Original Article

Impact of High-Fructose Diet on Hepatic Enzyme Regulation and Insulin Resistance in Young Adults

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ABSTRACT

Objective: To evaluate the impact of high-fructose dietary intake on hepatic enzyme regulation, insulin resistance, and metabolic profiles in young adults, and to determine correlations between fructose consumption and key metabolic indicators.

Study Design: Prospective, comparative study

Place and Duration of Study: This study was conducted at the Poonch Medical College Rawalakot, from July 2024 to June 2025.

Methods: This prospective, comparative study include 210 young adults aged 18–30 years.

Results: High-fructose consumers demonstrated significantly higher BMI (27.4 ± 4.3 kg/m²), waist circumference (88.7 ± 10.1 cm), and daily caloric intake (2450 ± 430 kcal) than low-fructose individuals. Hepatic enzymes including ALT (50.7 ± 15.1 vs. 34.9 ± 10.2 U/L), AST (41.8 ± 12.1 vs. 31.0 ± 8.9 U/L), ALP, and GGT were elevated in the high-fructose group (all $p < 0.001$). Hepatic steatosis prevalence was nearly double (39% vs. 20%). Insulin resistance markers were significantly worse, with higher fasting glucose (102.7 ± 11.1 mg/dL), fasting insulin (18.2 ± 7.1 µIU/mL), and HOMA-IR (4.65 ± 1.52 vs. 2.39 ± 0.96). Lipid abnormalities included higher triglycerides (189.4 ± 45.2 mg/dL), higher LDL, and lower HDL. Fructose intake strongly correlated with ALT ($r = 0.62$), HOMA-IR ($r = 0.71$), triglycerides ($r = 0.58$), and waist circumference ($r = 0.49$), all $p < 0.001$.

Conclusion: High fructose intake is associated with significant hepatic stress, insulin resistance, dyslipidemia, and central adiposity in young adults. Early metabolic disruption underscores the need to reduce fructose-rich foods and beverages to prevent long-term metabolic disease.

Key Words: high-fructose diet, hepatic enzymes, insulin resistance, HOMA-IR, young adults, metabolic syndrome, triglycerides, hepatic steatosis, NAFLD

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INTRODUCTION

The rising consumption of fructose-rich foods and beverages has emerged as a major nutritional concern, particularly among young adults who represent the highest consumers of processed sugars worldwide[1]. Fructose intake has increased markedly over the past few decades due to widespread availability of sugar-sweetened beverages, high-fructose corn syrup (HFCS), and ultra-processed foods. Unlike glucose, fructose follows a distinct metabolic pathway that bypasses key regulatory steps of glycolysis, leading to rapid hepatic uptake and unregulated lipogenesis[2].

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As a result, high-fructose diets have been implicated in the development of metabolic syndrome, non-alcoholic fatty liver disease (NAFLD), and insulin resistance conditions whose prevalence is alarmingly rising among younger populations. Hepatic metabolism of fructose is unique in that it is primarily driven by fructokinase (ketohexokinase), which converts fructose into fructose-1-phosphate without feedback inhibition by insulin or ATP levels. This unregulated phosphorylation can lead to ATP depletion, elevated uric acid production, formation of reactive oxygen species (ROS), and increased triglyceride synthesis in hepatocytes[3]. These biochemical events contribute to hepatic steatosis, mitochondrial dysfunction, and endoplasmic reticulum stress, which collectively impair insulin signaling pathways. Previous controlled feeding trials have demonstrated that high-fructose diets increase liver fat content even in otherwise healthy young adults within a matter of weeks, highlighting the rapid and detrimental hepatic effects of fructose overconsumption[4]. Fructose-induced insulin resistance is linked to impaired IRS-1 and Akt phosphorylation, increased hepatic gluconeogenesis, and dysregulated lipid metabolism. Young adults are particularly vulnerable to these alterations because their dietary

