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THE THERAPEUTIC EFFECTS OF MAGNESIUM SUPPLEMENTATION ON GLYCEMIC CONTROL AND LIPID PROFILE IN TYPE II DIABETES

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Magnesium, Type II diabetes mellitus, FSG, HbA1c%, lipid profile.

ABSTRACT

Individuals with type II diabetes mellitus use dietary supplements on a regular basis. The aim of study was to investigate the therapeutic effect of magnesium supplementation on glycemic control and lipid profile in adult type II diabetes mellitus patients. Seventy type II diabetes patients were allocated into: The intervention group (n=35) was received oral Magnesium oxide 250 mg once daily, and the control group (n=35) was received corn starch as a placebo. The duration of treatment for both groups was two months. After 2 months, the magnesium treated group demonstrated a significant reduction in FSG, HbA1c%, VLDL-C and triglyceride level, while insignificant change in TC, LDL-C and HDL-C, when compared to their pre-supplementation levels and the control group. There is no statistically significant difference between the two studied groups in the mean of age, BMI, systolic and diastolic blood pressure. The intervention group had a significant reduction in FSG ($p= 0.034$), HbA1c% level was significantly reduced in the magnesium treated group ($p = 0.01$) while in the control group HbA1c level is increased. Serum triglyceride levels decreased significantly ($p < 0.05$) in the magnesium supplemented group, but it is increased in the control group (p=0. 54). Oral magnesium supplementation has been shown to be effective in lowering glycaemic control and serum triglyceride level in patients with type 2 diabetes mellitus, and thus may be used as adjuvant therapy for management of patients with type II diabetes mellitus.

1. Introduction

Diabetes mellitus (DM) is a chronic endocrine disease characterized by hyperglycemia [1], [2] with abnormalities in carbohydrate, protein and lipid metabolism [3]. The pathophysiology of DM is related to insulin secretion or action abnormalities with gradual elevation of blood glucose level, The prevalence of DM has increased in the last 30 years, particularly in low and middle income countries [4]. Globally, the prevalence of DM in 2017 was about 425 million adult patients and in Iraq was about 1.4 million adult

patients, according to the International Diabetes Federation (IDF). DM is the eighth cause of death worldwide with a mortality rate of 10.7% of adult patients in 2017 [4]. Diabetic patients need more frequent follow up to maintain normal blood glucose level and to prevent or delay long term complications including micro vascular complications [5]. The goal of treatment is to gain and maintain normal blood glucose level that prevent diabetic complications by using different mechanisms and different drugs. The drug choice depends on many factors, including therapeutic efficacy, possible side effects, especially hypoglycemia and their severity, cost, weight, patient preference, and other patients' current diseases [5- 7]. The management decision should be made according to many factors overviewed in the Figure (1). The glycated hemoglobin HbA1c goal in diabetic patients is less than 7 percent unless there is a high risk of hypoglycemia. That higher percent is considered acceptable in this patient group [8].

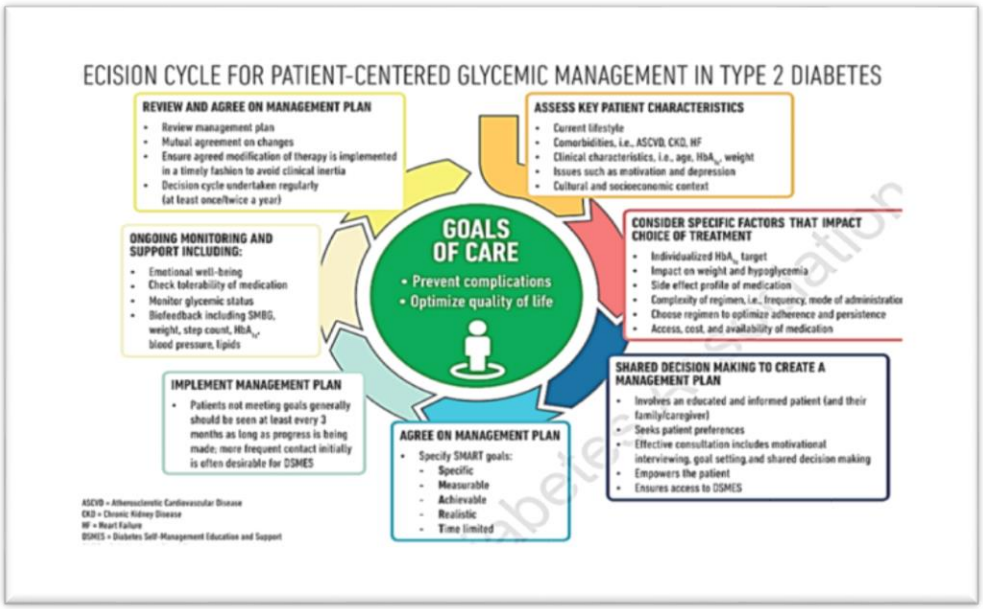

Figure 1. Decision cycle for glycemic control in Type 2 diabetes, Reprinted from American Association of Diabetes [9]

It has been shown that minerals and vitamins may improve the glycemic state in patients with diabetes mellitus. Magnesium is an essential trace mineral that plays a number of roles in human nutrition. Magnesium's critical role as a component of the body's antioxidant system in slowing the oxidative process is particularly important in the context of diabetes. Magnesium is required as a cofactor in a variety of enzymes, aids in the maintenance of the cell membrane's stability, and protects against the effects of oxidative stress [10], [11].

