History of Medicine, 2023, 9(1): 1519–1525
DOI: 10.17720/2409-5834.v9.1.2023.185

The Role of collagen Supplement to The Improvement of Insulin Resistance

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Received: 20 January 2023 **Accepted:** 15 April 2023

Citation: Taha BE, Majeed MJ (2023) The Role of collagen Supplement to The Improvement of Insulin Resistance. History of Medicine 9(1): 1519−1525. https://doi.org/10.17720/2409-5834.v9.1.2023.185

Abstract

Background Insulin resistance is a problem that many of us suffer from. It has been studied from several aspects, including changing the lifestyle through exercise, limiting the high-carbohydrate diet, and through proven facts about glycine through its role as a precursor for several crucial metabolites, including creatine, haem, porphyrins, and glutathione. Glycine functions as a neurotransmitter in the central nervous system and has a variety of functions in peripheral and nervous tissue, including immunomodulatory, cryoprotective, antioxidant, and anti-inflammatory effects. These facts have sparked research into the role of glycine in lowering insulin resistance. Objective: Studying the level of glycine as a major amino acid in the formation of collagen in the case of insulin resistance and, simultaneously, studying the possibility of using it as a treatment for the condition. Subjects, Material, and Method: Analytical cross-sectional and cohort designs are the two types of statistical designs. The study was conducted on 160 volunteers, recruited at the beginning of the study and chosen from an age group based on the study data and the preliminary analysis, with ages ranging from (40-70 years). They were separated into two groups: the first group includes 80 individuals, after adopting an average body mass index of more than 25, who suffer from insulin resistance, and the second group includes 80 healthy individuals who do not suffer from insulin resistance and whose body mass index is less than 25. It was determined Blood glucose, lipid profile, and HBA1C using Cobas c111 on serum samples from both groups. Fasting insulin was determined using Cobas E411 and serum glycine using ELISA kits. Results: Individuals with insulin resistance have significantly lower serum glycine levels (p≤ and diabetes finding of studied (0.05) in comparison with healthy individuals without insulin resistance, and after collagen (1tab/day) at fasting state supplement show a significant decrease in the level of serum fasting glucose, triglyceride, fasting insulin, homeostatic model of assessment insulin resistance (HOMA-IR) and triglyceride-Glucose index (TyG). Conclusion: The level of glycine is low in people who have insulin resistance, and at most, according to the results, its decrease is one of the causes of insulin resistance. At the same time, collagen pills can be adopted as a preventative treatment for insulin resistance.

Keywords

insulin resistance, Type 2 diabetes, TyG index, glycine, collagen, insulin secretion, HOMA-1.

The tart with treatment as soon as possible, and type 2 diabetes (T2D) can be stopped in its progression. As a result, great efforts have been made to find indicators that can predict the onset or progression of diabetes and prediabetes. The lowest molecular weight amino acid, glycine, which has a hydrogen atom as a side chain, are proteolytic and glucose-dependent. Glycine serves as a protein building block and is also required for several metabolic processes, including the production of glutathione and the control of one-carbon metabolism (1). Insulin resistance is a disruption of metabolism and is a major and well-established risk factor for heart