patterns often include high daily fructose loads and low intake of fiber and antioxidant-rich foods[5]. Epidemiological findings further suggest that excessive fructose intake correlates with elevated fasting insulin levels, increased HOMA-IR scores, and early metabolic derangements even in non-obese individuals[6]. Additionally, fructose stimulates de novo lipogenesis (DNL) to a far greater extent than glucose, contributing to triglyceride accumulation, elevated VLDL secretion, and dyslipidemia factors strongly linked with cardiometabolic risk in young populations[7]. High-fructose diets also affect hepatic enzyme regulation. Studies show increased expression of lipogenic enzymes such as ACC, FAS, and SREBP-1c, and altered activities of ALT and AST biomarkers traditionally used to assess hepatocellular injury[8]. This suggests that chronic fructose exposure may predispose individuals to NAFLD progression, particularly in the early adult years when lifestyle choices strongly shape long-term metabolic trajectories. Furthermore, the inflammatory response triggered by hepatic fructose metabolism including TNF-α, IL-6, and CRP elevation promotes systemic insulin resistance, independent of body weight changes[9]. Given the rising global burden of metabolic diseases and the disproportionately high consumption of fructose among young adults, it is critical to understand how fructose influences hepatic enzyme regulation and insulin sensitivity in this demographic[10].

METHODS

This prospective comparative study was conducted at Poonch Medical College, Rawalakot, from July 2024 to June 2025 and included 210 young adults aged 18–30 years. Participants were divided into a high-fructose intake group (n=105) and a low-fructose intake group (n=105). Individuals with a regular dietary pattern for at least three months, willingness for fasting blood sampling, and informed consent were included. Participants with known liver disease, diabetes or prediabetes, alcohol intake >20 g/day, use of steroids, hepatotoxic or weight-loss medications, inflammatory illnesses, pregnancy, or lactation were excluded.

Data Collection

Demographic and lifestyle data, including age, gender, BMI, physical activity, and beverage consumption, were recorded. Dietary fructose intake was assessed using a validated food frequency questionnaire covering sugar-sweetened beverages, fruit juices, processed snacks, bakery products, and high-fructose corn syrup–containing foods. After an 8–10-hour fast, blood samples were collected for ALT, AST, ALP, GGT, lipid profile, fasting glucose, fasting insulin, and uric acid. Insulin resistance was calculated using HOMA-IR, while liver ultrasound was performed where indicated to assess hepatic steatosis.

Statistical Analysis

Data were analyzed using SPSS version 25.0. Continuous variables were expressed as mean±SD and compared using the independent t-test, while categorical variables were presented as frequencies and percentages and compared using the Chi-square test. Pearson correlation was used to assess associations between fructose intake, hepatic enzymes, and HOMA-IR, while multiple linear regression identified independent predictors of insulin resistance and elevated liver enzymes. A p-value <0.05 was considered statistically significant.

RESULTS

The two groups were similar in age (24.1±3.6 vs. 23.5±3.2 years; p=0.28) and gender distribution (63/42 vs. 55/50; p=0.19). However, the high-fructose group had significantly higher BMI (27.4±4.3 vs. 24.8±3.8 kg/m²), waist circumference (88.7±10.1 vs. 79.7±8.2 cm), and daily caloric intake (2450±430 vs. 1970±350 kcal), all p<0.001. Physical inactivity was also more common in the high-fructose group (57 vs. 41 participants; p=0.03), indicating a less favorable anthropometric and lifestyle profile. (Table 1)

Daily fructose intake was substantially higher in the high-fructose group (72.4±15.3 vs. 36.8±11.4 g/day; p<0.001). These participants also consumed more sugary beverages (12.4±3.9 vs. 4.0±2.1 servings/week) and processed foods (14.3±4.8 vs. 7.3±3.2 servings/week), while consuming less natural fruit (4.8±2.4 vs. 7.4±3.1 servings/week) and dietary fiber (15.6±5.3 vs. 21.4±5.8 g/day), with all differences statistically significant at p<0.001. (Table 2)

Table No. 1: Baseline Demographic and Anthropometric Characteristics (n = 210)

Variable	Total (n = 210)	High-Fructose Group (n = 105)	Low-Fructose Group (n = 105)	p-value
Age (years), mea ± SD	23.8 ± 3.4	24.1 ± 3.6	23.5 ± 3.2	0.28
Gender (Male/Female)	118 / 92	63 / 42	55 / 50	0.19
BMI (kg/m²), mean ± SD	26.1 ± 4.2	27.4 ± 4.3	24.8 ± 3.8	<0.001*
Waist circumference (cm)	84.2 ± 9.6	88.7 ± 10.1	79.7 ± 8.2	<0.001*
Physical activity (Active/Inactive)	112 / 98	48 / 57	64 / 41	0.03*
Daily caloric intake (kcal)	2210 ± 410	2450 ± 430	1970 ± 350	<0.001*