Major processes in which magnesium is involved include protein synthesis, blood glucose control, hormone receptor interaction and many others. Regarding energy production, magnesium plays a vital role in the synthesis of Adenosine triphosphate (ATP) from Adenosine diphosphate (ADP) [10]. In the view point of DM, there is an inverse relationship between magnesium level and the occurrence of DM or insulin resistance [10]. Many studies have shown an improvement in insulin sensitivity and glucose may be controlled by magnesium intake. The molecular mechanism that correlates magnesium deficiency with insulin resistance hasn't been clarified yet, but there are many explanations. One of them links Mg+2 with insulin secretion by affecting glucokinase, as the latter is considered as a glucose-sensor. Mg+2 directly activates it as an enzyme cofactor and increases intracellular ATP. Mg deficiency affects insulin action by

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causing alteration of signaling pathways such as a reduction in phosphoinositide 3 kinase activity, and defects in GLUT4 expression and function as shown in Figure (2)

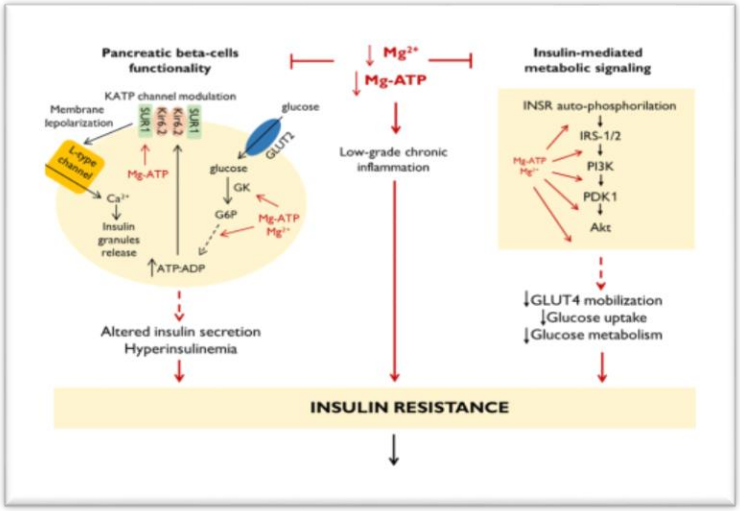

Figure 2. The link between magnesium and insulin signaling [12]

The aim of the current study is to evaluate the significance of the effects of magnesium supplements on glycemic control and lipid homeostasis in type 2 diabetes mellitus by measurement of many parameters including fasting serum glucose, HbA1c, and lipid profile.

2. Materials and Methods

1) Study settings

This case-control study was approved by the Local Health Committee and Ethics Committee at Nineveh Health Directorate, Mosul, Iraq. Patients were collected from Al-Salam Teaching Hospital in Mosul, Iraq and the study also involved out patients. The biochemical analysis was performed at a private laboratory.

2) Study period

This study was conducted at the College of Pharmacy, University of Mosul, Mosul, Iraq. From the 1st of October 2020 to the 1st of March 2021.

3) Ethical approval

An approval was made from the Scientific Committee at College of Pharmacy, University of Mosul which was obtained before conducting the study. Moreover, the participants in this study were completely voluntary. Both verbal and written consent were obtained from them and they were assured that their data would only be used for scientific research.

4) Participants

Seventy diabetic patients were divided randomly into two groups:

I. The Intervention group: This group consists of 35 patients with type 2 diabetes mellitus. They were supplemented with oral Magnesium oxide 250 mg (equivalent to 150 mg elemental magnesium) once daily for a period of 2 months in addition to the oral anti diabetic drugs.

II. The Control group: This group consists of 35 patients with type 2 diabetes mellitus who did not receive magnesium therapy, was supplemented with corn starch as a placebo once daily for three months in addition to the oral anti diabetic drugs.

Participants ranged in age from 24 to 75, with a mean age of 55 years old. The majority of participants were male (60%) and female (40%), and the percentages remained the same after splitting into two groups. Also, all the participants are from Mosul-Iraq with various educational level and different occupations.