disease(2). Lifestyle factors such as poor diet and improper daily activities are among the most important factors which leads to weight gain and thus leads to obesity (3). Obesity is considered a pandemic of the current century by international and global organizations (4). One of the complications of insulin resistance and diabetes is the occurrence of osteoporosis and thus its fracture (5). According to a growing body of studies, one such sign might be a change in plasma glycine (6). As a result, numerous studies have concentrated on T2D prevention and early prediabetes biomarker detection (6)(7). Insulin resistance and obesity negatively correlate with this non-essential amino acid (8). Plasma glycine increases in response to therapies that enhance glucose homeostasis, such as exercise and bariatric surgery, and favorably correlates with glucose elimination. Glycine may be a biomarker, although its function in glucose control is less certain. Supplementing with dietary glycine raises insulin levels, lowers systemic inflammation, and enhances glucose tolerance (9). Supplementing with glycine helps the metabolic syndrome's numerous symptoms, including diabetes, obesity, hyperlipidemia, and hypertension. In the future, using glycine may significantly impact the clinical management of individuals with metabolic syndrome (10). Collagen's fundamental structure comprises three amino acids repeated in a certain order. Glycine, a little amino acid that fits perfectly inside the helix, makes up every third amino acid. Proline and a modified form of proline, two amino acids, occupy most of the chain's gaps (11). Glycine performs various activities in peripheral and neurological tissue, including antioxidant, anti-inflammatory, cryoprotective, and immunomodulatory. It also serves as a neurotransmitter in the brain (12). Several factors, including metformin doses, may contribute to glycemic control and signs of obesity (13)

Subjects, Material, and Method

Patients at the (Specialized Center for Endocrinology and Diabetes in Al-Rusafa /Baghdad) were thought to have T2DM between November 2022 and the end of February 2023. The American Diabetes Association (ADA) and the WHO criteria for diagnosing diabetes mellitus use plasma glucose (FPG or OGTT) or HbA1c estimates. When combined with symptoms of hyperglycemia, the random plasma glucose of 200 mg/dL (11.1 mmol/L), the 2-h OGTT plasma glucose of 200 mg/dL (11.1 mmol/L), the FPG of 126 mg/dL (7.0 mmol/L), or the HbA1c of 6.5 percent (48 mmol/mol) are diagnostic of DM. This study excluded patients with T2DM, insulin therapy, cardiovascular conditions, Cushing disease, and PCOS in women.

BMI ≥ 25 kg/m2 and waist circumference 102 cm in males and 88 cm in women qualified for the insulin resistance test. Age 40 years, plus two or more of the following requirements 150 mg/dl of triglycerides, fasting glucose should be between 110 and 125 mg/dl if it meets the accepted insulin resistance guidelines, and HDL cholesterol should be below 40 mg/dl in men and 50 mg/dl in women (14). (Men comprised 50% of them, and women represented 50%). The study's 80 individuals with IR and 80 healthy controls ranged in age from 40 to 69. based on the spectrum of ages of those who suffer from insulin resistance. The 25 donors were collected from 80 who had insulin resistance, and they were given collagen at the rate of 1 pill each day. They were followed up for 45 days, and the changes in insulin resistance markers were monitored.

To extract the serum from the blood samples and collect it for measuring fasting serum insulin, the blood samples were centrifuged at 3000 rpm for 10 minutes, lipid profile, and fasting serum blood glucose using COBAS C 111 immunoassay analyzers. The remaining serum was kept at (- 20 Co) for automatic ELISA tests to measure glycine levels. The COBAS C 111 analyzer was used to estimate the HbA1c level.

Version twenty-six of SPSS and Minitab version 19 was used to complete the statistical analysis (80). Mean ± standard deviation was used to represent the variables. We tested the chi-square distribution for categorical variables. Three square studies were compared using the student's t-test, and fisher's less significant difference (LSD) between the two groups was calculated using the student's t-test. Bar charts were used to represent the Mean distribution graphically. The correlation between two variables was investigated using a person's correlation coefficient (r). At the level of ($P>0.05$) and ($p0.05$), the differences and correlations between the values were deemed statistically non-significant, respectively. The best serum fasting insulin, glycine, HOMA-IR, IS, and TyG indices were determined using receiver operator curve analysis (ROC).

Results

The matching of the study's population age is accentuation by the non-significant result ($p> 0.05$), as table 1 shows. As a result of choosing the range of the BMI and waist circumference for the research population, it is found a significant ($p\leq 0.05$) difference between the healthy individual without insulin resistance and the individual with insulin resistance, and that serves the purpose of the study(as table 1 present).

Table (1): Age, BMI, and W.C. general characteristics for the mean SD to a person without and with IR.

