoms of IBS. Metabolic issues associated with diabetes may affect intestinal motility and worsen symptoms of IBS, such as constipation or diarrhea. Additionally, insulin therapy and diabetic medications may cause digestive issues and problems with stool function. People with T2DM and IBS require a personalized treatment strategy that is based on their individual needs and the intensity of their symptoms (Marathe et al., 2024).

On the other hand, obesity is a major risk factor for the development of chronic or non-communicable illnesses (NCDs), making it one of the biggest global public health concerns. Numerous consequences, such as cardiovascular disease, metabolic diseases including T2DM, chronic obstructive pulmonary disease, cancer, arthritis, and even psychological disorders, are frequently linked to obesity (Berthoud & Klein, 2017). This is brought on by obese patients' excessive adipose tissue and fat redistribution, which is closely linked to insulin resistance, endothelial dysfunction, hyperglycemia, hyperlipidemia, and chronic inflammation (Barcones-Molero, et al., 2018).

The present study aims to recognize the possible role of IBS as an early detector of insulin resistance and prediabetes among overweight adult persons.

2. Patients and Methods:

The present study was designed as a comparative trial that included 200 participants who were divided into 2 groups, each group included 100 individuals. Group A (IBS group) included both male and female individuals of varying nationalities, with age range between 18 to 60 years, who presented symptoms consistent with IBS and were following their IBS condition in the internal medicine department in NMC Royal hospital from 2022 to 2024. Group B (Non-IBS group) included 100 individuals without any symptoms of IBS with similar demographic characters of Group A. All participants provided informed consent. Exclusion criteria included participants with Diabetes Mellitus (DM), history of gestational DM, older than 60 years, had hypertension, and any other evidence of other diseases within any other organ.

To evaluate the potential association between IBS and metabolic syndrome, the following measurement techniques were employed:

1- Physical evaluation: Body Mass Index (BMI) was calculated for all participants based on their weight and height to determine obesity levels, specifically targeting a BMI threshold of 25 or more.

2- Laboratory evaluations: Blood tests were conducted to measure fasting blood glucose (FBG), glycated hemoglobin (HbA1c), liver enzymes (alanine aminotransferase [ALT] and aspartate aminotransferase [AST]), as well as lipid profiles, which included low-density lipoprotein (LDL), and triglycerides. Specific thresholds were set for each test: FBG levels were deemed abnormal if they exceeded 99 mg/dL, HbA1c levels above 5.7%, ALT and AST levels exceeding 50 U/L, LDL cholesterol levels above 100 mg/dL, HDL cholesterol levels below 40 mg/dL, and triglycerides above 150 mg/dL.

3- Clinical evaluation of IBS symptoms: Each participant in Group A underwent a thorough clinical evaluation to record the specific IBS symptoms, such as abdominal pain or discomfort, bloating, gas, and altered bowel movements.

4- Abdominal Ultrasound: An ultrasound was performed on all participants to assess for the presence and degree of fatty liver disease, which can be an indicator of fat accumulation in the liver associated with metabolic disturbances.

Statistical analysis:

The Statistical analysis was conducted by SPSS for data entry and analysis. Descriptive data (e.g., frequencies and percentages) were calculated, and the x 2 test and t test were applied accordingly. A statistically significant difference was considered when the p-value was less than 0.05.

3. Results

The findings of the clinical evaluation revealed that Group A with IBS reported various IBS symptoms, including fatigue, abdominal distension, and irregular bowel function. The effect of sex-specific factor for Group A (with IBS) and Group B (Non-IBS group) was shown in Table 1, 2 respectively. In the initial sample of 100 participants with IBS, 24% were female, and 76% were male (Table 1). This indicates that the participants with IBS had a higher male representation, which may influence the generalizability of certain outcomes, as IBS-related health risks and responses to interventions may differ by sex. On the other hand, in the follow-up sample of 100 participants who had no IBS status, the gender composition shifted slightly, with 9% female and 91% male (Table 2).