The main source of data is participants themselves by filling out a questionnaire and taking simple measures. The questionnaire form contains sample number, patient name, phone number, gender, age (year), height (cm), duration of diabetes mellitus (year), other co-morbidities, and chronic medication, Also, have two measurements taken, one at the beginning and one at the end of the study, of the following: body weight (kg), systolic and diastolic blood pressure (mmHg), and sleep duration (hour).

a) Inclusion criteria include patients with diabetes mellitus type 2, who didn't use insulin.

b) Exclusion criteria include patients with type 1 diabetes, type 2 diabetes using insulin, or patients with impaired kidney function as measured by creatinine > 1.4 mg/dl in males and > 1.2 mg/dl in females were excluded.

All participants were asked to maintain their usual diet and physical activity during the period of the study.

5) Sampling

Venous blood samples)5 ml) were collected from all patient groups (Magnesium and control groups) at baseline and after 3 months of supplement to determine the biochemical changes under the study.

6) Anthropometry

The weight and height of each patient enrolled in the study were measured to calculate the Body Mass Index (BMI) according to the following equation:

$$BMI = \text{Weight (kg)}/\text{Height (m)}^2$$ [13].

7) Materials

Materials used for measuring of Biochemical parameters under the study studied were shown in Table.1. using standard (commercial) kits that were chosen according to their accuracy, dependability, and availability.

Table 1. Biochemical kits used in this study

Kit type	Kit name	Source
HbA1c	Ichroma HbA1c Kit	Korea
Fasting Serum Glucose	Glucose God/Pap Kit	Uk
Triglyceride	Triglycerides Gpo Method Kit	France
Total Cholesterol	Cholesterol Chod Pap Kit	France
HDL-Cholesterol	HDL-Cholesterol (Pta) Kit	France

Fasting serum glucose was measured by the enzymatic method [14], [15], glycated HbA1c was estimated by Immunoassay detection method [15], [16], serum triglyceride and serum total cholesterol were measured by the enzymatic method [18], [19], while serum HDL-Cholesterol was measured by Chemical precipitation method, [14], [17]. VLDL-cholesterol is measured in mg/dl using an indirect method that involves dividing the triglyceride level by 5 (when using mg/dl units) [17].

VLDL-Cholesterol = [Triglyceride]/5

LDL-Cholesterol concentration is calculated by indirect method through the Friedewald equation. Total serum cholesterol, triglyceride and HDL-Cholesterol are quantified as mentioned previously [14], [15]. The calculated VLDL-C and measured HDL-C are subtracted from total serum cholesterol to estimate LDL-C. according to the following equation:

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LDL-Cholesterol (mg/dl) = [Total cholesterol] – [HDL-C] – [VLDL-C]

The Statistical Package for Social Science (SPSS) version 25 was used to analyse the data statistically (SPSS Inc., Chicago, IL, USA). The data was presented as Mean Standard Deviation. If the distribution of the data between the two groups was normal, the student' t test was used; otherwise, a nonparametric test was used (Mann Whitney test). For qualitative comparison between the two patient groups, Pearson's Chi square (x 2) test was used. Statistical significance was defined as a P value of less than (0.05) [17].

3. Results

A total of 70 patients with type II diabetes mellitus participated in the study, 35 (21 males, 14 females) patients with type 2 diabetes mellitus receive magnesium supplements for two months considered as intervention group and the other 35 (21 males, 14 females) patients with diabetes mellitus receive corn starch as control group visited Al-Salam Teaching Hospital in the morning, and after taking the participants' acceptance, questioners were given and important information were filled.

3.1 Demographic characteristics

Participants show no significant difference in age. duration of diabetes, body mass index (BMI), systolic and diastolic blood pressure between the studied groups at the beginning of study as shown Table. 2 and Figure .3.

Table 2. Demographic Characteristics of patients

Parameters	Intervention [n = 35] Mean ± SD	Control [n = 35] Mean ± SD	P-value*
Age (years)	55.49 ± 9.84	53.77 ± 10.16	NS
Duration of DM (years)	8.17 ± 6.16	5.59 ± 6.61	NS
BMI (kg/m^2)	31.79 ± 5.27	32.85 ± 7.39	NS
Systolic bl. pressure (mmHg)	143.0 ± 17.6	137.5 ± 18.0	NS
Diastolic bl. pressure (mmHg)	92.1 ± 9.8	89.0 ± 12.2	NS

* Independent T-test of two means was used.