Parameter	Individual without IR (N= 80) mean ± SD	Individuals with IR (N= 80) mean ± SD	P-Value
Age (years)	53.59±8.63	53.27±8.83	0.82 (N.S)
BMI ($Kg/M^{2)}$	21.3±1.76	32.14±3.7	0.000 (S)
Waist circumference (cm)	76.75±11.06	113.4±8.91	0.000 (S)

N.S: Non-Significant, S: Significant, BMI: body mass index, IR: Insulin resistance, N: number

The American College of Endocrinology (AACE) criteria and the following tests are used to validate the diagnosis of insulin resistance: blood HbA1c, serum fasting glucose, fasting insulin, lipid profile, triglyceride-glucose index, HOMA-IR, and insulin secretion (14). The results in table (2) align with the insulin resistance definition. Also, it's absent.

Table (2): Mean ± SD of the insulin resistance diagnostic sign for a healthy person without and with IR.

Markers	Healthy individuals without IR (N= 80) mean ± SD	Individuals with IR (N= 80) mean ± SD	P-Value
S.F.G (mg/dl)	71.25±9.74	120.85±4.76	0.000 (s)
Blood HbA1c (%)	4.81±0.52	6.34±0.23	0.000 (s)
Serum Fasting Insulin (µU/Ml)	6.75±1.31	20.80±24	0.000 (s)
Serum.T.Cholesterol (mg/dl)	135.86±10.24	174.24±43.40	0.000 (s)
Serum Triglyceride (mg/dl)	76.44±8.21	217.82±72.31	0.000 (s)
Serum LDL cholesterol (mg/dl)	72.53±11.63	97.33±38.17	0.000 (s)
Serum HDL cholesterol (mg/dl)	47.70±5.43	35±6.80	0.000 (s)
HOMA-IR	1.16±0.10	7.24±1.11	0.000 (s)
TyG Index	4.30±0.09	5.05±0.14	0.000 (s)

S.F.G: serum fasting glucose, S.T. Cholesterol: total serum cholesterol, LDL: low-density lipoprotein, HDL: high-density lipoprotein, HOMA-IR: homeostatic model assessment of insulin resistance, HbA1c: glycated hemoglobin, TyG Index: triglyceride − Glucose Index, N: number, s: significant, TG: triglyceride.

An individual with insulin resistance has a significantly lower serum glycine level ($p \leq 0.05$) in comparison with a healthy individual without insulin resistance, as table (3) shows.

Table (3): Mean ± SD Serum glycine averages without and with IR for healthy individuals.

Parameter	A healthy individual without IR (N= 80) mean ± SD	Individual with IR (N= 80) mean ±SD	P-Value
serum Glycine (Pg/ml)	115.6±28.73	44.27±8.85	0.000(s)

IR: insulin resistance, N: number, s: significant.

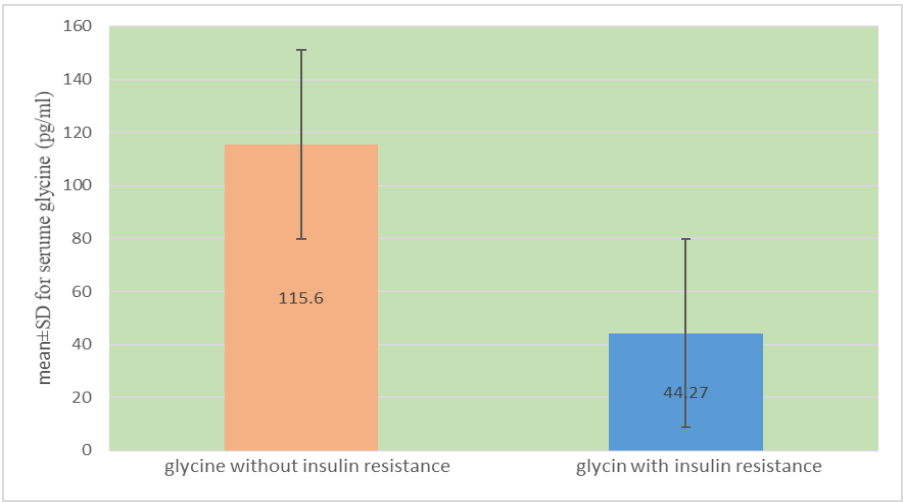

Figure (1): Mean ± Standard deviation (SD) of glycine in healthy individuals and those without insulin resistance.