Table 1: Sex-specific factor for Group A:

Sex for Group A					
		Frequency	Percent	Valid Percent	Cumulative Percent
Valid	F	24	24.0	24.0	24.0
	M	76	76.0	76.0	100.0
	Total	100	100.0	100.0	

Table 2: Sex-specific factor for Group B:

Sex for Group B					
		Frequency	Percent	Valid Percent	Cumulative Percent
Valid	F	9	9.0	9.0	9.0
	M	91	91.0	91.0	100.0
	Total	100	100.0	100.0	

HbA1c levels for Group A and Group B were revealed in Tables 3,4. The mean baseline HbA1c level among Group A

participants with IBS was 5.945 (t = -29.070, p < 0.001), which is significantly lower than the test value of 7.5. (Table 3).

At follow-up, the mean HbA1c among Group B (Non-IBS group) decreased further to 5.314 (t = -76.992, p < 0.001), indicating substantial improvement in glycemic control (Table 4).

Additionally, HbA1c levels indicated prediabetes, with many individuals exceeding the 5.7% threshold, and FBG levels were frequently elevated beyond 99 mg/dL (Table 4)

Table 3: Descriptive statistics of HbA1c for Group A and Group B:

One-Sample Statistics				
Item	N	Mean	Std. Deviation	Std. Error Mean
HbA1c for Group A	100	5.94500	0.534917	0.053492
HbA1c for Group B	99	5.31414	0.282485	0.028391

Table 4: The one-sample t-test results for HbA1c for Group A and Group B:

One-Sample t-Test						
Item	Test Value = 7.5					
	t	df	Sig. (2-tailed)	Mean Difference	95% Confidence Interval of the Difference	
					Lower	Upper
HbA1c for Group A	-29.070	99	0.000	-1.555000	-1.66114	-1.44886
HbA1c for Group B	-76.992	98	0.000	-2.185859	-2.24220	-2.12952

The analysis of liver enzymes was shown in Tables 5-7. Elevated liver enzymes were noted, with levels exceeding 50 U/L in a significant proportion of participants (Table 6,7).

The mean ALT level for participants of Group A with IBS was 42.54, which is close to normal with no significant difference from the test value of 45 (t = -1.064, p = 0.290) (Table 6).

In Group B, the follow-up mean of ALT level decreased significantly to 36.79 (t = -9.137, p < 0.001), suggesting an improvement in liver function upon transitioning to a Non-IBS status (Table 6). On the other hand, the mean AST level in Group A (the IBS group) was 4.78, which was close to to normal with no significant difference from the test value of 45 (t = -1.850, p = 0.067) (Table 7). At follow-up, AST levels in Group B were significantly lower, with a mean of 5.46 (t = -5.608, p < 0.001) (Table 7).

Table 5: Descriptive statistics of ALT levels in Group A and Group B:

One-Sample Statistics				
	N	Mean	Std. Deviation	Std. Error Mean
ALT for Group A	100	42.54000	23.127848	2.312785
ALT for Group B	100	36.79000	8.985167	0.898517

Table 6: The one-sample t-test results for ALT levels in Group A and Group B:

One-Sample t-Test						
Item	Test Value = 45					
	t	df	Sig. (2-tailed)	Mean Difference	95% Confidence Interval of the Difference	
					Lower	Upper
ALT for Group A	-1.064	99	0.290	-2.460000	-7.04907	2.12907
ALT for Group B	-9.137	99	0.000	-8.210000	-9.99285	-6.42715

Table 7: The one-sample t-test results for liver enzymes levels in Group A and Group B:

One-Sample t-Test						
Item	Test Value = 45					
	t	df	Sig. (2-tailed)	Mean Difference	95% Confidence Interval of the Difference	
					Lower	Upper
ALT for Group A	-1.064	99	0.290	-2.460000	-7.04907	2.12907
ALT for Group B	-9.137	99	0.000	-8.210000	-9.99285	-6.42715
AST for Group A	-1.850	98	0.067	-4.777778	-9.90233	0.34677
AST for Group B	-5.608	99	0.000	-5.460000	-7.39170	-3.52830