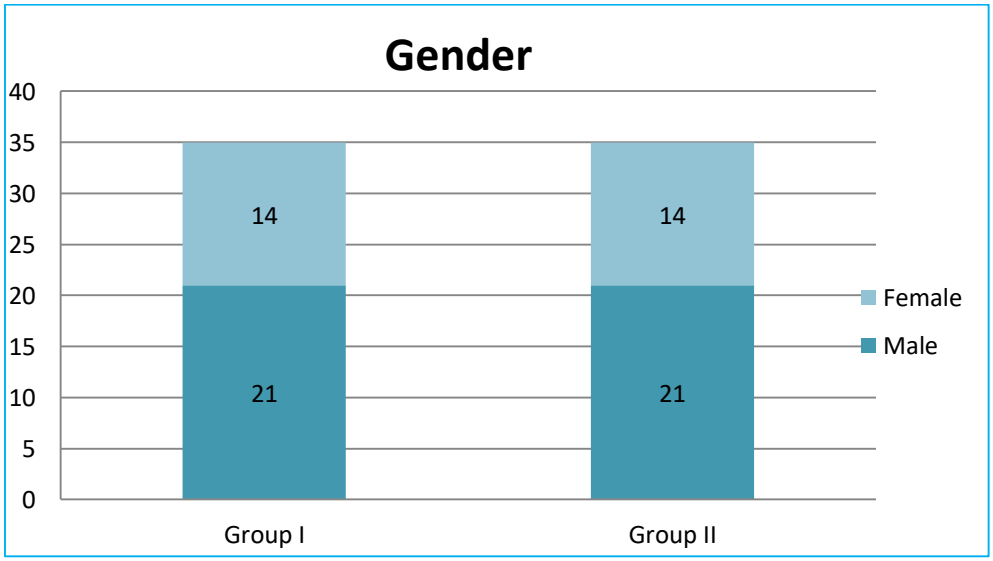

Figure 3. Gender distribution of study sampled population.

Additional data for participants: included: 16.7% of diabetic patients on diet only with no medication, 28.3% on Metformin, 8.3% use multiple medications and 13.3% of participants on Glibenclamide, similar percent on Glibenclamide and Metformin, also 13.3% on Glimipride and Metformin. Only 3.3% on Glimpride alone or Sitagliptin and Metformin. That means in 65.5% of diabetic patients, Metformin was the hypoglycemic treatment alone or with other medications.

The most important comorbidities in the participants were hypertension (45%) and dyslipidemia (16.7%). 43.3% of the participants had no associated comorbidities. The remaining 5% of patients exhibited other comorbidities. Additionally, 61.7% of patients had diabetes for less than 10 years, 21.7% 10-14 years, 10% 15-19 years, and 6.7% 20-25 years.

Table 3. The effect of duration of DM on type of therapy

Duration of DM	Medication %				
	No medicine	Metformin	Sulfonylurea	Metformin+ Sulfonylurea	Sitagliptin , Glucophage
Less than 5 years	15%	20%	3%	2%	0%
5-10 years	2%	2%	5%	12%	0%
10 – 15 years	0%	5%	3.5%	8.5%	5.5%
15 – 20 years	0%	0%	3.5%	3.5%	3.5%
20-25 years	0%	0%	2%	2%	2%

Magnesium supplements were well tolerated and no side effects have been reported by participants, and the compliance of the intervention group was detected by counting the remaining tablets at the end of the study. Figure .4 shows the compliance of the intervention group to magnesium tablet during the study period. About 20% of patients have a low level of compliance, less than 70%, but the majority of patients have a good compliance level.

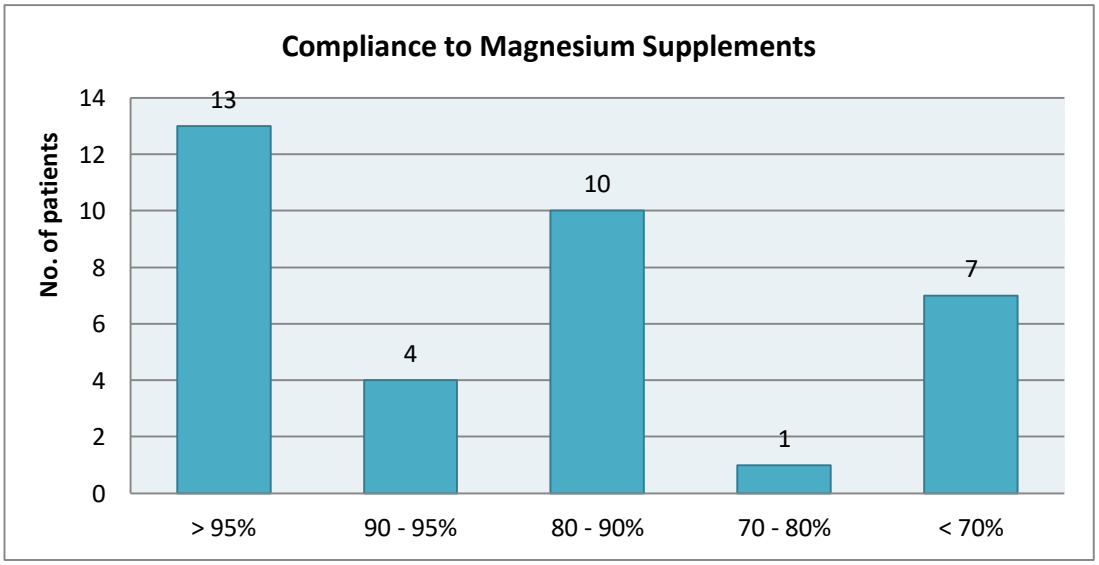

Figure 4. Compliance of intervention group to magnesium supplements, [n = 35].