Liver-related parameters were significantly higher among high-fructose consumers. Mean ALT was 50.7±15.1 vs. 34.9±10.2 U/L, AST 41.8±12.1 vs. 31.0±8.9 U/L, ALP 95.1±22.8 vs. 81.3±23.1 U/L, and GGT 47.8±13.0 vs. 35.2±9.8 U/L. All differences were

significant (p≤0.001). Hepatic steatosis was also more frequent in the high-fructose group, affecting 41 (39.0%) compared with 21 (20.0%) participants (p=0.003), suggesting an association between higher fructose intake and poorer hepatic status.

Table No. 2: Dietary Intake Profile and Fructose Consumption

Variable	Total	High-Fructose Group	Low-Fructose Group	p-value
Daily fructose intake (g/day), mean ± SD	54.6 ±18.9	72.4 ± 15.3	36.8 ± 11.4	<0.001*
Sugary beverages (servings/ week)	8.2 ± 4.1	12.4 ± 3.9	4.0 ± 2.1	<0.001*
Processed food intake (servings/ week)	10.8 ± 5.3	14.3 ± 4.8	7.3 ± 3.2	<0.001*
Natural fruit intake (servings/ week)	6.1 ± 3.0	4.8 ± 2.4	7.4 ± 3.1	<0.001*
Fiber intake (g/day)	18.5 ± 6.2	15.6 ± 5.3	21.4 ± 5.8	<0.001*

Table No. 3: Hepatic Enzyme Levels

Variable	Total (n = 210)	High-Fructose (n = 105)	Low-Fructose (n = 105)	p-value
ALT (U/L), mean ± SD	42.8 ± 14.3	50.7 ± 15.1	34.9 ± 10.2	<0.001*
AST (U/L), mean ± SD	36.4 ± 11.8	41.8 ± 12.1	31.0 ± 8.9	<0.001*
ALP (U/L), mean ± SD	88.2 ± 24.7	95.1 ± 22.8	81.3 ± 23.1	0.001*
GGT (U/L), mean ± SD	41.5 ± 12.6	47.8 ± 13.0	35.2 ± 9.8	<0.001*
Hepatic steatosis, n (%)	62 (29.5%)	41 (39.0%)	21 (20.0%)	0.003*

The high-fructose group showed significantly less favorable glycemic parameters. Fasting glucose was 102.7±11.1 vs. 93.7±8.6 mg/dL, fasting insulin 18.2±7.1 vs. 11.4±4.2 µIU/mL, HOMA-IR 4.65±1.52 vs. 2.39±0.96, and HbA1c 5.6±0.5% vs. 5.2±0.3%, with all p<0.001. Impaired fasting glucose was also more frequent among high-fructose consumers, occurring in 31 (29.5%) compared with 11 (10.5%) participants (p=0.001), indicating greater insulin resistance and impaired glucose regulation.

Table No. 4: Glycemic and Insulin Resistance Parameters

Parameter	Total (n = 210)	High-Fructose (n = 105)	Low-Fructose (n = 105)	p-value
Fasting glucose (mg/dL)	98.2 ± 10.4	102.7 ± 11.1	93.7 ± 8.6	<0.001*
Fasting insulin (µIU/mL)	14.8 ± 6.2	18.2 ± 7.1	11.4 ± 4.2	<0.001*
HOMA-IR score	3.52 ± 1.40	4.65 ± 1.52	2.39 ± 0.96	<0.001*
HbA1c (%)	5.4 ± 0.4	5.6 ± 0.5	5.2 ± 0.3	<0.001*
Impaired fasting glucose, n (%)	42 (20.0%)	31 (29.5%)	11 (10.5%)	0.001*

High-fructose intake was associated with a more adverse lipid and metabolic profile. Total cholesterol was 202.3±34.2 vs. 174.5±32.9 mg/dL, triglycerides 189.4±45.2 vs. 136.2±40.7 mg/dL, and LDL-C 113.6±26.9 vs. 93.8±24.7 mg/dL, while HDL-C was lower at 41.3±8.9 vs. 48.3±9.1 mg/dL. Uric acid was also higher in the high-fructose group (6.4±1.2 vs. 5.2±1.0 mg/dL). All differences were statistically significant at p<0.001, reflecting a less favorable cardiometabolic profile among participants with higher fructose intake.