The descriptive statistics and one-sample t-test results for triglycerides and ultrasound for individuals in Group A and Group B were displayed in Tables 8,9. In Group A, triglycerides and ultrasound shows a mean of 191.58 (SD = 66.68) (Table 8) and significantly exceeds the test value (t = 6.236, p < 0.001), with a confidence interval (28.35, 54.81) entirely above zero, indicating a substantial deviation from 150 (Table 9). This result highlights the elevated triglyceride and ultrasound levels in the IBS group compared to the test benchmark. In contrast, in Group B, the results for triglycerides and ultrasound were compared against a benchmark value of 150 with a mean of 154.41 (SD = 28.85), showed no statistically significant difference from the test value (t = 1.529, p = 0.130) (Table 8), as its confidence interval (-1.31, 10.13) includes zero (Table 9). This suggests that TG/US for Non-IBS group values are not meaningfully different from 150. In addition, a concerning number of

participants had triglyceride levels above 150 mg/dL.LDL cholesterol levels LDL were found to exceed 100 mg/dL (Table 8)

Table 8: Descriptive statistics for triglycerides and ultrasound in Group A and Group B:

One-Sample Statistics				
	N	Mean	Std. Deviation	Std. Error Mean
Triglycerides and ultrasound in Group A	100	191.58000	66.675027	6.667503
Triglycerides and ultrasound in Group B	100	154.41000	28.851797	2.885180

Table 9: The one-sample t-test results for triglycerides and ultrasound in Group A and Group B:

One-Sample t-Test						
Item	Test Value = 150					
	t	df	Sig. (2-tailed)	Mean Difference	95% Confidence Interval of the Difference	
					Lower	Upper
Triglycerides and ultrasound in Group A	6.236	99	.000	41.580000	28.35023	54.80977
Triglycerides and ultrasound in Group B	1.529	99	.130	4.410000	-1.31482	10.13482

Table 10, 11 revealed BMI figures that indicated that many participants fell into the overweight or obese categories. The mean BMI at baseline for Group A was 29.33 (Table 10), significantly higher than the reference test value of 25 ($t = 8.883$, $p < 0.001$) (Table 11). At follow-up, the mean BMI for Group B (Non-IBS) was 24.316 (Table 10), significantly lower than the test value of 25 ($t = -2.793$, $p = 0.006$) (Table 11).

Table 10: Descriptive statistics for BMI in Group A and Group B:

One-Sample Statistics				
	N	Mean	Std. Deviation	Std. Error Mean
BMI for Group A	100	29.33090	4.875483	.487548
BMI for Group B	100	24.31600	2.448612	.244861

Table 11: The one-sample t-test results for BMI in Group A and Group B:

One-Sample t-Test						
Item	Test Value = 25					
	t	df	Sig. (2-tailed)	Mean Difference	95% Confidence Interval of the Difference	
					Lower	Upper
BMI for Group A	8.883	99	.000	4.330900	3.36350	5.29830
BMI for Group B	-2.793	99	.006	-.684000	-1.16986	-.19814

4. Discussion

IBS is a prevalent and serious health issue. It has a major detrimental influence on social functioning and life quality, so it shouldn't be neglected (Camilleri, 2021). The effect of sex-specific factor indicated that the reduction in the percentage of female participants may reflect different responses to the intervention or could be attributed to attrition rates among females. This trend may warrant further exploration to determine whether sex-specific factors influenced the intervention outcomes or participant retention rates. According to studies, IBS is more common in females than in males. In the context of medical care, a more sex-gender-oriented approach may enhance comprehension of diverse IBS patients (Kim & Kim, 2018).

The comparative analysis from the present study indicatesd a significant relationship between IBS and metabolic syndrome. The results of the present study revealed that markers of metabolic syndrome were substantially lower in Non-IBS individuals, showcasing that participants with IBS were more likely to exhibit metabolic dysregulations. Although the mean HbA1c was within the controlled levels in the present results, the variability indicated potential risks associated with IBS, as IBS is commonly associated with higher risks of dysregulated glucose metabolism. This was in agreement with Chen et al. (2024), Jess et al. (2020), and Yorulmaz et al. (2011). Also, it was found that individuals with IBS are more susceptible to early signs of insulin resistance and prediabetes, highlighting that IBS could serve as a potential early warning signal for metabolic dysfunction (Dragasevic et al., 2020; Hemminki, et al., 2010). As it was shown in the results, at follow-up, the mean HbA1c among Non-IBS group decreased indicating substantial improvement in glycemic control. This decrease aligns with the beneficial effects anticipated from a reduction in IBS and highlighted the effectiveness of the intervention in achieving optimal HbA1c levels. Lowering HbA1c values suggest reduced risk for diabetes-related complications in the group without IBS Patients with IBS symptoms may benefit from an initial metabolic syndrome assessment, which could result in

preventive measures to avoid the development of type 2 diabetes and cardiovascular disorders (Lemieux & Després, 2020, Frankenberg et al., 2017).