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In order to identify association between age, gender, duration of diabetes and type of medication and the main variable of interest (HbA1c, FSG, TG, TC, LDL-C, and other) a series of preliminary analyses were performed. There is a correlation between age and HbA1c as shown in following graph but it is nonsignificant.

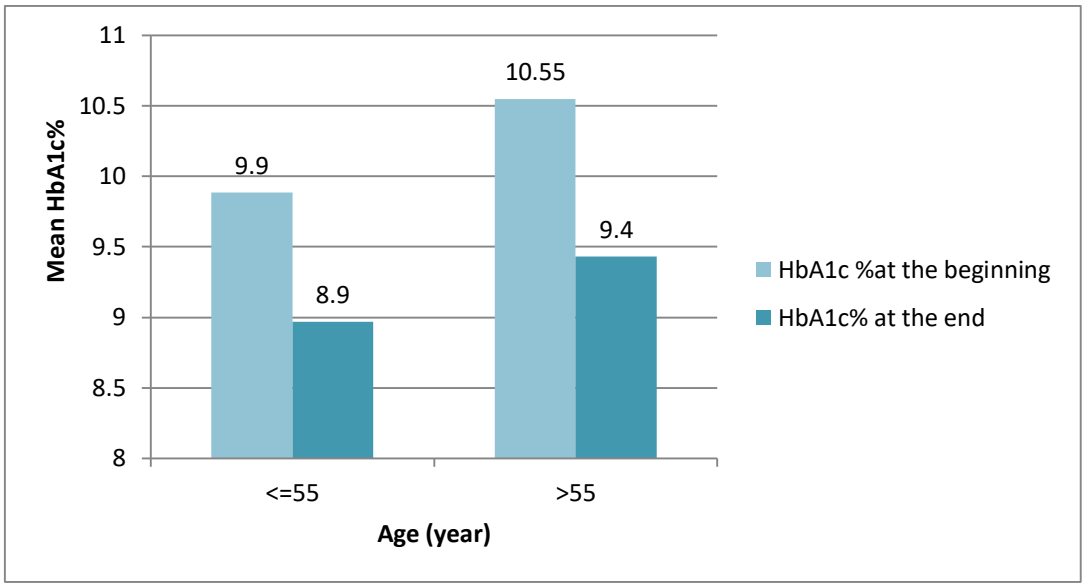

Figure 5. The relation between change in HbA1c% of intervention group with age, [n = 35].

Table 4 and Figure 6 Show the comparison between HbA1c% with duration of DM as during first five years of diagnosis HbA1c% is 7.4% but after that HbA1c% is about 10%.

Table. 4: Comparison of Duration of DM and HbA1c%.

Duration of DM	HbA1c%			
	Mean	**SD**	**%**	**P-value***
Less than 5 years	7.4	1.82	40.7	0.33
5-10 years	10.88	3.22	20.3	0.74
10 – 15 years	9.95	2.89	22.0	0.05
15 – 20 years	9.8	1.65	10.2	0.03
20-25 years	10.52	2.07	6.8	0.96

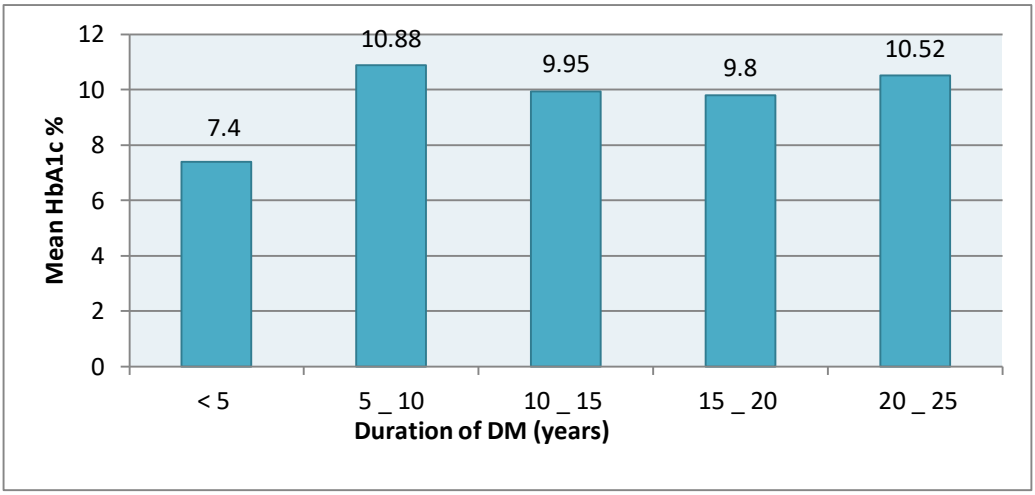

Figure 6. HbA1c% in participants at the beginning of the study with duration of DM (n=70)

3.2 The effects of magnesium supplements on glycemic control

Table 5. shows a positive significant change in HbA1c percent after taking magnesium supplements for months with reduction 0.9% in HbA1c (p-value < 0.05) and when compared with control group found that HbA1c is increased.