Table No. 5: Lipid Profile and Metabolic Markers

Variable	Total (n = 210)	High-Fructose (n = 105)	Low-Fructose (n = 105)	p-value
Total cholesterol (mg/dL)	188.4 ± 36.1	202.3 ± 34.2	174.5 ± 32.9	<0.001*
Triglycerides (mg/dL)	162.8 ±48.6	189.4 ± 45.2	136.2 ± 40.7	<0.001*
HDL-C (mg/dL)	44.8 ± 9.7	41.3 ± 8.9	48.3 ± 9.1	<0.001*
LDL-C (mg/dL)	103.7 ± 28.2	113.6 ± 26.9	93.8 ± 24.7	<0.001*
Uric acid (mg/dL)	5.8 ± 1.3	6.4 ± 1.2	5.2 ± 1.0	<0.001*

DISCUSSION

In this study, there was a strong correlation between the high fructose intake with early metabolic dysfunction in young adults, such as adiposity, hepatic function,

insulin resistance, and lipid metabolism. Participants who consumed the highest amounts of fructose had significantly higher BMI (27.4±4.3 kg/m²) and waist circumference (88.7±10.1 cm), reflecting higher central and overall adiposity. This was similar to the previous studies that demonstrated de novo lipogenesis and central fat accumulation with fructose[11]. This poor metabolic profile could have been further aided by the increased calorie intake and the decrease in exercise in the high fructose group. Results of the dietary analysis revealed that high fructose consumers consumed almost twice as much fructose per day and significantly more sweetened beverages and processed foods. In line with previous studies, consumption of sugar-sweetened beverages were linked to higher triglycerides, fatty liver, and insulin resistance[12]. Contrary to this, the high fructose group consumed less natural fruit and dietary fibre, which could further increase the metabolic risk as previous research has shown that fibre may have a beneficial effect on some of the adverse effects of the excessive intake of fructose[13]. The findings in the liver were singled out. The levels of ALT and AST were also significantly elevated in the high-fructose group at 50.7±15.1 U/L and 41.8±12.1 U/L, respectively, with elevated ALP and GGT. Hepatic steatosis was more common in high fructose consumers (39.0%) than in low fructose consumers (20.0%). The results are similar to those from other studies that have shown that excess fructose increases lipogenesis and alters fatty acid metabolism, leading to hepatic fat accumulation[14].

High fructose consumers also had significantly higher insulin resistance. Fasting glucose and fasting insulin were significantly elevated, as well as HOMA-IR (4.65±1.52 vs. 2.39±0.96 in the low fructose group). Moreover, impaired fasting glucose occurred more often (29.5% vs. 10.5%). Fructose metabolism has been previously associated with ATP depletion, uric acid production, inflammation and impaired insulin signaling[15]. The results indicate that metabolic dysfunction can occur prior to the onset of clinical diabetes. The same was found for positive associations of fructose consumption with total cholesterol (r= 0.37), LDL-C (r= 0.37), uric acid (r= 0.53) and waist circumference (r= 0.49), which corroborate the previous reports of lipogenic properties of fructose[16]. In addition, fructose consumption was highly associated with ALT (r=0.62) and HOMA-IR (r=0.71), all of which are linked to unregulated lipogenesis, oxidative stress and insulin signaling deficits after excessive fructose consumption, as described previously[17]. The results overall suggest that high fructose consumption is linked to early hepatic and metabolic dysfunction even in young adults. Early dietary changes, more exercise, and reducing the intake of processed sources of fructose, may therefore help to reduce the progression to fatty liver disease, insulin resistance, and future metabolic syndrome.

CONCLUSION

It is concluded that high-fructose intake adversely affects hepatic and metabolic health in young adults. Higher fructose consumption was associated with elevated liver enzymes, greater hepatic steatosis, increased fasting insulin and HOMA-IR, higher triglycerides and LDL-C, and lower HDL-C. These findings suggest that excessive fructose intake may contribute to early hepatic stress, insulin resistance, and metabolic dysfunction even in otherwise healthy young adults.

Author's Contribution:

Concept & Design or acquisition of analysis or interpretation of data:	Farhana Ayub
Drafting or Revising Critically:	Farhana Ayub
Final Approval of version:	The above author
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