A person 's correlation for both markers of insulin resistance (TyG index and HOMA-IR) was studied. It found that TyG index and HOMA-IR had a significant positive correlation with each of serum fasting glucose, insulin, and blood HbA1c% (as was expected) with (p≤ 0.05) (r = 0.63, r = 0.35, r = 0.41) (r = 0.65, r = 0.30, r = 0.32). Also, both insulin resistance marker TyG index and HOMA-IR show a significant negative correlation with serum glycine with (p≤ 0.05) (r = -0.21, r = -0.24) consequently. Insulin resistance markers don't show a significant association with insulin secretion (p> 0.05), as table (4,5) shows.

Table (4): correlation between TyG index and each of S.F.G, blood HbA1c, serum insulin, glycine, and insulin secretion for individuals with insulin resistance.

Parameter	TyG index N= 80 r =	P-Value
S.F.G (mg/dl)	0.63	0.000 (S)
Blood HbA1c (%)	0.41	0.000 (S)
Serum Fasting Insulin (µU/Ml)	0.35	0.001(S)
Serum Glycine (Pg/ml)	-0.21	0.05 (S)
Insulin secretion	0.06	0.54 (N.S)

S.F.G: serum fasting glucose, TyG Index: triglyceride − Glucose Index, HbA1c: glycated hemoglobin, N: number, s: significant, N.S: non-significant.

Table (5): correlation between HOMA-IR and each of S.F.G, blood HbA1c, serum insulin, glycine, and insulin secretion for an individual with insulin resistance.

arameter	HOMA-IRN= 80 r =	P-Value
S.F.G (mg/dl)	0.65	0.000 (S)
Blood HbA1c (%)	0.32	0.02 (S)
Serum Fasting Insulin (µU/Ml)	0.30	0.01 (S)
serum Glycine (Pg/ml)	-0.24	0.03 (S)
Insulin secretion	0.04	0.71 (N.S)

S.F.G: serum fasting glucose, HOMA-IR: homeostatic model assessment of insulin resistance, HbA1c: glycated hemoglobin, N: number, s: significant, N.S: non-significant.

It was agreed with 25 donors from an individual with an insulin resistance group, from a total of 80 who obtained their consent to take a collagen supplementation according to FAD, the details of which are mentioned in the second chapter. Individuals with insulin resistance after collagen (1 tab/day) at fasting state supplement show a significant decrease in the level of serum fasting glucose, TG, insulin, HOMA-IR, TyG index, and blood HbA1c (p≤ 0.05). But didn't show a significant difference with total serum cholesterol, LDL-cholesterol, HDL-cholesterol, and insulin secretion (p> 0.05), as table (6) shows.

Table (6): Mean ± SD of the diagnostic marker of insulin resistance for individuals with IR before and after supplementation collagen.