Table 5. HbA1c % at the beginning and at the end of study in Intervention and control group

Parameters	Intervention group [n = 35]		P-value*
	Baseline Mean ± SD	After two months Mean ± SD	
HbA1c %	9.979 ± 2.6	9.026 ± 2.2	0.01
Parameters	**Control group [n = 35]**		P-value*
	Baseline Mean ± SD	After two months Mean ± SD	
HbA1c %	8.162± 2.77	8.398 ± 2.8	0.058

* Paired T-test of two means was used.

Table. 6 Comparing of HbA1c % at the end of study in intervention and control group found there is a significant difference.

Table 6. HbA1c % at the end of study in intervention and control group

	Intervention group [n = 35] Mean ± SD	Control group [n = 35] Mean ± SD	P-value*
HbA1c %	9.026 ± 2.2	8.398 ± 2.8	0.01

* Univariate Analysis of Variance is used

Table 7 shows that difference in HbA1c% between patients determine the percent of improvement in HbA1c. When HbA1c% equal or higher than 10 the improvement is about 15% but if HbA1c less than 10

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the reduction is only 5%.

Table 7. The relation between baseline HbA1c% and percent of improvement

Intervention Group	% of patients	HbA1c% at the beginning	HbA1c% at the end	% of improvement	P-value*
		Mean ± SD	Mean ± SD		
HbA1c% <10	59%	8.47 ± 0.91	7.98 ± 1.05	5.55%	0.45
HbA1c% >= 10	41%	12.92 ± 1.71	11.08 ± 2.16	14.24%	0.03

* Paired T-test of two means was used.

Table 8. shows change in fasting blood glucose in Intervention group from 170.59 to 147.26 mg/dl which is statistically significant, While in control group there is increase in FBG from 121.28 to 134.03 mg/dl.

Table 8. Fasting blood glucose at the beginning and at the end of study in Intervention and control group

Parameters	Intervention group [n = 35]		P-value*
	Baseline Mean ± SD	After two months Mean ± SD	
Fasting blood glucose (mg/dl)	170.59 ± 65.41	147.26 ± 47.51	0.034
Parameters	**Control group [n = 35]**		**P-value***
	Baseline Mean ± SD	After two months Mean ± SD	
Fasting blood glucose (mg/dl)	121.28 ± 56.28	134.03 ± 84.98	0.178

* Paired T-test of two means was used.

Table .9 shows the relation of baseline fasting serum glucose with percent of improvement as FSG higher than 200 mg/dl is associated with improvement 27% while FSG lower than 200 mg/dl have only 2% of improvement.

Table 9. The relation between baseline fasting serum glucose and percent of improvement

Intervention Group	% of patients	FSG at the beginning	FSG at the end	% of improvement	P-value*
		Mean ± SD	Mean ± SD		
FSG <200 mg/dl	70%	136.58 ± 31.2	133.89 ± 38	2 %	0.69
FSG >= 200 mg/dl	30%	263.38 ± 29.3	191.88 ± 56	27 %	0.02

3.3 The effects of magnesium supplements on Lipid profile

Table. 10 shows changes in lipid profile in intervention group and control group. The results found significant reduction in triglyceride and VLDL in Intervention group after two months of magnesium

supplement. The total cholesterol, LDL reduction is nonsignificant. While in control group there are elevation in lipid profile parameter. HDL level decreased in both Intervention and control groups mean that is not affected by magnesium.

Table 10. Lipid profile at the beginning and at the end of study in Intervention and control group

Lipid profile parameters	Intervention group [n = 35]		P-value*
	Baseline Mean ± SD	After two months Mean ± SD	
Cholesterol (mg\dl)	184.78 ± 56.62	186.07 ± 51.74	0.95
Triglyceride (mg\dl)	168.37 ± 110.83	129.07 ± 72.36	0.04
HDL (mg\dl)	32.30±	28.48± 10	0.01
LDL (mg\dl)	121.93 ± 51.51	130.48 ± 48.22	0.52
VLDL (mg\dl)	33.7 ± 23.56	25.19 ± 14.53	0.045
Parameters	**Control group [n = 35]**		**P-value***
	Baseline Mean ± SD	After two months Mean ± SD	
Cholesterol (mg\dl)	165.22 ± 48.9	181.91± 59.48	0.031
Triglyceride (mg\dl)	101.28 ± 46.16	107.47± 49.87	0.542
HDL (mg\dl)	30.13 ± 11.99	28.91± 11.07	0.630
LDL (mg\dl)	114.28 ± 45.963	132.06 ± 58.12	0.029
VLDL (mg\dl)	20.03 ± 9.16	22.84 ± 14.6	0.296

* Paired T-test of two means was used.