According the present findings, elevated ALT levels are often associated with liver strain or non-alcoholic fatty liver disease, which is a common comorbidity in IBS. These levels indicate that the IBS group was at a mild risk for liver-related conditions. Although within the normal range, higher AST levels could indicate early hepatic stress or metabolic dysfunction associated with IBS. On the other hand, the follow-up mean of ALT and AST levels decreased significantly suggesting an improvement in liver function upon transitioning to a non-IBS status. This reduction in ALT reflects decreased hepatic strain and an improvement in overall liver health, likely attributable to weight loss and metabolic improvements in the Non-IBS Syndrome group, supporting the benefit of weight management on liver function. This was in consistent with AbdAl-Rhman (2023) and Gadour et al. (2021). Indeed, it was mentioned that intestinal permeability is higher in those with IBS (Hanning et al., 2021). Thus, the current study confirms the positive correlation between liver enzymes and IBS, and it is probable that IBS itself could be the cause of elevated liver enzymes. The present results also highlighted the elevated triglyceride and ultrasound levels in the IBS group compared to the test benchmark, indicating the relation between elevated levels of triglycerides and IBS. This was in agreement with Helvaci, et al. (2022) and Bayrak (2020). According to Guo et al. (2014), increased triglycerides levels in addition to higher rates of metabolic syndrome are independently associated with IBS.

With regard to BMI, the present results revealed a high mean BMI that aligns with an overweight/IBS classification, indicating increased risk for metabolic disorders, cardiovascular disease, and other IBS-related conditions. However, at follow-up, the mean BMI for Non-IBS was significantly lower than the test value and this transition into a healthier BMI range signifies the success of weight management interventions, reducing BMI-related health risks and supporting overall wellness in participants. In line with these findings, it was reported that individuals who are obese with high BMI are more likely to suffer from severe IBS and many other major chronic illnesses such as DM (AbdAl-Rhman, 2023; Emerenziani al., 2019; Nuaman, 2017).

This study suggests that those presenting with IBS should be monitored closely for changes in metabolic health, allowing for dietary and lifestyle interventions that could mitigate the risks associated with metabolic syndrome (van Namen et al., 2019). Furthermore, engaging in early lifestyle modifications can be greatly beneficial. For instance, weight management, dietary changes such as an increase in fiber intake, and regular physical activity may help not only reduce IBS symptoms but also assist in controlling body weight and improving insulin sensitivity. These interventions may serve as both primary and secondary preventive strategies (Sayon-Orea et al., 2019).

The implications of our findings underscore the need for heightened awareness among healthcare professionals about the connection between gastrointestinal symptoms and metabolic health. Expanding our understanding of IBS as an early indicator for metabolic syndrome can support the development of targeted screening protocols, fostering a more integrated approach to patient care for those presenting with IBS symptoms (Najjar & Russo, 2014).

Through systematic screening and proactive management, it is feasible to anticipate and avert the debilitating consequences of diabetes and metabolic syndromes, making a compelling case for the association between IBS and insulin resistance as a significant area of research in the field of metabolic health. Hence, insulin resistance, a core component of Metabolic Syndrome, can manifest through various symptoms, including the gastrointestinal distress often seen in patients with IBS. The connection between these two syndromes reveals the importance of considering IBS not just as a digestive disorder but also as a potential warning sign for broader metabolic issues. Individuals with IBS may unknowingly be at an increased risk for developing insulin resistance, which could lead to more serious metabolic diseases if left unaddressed (Yao et al., 2014; Gulcan et al., 2009).

5. Conclusion:

It is concluded that understanding the relationship between IBS and other disorders can provide vital insights into early intervention strategies that may prevent the progression to more severe health complications, such as diabetes. IBS can be not only as a digestive disorder but also as a potential warning sign for broader metabolic issues like insulin resistance.

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