Parameter	individuals before supplementation N= 25 mean ± SD	individual's after supplementation N= 25 mean ± SD	P-Value
S.F.G (mg/dl)	120.7±4.37	106.1±11.74	0.000 (S)
Blood HbA1c (%)	6.26±0.26	5.80±0.31	0.000 (S)
Serum Fasting Insulin (µU/Ml)	24.16±4.5	21.9±3.45	0.001 (S)
Serum .T. Cholesterol (mg/dl)	186±53.5	172.5±55.2	0.10 (N.S)
Serum Triglyceride (mg/dl)	209.9±75.7	180±74	0.009 (S)
Serum LDL cholesterol(mg/dl)	105.2±45.2	99.4±46.6	0.32 (N.S)
Serum HDL cholesterol(mg/dl)	37.35±6.84	37.01±8.66	0.86 (N.S)
HOMA-IR	7.75±1.26	5.73±1.06	0.000 (S)
TyG Index	5.04±0.15	4.90±0.18	0.000 (S)
Insulin secretion	0.19±0.04	0.20±0.04	0.50 (N.S)

S.F.G: serum fasting glucose, S.T. Cholesterol: total serum cholesterol, LDL: low-density lipoprotein, HDL: high-density lipoprotein, HOMA-IR: homeostatic model assessment of insulin resistance, HbA1c: glycated hemoglobin, TyG Index: triglyceride − Glucose Index, N: number, s: significant, N.S: Non-Significant.

Table (7): correlation between HOMA-IR and each of S.F.G, blood HbA1c, serum insulin, and insulin secretion for an individual with insulin resistance after collagen supplementation.

Parameter	HOMA-IR N= 25 r =	P-Value
S.F.G [mg/dl]	0.57	0.003 (S)
Blood HbA1c (%)	0.21	0.41 (N.S)
Serum Fasting Insulin (µU/Ml)	0.63	0.001(S)
Insulin secretion	0.35	0.17 (N.S)

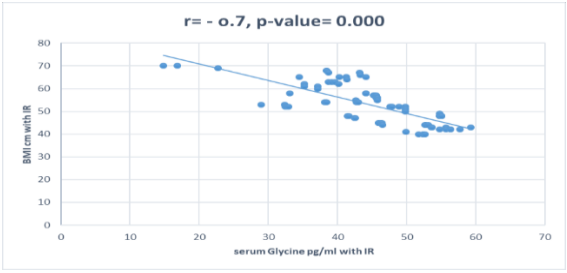

Figure (1): Correlation between serum glycine and BMI for an insulin-resistant individual.

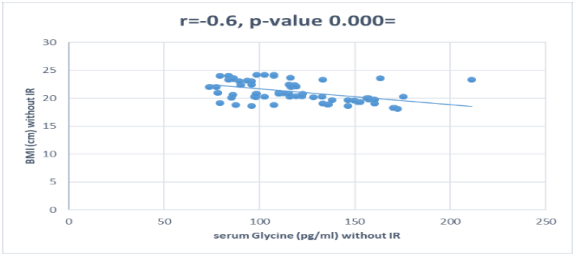

Figure (2): Correlation between serum glycine and BMI for a healthy individual without insulin resistance

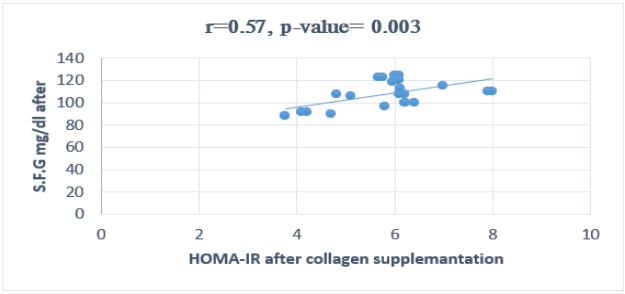

Figure (3): Correlation between HOMA-IR and serum fasting glucose (S.F.G) for an individual with insulin resistance after collagen supplementation.