4. Discussion

Diabetes mellitus is one of the most important medical conditions that influences patients' quality of life [18] Diabetes mellitus is a complex disease with many genetic, behavioral, lifestyle and other risk factors [19].

Accordingly, many studies were performed to better understanding of the pathogenesis of DM. Recently, the impact of magnesium supplementation on glycemic control in diabetic patients has been viewed by many studies to observe the association between magnesium status and glycemic control or lipid profile in pre-diabetics or diabetic patients.

Magnesium is an important micronutrient with many beneficial effects on the human body by regulating several important functions such as neuromuscular conduction, glycemic control, muscle contraction, and myocardial contraction. Additionally, it has a role in ion channels regulation, energy production, and DNA synthesis [20].

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Magnesium deficiency is a predisposing factor for insulin resistance by its effect on insulin secretion and action, glucose metabolism, and synthesis of proteins [21].

Magnesium has an effect on dyslipidemia by its effect on insulin resistance as the latter is associated with increased free fatty acid efflux from fat cells and higher level of triglyceride and low level of HDL-C [22].

The correlation of magnesium supplementation with glycemic control and lipid profile is observed in our study to examine the effect of magnesium supplements in Type 2 diabetic patients who don't use insulin.

4.1 Effects of Magnesium on Fasting Serum Glucose in diabetic patients

Magnesium deficiency is associated with defects in insulin action by interfering with insulin receptor associated tyrosine kinase activity, which also affects intracellular glucose transport that finally impairs insulin sensitivity [23].

In the current study, there is a significant reduction in serum fasting glucose with values higher in the control group than in the intervention group at the end of study, also higher in the intervention group at the beginning of study than at the end of the study. Additionally, FSG increased in the control group during the period of study as shown in Table 8. Also, the improvement level is associated with baseline FSG level. In patients with FSG higher than 200 mg/dl the improvement percent is 27%, while in patients with FSG lower than 200 mg/dl the improvement is only 2% as shown in Table 9.

This agrees with a meta-analysis study performed by [23] conducted on 21 randomized clinical trials with different forms of magnesium and different duration of magnesium supplementation from 1 to 4 months found reduction in fasting serum glucose although it was statistically nonsignificant, while taking only those studies with 4 months of magnesium supplementation observed significant reduction of FSG.

Other studies with similar results are [24] who observed the effects of 300 mg Magnesium daily for 3 months and found a significant reduction in fasting serum glucose ($p < 0.0001$) [25] conducted a clinical trial on 40 participants. 20 of them were in the intervention group taking Magnesium supplements for three months and the other 20 as a control group. All the participants follow a specific dietary regimen. This study found a reduction of FSG in the intervention group of 10.55 mg/dl while increased in the control group of 10 mg/dl but the reduction is statistically nonsignificant ($p = 0.06$).

[26] cross sectional meta-analysis study involved more than 50,000 non diabetic participants of 15 cohort studies. These studies document dietary intake of magnesium by those participants and correlate it with FSG. The result of this meta-analysis was that each 50 mg increase in dietary intake of magnesium reduces FSG by 0.009 mmole/L.

This improvement in glycemic status by magnesium treatment is expected by the role of magnesium in enhancing insulin sensitivity by its effects as a cofactor on tyrosine kinase activity affecting glycolysis or by inhibiting IP3 calcium channels altering secretion of insulin [27- 30].

4.2 Effects of Magnesium on HbA1c% in diabetic patients

As shown in Tables 5 and 6, there is a statistically significant reduction in HbA1c% of about 1% after Magnesium supplementation in the intervention group, while HbA1c% is increased in the control group, despite the fact that their HbA1c% is lower than the intervention group. In addition, as shown in Table 7, patients with HbA1c% greater than 10 achieve a greater improvement percentage of about 14%, while

patients with HbA1c% less than 10 achieve a 5% improvement percentage.

These findings are consistent with (Labban, 2019) who found a direct relationship between the degree of reduction of HbA1c percent with Magnesium intake and the baseline HbA1c level as the higher the degree of improvement in HbA1c will be greater that in patients with HbA1c higher than 8% the improvement of HbA1c % [31].

Another study that is consistent with these results is [25], a study conducted on 40 diabetic patients. 20 patients take 250 mg of magnesium for three months and the other 20 patients as a control group don't use any supplements. The results of this study were a significant reduction of HbA1c% ($p < 0.001$).

A meta-analysis study of 18 randomized clinical trials that examined the effects of magnesium supplementation on glycemic control, only 8 of these studies measure HbA1c% and the reduction in HbA1c was statistically nonsignificant ($p= 0.26$), But in 3 of these 8 studies the improvement in HbA1c was significant ($p= 0.04$) [32].

The study by [33] conducted in Iraq-Kirkuk on 52 diabetic patients and compared with 24 healthy individuals correlated the low magnesium level in diabetic patients with high HbA1c%.

This contradicts a study conducted in Iraq-Duhok by [34], which found a nonsignificant correlation between HbA1c% and magnesium level in 100 diabetic patients in a cross-sectional study.

4.3 The effects of Magnesium on Serum Triglyceride level

The improvement in serum triglyceride level after magnesium supplementation is statistically significant, which is consistent with the results of the Labban 2019 study with P 0.05. Furthermore, when the degree of improvement in serum TG level is correlated to the initial HbA1c%, higher HbA1c% is associated with better reduction of TG level [31].

Other studies [35] measured magnesium levels and lipid profiles in 71 type 1 diabetic patients and compared them to 71 healthy individuals. The findings of this study revealed that patients with low magnesium levels 1.67 mg/dl have high triglyceride levels, which is a statistically significant difference (p 0.001).

Other studies with similar results are [36] examined the relationship between triglyceride and magnesium level in 45 diabetic patients and found a significant correlation between them ($p = 0.002$) [36- 38].

High serum triglyceride concentration is associated with insulin resistance. Insulin resistance leads to increased triglyceride synthesis by increased free fatty acids entry into the liver. So the beneficial effects of magnesium on lipid profile is associated with the ability of magnesium to enhance insulin sensitivity. Another role of magnesium is in reduction in TG by impairing absorption and increased fecal excretion [22], [39].

On the other hand, [40] performed on more than 200 diabetic patients by measuring serum Mg level and serum TG level and found a statistically nonsignificant correlation between TG level and Mg level.

4.4 The effects of Magnesium on Serum Total Cholesterol level

The current study observes no change in serum total cholesterol between patients at the beginning of study

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and after taking magnesium supplements. whereas in the control group, cholesterol levels increased by about 20 mg/dl between two measurements. This result is similar to the results of a study conducted by [36] of a nonsignificant correlation between magnesium level and cholesterol status (P = 0.146).

The meta-analysis of 15 studies by [41] examining the effects of different magnesium supplements in many population groups (diabetics, overweight, hypertensive and others) found similar results of a nonsignificant relationship between magnesium level and total cholesterol (p = 0.67).

Also, this result agrees with results of a study performed in Pakistan by [40] that found a negative correlation between cholesterol and magnesium but still statistically nonsignificant [42] conducted a similar study and obtained similar results.

These various results are associated with the dose of magnesium and duration of magnesium treatment [43].

4.5 The effects of Magnesium on Serum LDL level

In the present study, there is no association between serum LDL level and use of magnesium supplements in diabetic patients. This is similar to results of a previous study by [36] that found no significant inverse correlation (r=-0.34, p = 0.751) with magnesium level in type 2 diabetic patients.

The nonsignificant inverse relationship between serum LDL level and magnesium is also consistent with other previous studies performed by [40], [41].

This is in contrast to the findings of [25] of a significant correlation between magnesium supplementation and an improvement in LDL level in diabetic patients ($p < 0.01$).

4.6 The effects of Magnesium on Serum VLDL level

The result of the current study is a significant negative correlation between magnesium supplements and serum VLDL level ($p < 0.05$) as shown in Table 10. This finding is consistent with the findings of a previous study by [39], which included 80 diabetic patients divided into two groups of 40 patients each: an intervention group that received magnesium supplements for three months and a control group. This study found significant change in VLDL (p= 0.008).

This finding could be explained by the fact that released free fatty acids associated with insulin resistance increase hepatic synthesis of VLDL-C, resulting in high VLDL-C levels in diabetic patients. When magnesium improves insulin action, VLDL-C synthesis is reduced [22], [44].

4.7 The effects of Magnesium on Serum HDL level

Insulin resistance causes production of smaller and dense HDL that that is easily uptaked by the liver, leading to decreased level of HDL in diabetic patients [44].

In the present study, there is no correlation between intake of magnesium supplements with HDL-C as shown in Table 10 with similar values in the intervention and control group after two months. This result agrees with results of a previous study performed by [36] who found a nonsignificant relationship between HDL-C level and magnesium status (P = 0.228, r=-0.12).

Another study with similar results is [41] meta-analysis of 18 studies of the effect of magnesium supplementation on HDL-C status (p = 0.076) [24], [38].

In addition to [45], a double-blind randomized study of 98 type 2 diabetic patients taking magnesium supplements equal to 360 mg of elemental magnesium per day for three months in Mexico found no change in HDL-C level by magnesium supplementation study with similar results is [39].

The results of this study are in controversy with [46] meta-analysis study conducted on 20 studies that showed a significant positive correlation between HDL-C and magnesium treatment (P = 0.00032) and this result as mentioned by the study may be associated with baseline level of HDL-C which is low that can be easily increased by magnesium supplementation.

5. Conclusion

Magnesium supplementation in patients with type II diabetes mellitus results in significant improvement in glycemic control parameters (FDG and HbA1c%), VLDL-C and triglyceride level. Thus, magnesium may have additional benefits as adjuvant therapy in the routine management of DM, and may be a viable approach for those with risk factors for other diseases in addition to diabetes mellitus.

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