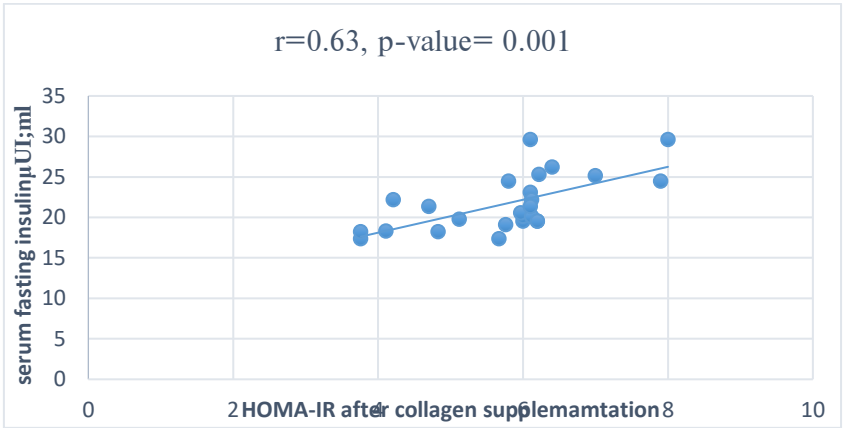

Figure (4): Correlation between HOMA-IR and serum fasting insulin for an individual with insulin resistance after collagen supplementation.

Discussion

Age is associated with insulin resistance, mitochondrial muscle dysfunction, and changes in body composition, which most likely contribute to the development of age-related insulin resistance. The effect of age was excluded by selecting the ages of the control, close to the ages of the patients, and this was documented by the non-significant results that were obtained (15)

To accompany weight with insulin resistance, people with different weights were selected, as shown in Table (1)

Obesity is a risk factor for diabetes that is associated with insulin resistance. Increased quantities of non-esterified fatty acids, glycerol, hormones, and pro-inflammatory cytokines are released by adipose tissue in obese individuals, which may help insulin resistance develop (16).

Although the origin of insulin resistance is unknown, the risk can be increased by having a family history of type 2 diabetes, being overweight (particularly around the waist), and not exercising. Insulin resistance is the most common cause of hyperinsulinemia. The pancreas generates more insulin to counteract increased blood sugar levels caused by improper insulin usage. Diabetes type 2 might be a result of insulin resistance (17).

A previous study found that the neurotransmitter glycine also directly affects the brain, the endocrine pancreas, and other target organs via attaching to the receptors for glycine and (N-methyl -D-aspartate glutamate), which control insulin synthesis and liver glucose output, respectively. Here, we investigate the evidence that glycine, through its central and peripheral actions and changes in T2D, may have a role in glucose homeostasis. (Endocrinology 158: 1064−1073, 2017) (6).

Obesity has an imperfect correlation with that glycine concentration. Previously, New Gard discovered lower glycine levels in 74 obese adults over 50. In a study of Japanese adults with appropriate glucose tolerance, the obese group also showed decreased glycine levels. Glycine demonstrated adverse relationships with the biochemical, hormonal, and clinical markers. These clusters persisted even after we only looked at the ill participants (18).

It was found to be a change in the improvement after giving individual supplementation collagen one pill a day on an empty stomach. The improvement represented decreased serum fasting glucose, fasting insulin, triglyceride, HOMA-IR, TyG index, and increased IS.

Generally, a decrease in glycine early in the disease's progression can exacerbate the disrupted glucose homeostasis. It is clear that glycine plays an important role in cellular signaling that controls glucose homeostasis in both the central nervous system and the periphery, and glycine supplementation increases insulin secretion and improves glucose tolerance (19).

The return of FBG and HbA1c to normal levels at the end of the study period in the study subjects who received oral supplements of collagen-derived peptides demonstrates that collagen peptide is an emerging treatment option to minimize the negative effects of such drugs by reducing the dosage of various types of drugs used to treat Type 2 diabetes (20).

Insulin resistance can cause hyperinsulinemia in anyone, and it can either be temporary or persistent. The two main contributors to insulin resistance and hyperinsulinemia appear to be too much body fat, particularly in the abdominal region, and a lack of activity (21).

Conclusion

The level of glycine is low in people who have insulin resistance, and at most, according to the results, its decrease is one of the causes of insulin resistance. At the same time, collagen pills can be adopted as a preventative treatment for insulin resistance.

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