Effect of magnesium and potassium on rheumatoid arthritis factor and quality of life in patients with type 2 diabetes mellitus: a randomized control trial

Hafiza Sonia Bibi,[1] Uzma Rafi,[1] Sidra Khalid,[2] Riffat Mehboob,[3] Anbreen Bibi,[4] Hani Sadaka Shalabi,[5] Mohammed A. Zaher,[6] Samy A. Abusikkien[7,8]

[1]Department of Biology, Lahore Garrison University, Lahore, Pakistan; [2]Institute of Diet and Nutritional Sciences, University of Lahore, Lahore, Pakistan; [3]Lahore Medical Research Center, Lahore, Pakistan; [4]University of Punjab, Lahore, Pakistan; [5]Department of Internal Medicine, College of Medicine, University of Jeddah, Jeddah, Saudia Arabia; [6]Department of Clinical Physiology, Faculty of Medicine, King Abdulaziz University, Jeddah, Saudi Arabia; [7]Department of Anatomy, Faculty of Medicine, King Abdulaziz University, Rabigh, Saudi Arabia; [8]Department of Anatomy, Faculty of Medicine, Ain Shams University, Cairo, Egypt

Correspondence: Riffat Mehboob, Lahore Medical Research Center, Lahore, Pakistan.
E-mail: mehboob.riffat@gmail.com

Key words: diabetes mellitus type 2, magnesium, potassium, rheumatoid arthritis, quality of life.

Contributions: RM, UR, conceived and designed the experiments; HSB, SK, performed the experiments; AB, HSS, analyzed and interpreted the data; HSB, MAZ, wrote the paper; UR, SAA, reviewed and edited the manuscript.

Conflict of interest: the authors declare no potential conflict of interest.

Ethics approval and consent to participate: ethical approval (IRB-UOL-FAHS/760/2020 - 27-10-2020) was gained from the Institutional Review Board, Faculty of Allied Health Sciences, University of Lahore.

Informed consent: written informed consent was obtained from patients.

Patient consent for publication: patients' consent was taken in written form for publication of outcomes obtained through their samples.

Availability of data and materials: data are available upon request due to privacy/ethical restrictions.

Funding: none.

Additional information: Clinical Trial Registration - NCT04642313.

Received: 6 December 2024.
Accepted: 23 February 2024.

Italian Journal of Medicine 2025; 19:1874
doi:10.4081/itjm.2025.1874

ABSTRACT

The management of type 2 diabetes mellitus (T2DM) and its related consequences, such as the prevalence of rheumatoid arthritis (RA) factor and overall quality of life, has drawn increased attention to the significance of micronutrients, particularly magnesium (Mg^{+2}) and potassium (K^{+}). The objective of this study is to investigate the effects of Mg^{+2} and/or K^{+} supplementation on the RA factor and quality of life in T2DM patients. This randomized controlled trial (single-blinded) was conducted at Lahore Garrison University and Lahore Medical Research Center. The sample size consisted of 80 diabetic patients. Four groups were formed based on the supplementation they received. Samples were taken before the use of Mg and K supplements and after 60 days of supplements taken. Quality of life assessments, including physical functioning, mental health, social functioning, and overall well-being, were measured in our study. Data were analyzed statistically by using GraphPad Prism 8.0.2. The study results show that group 2, which received Mg^{+2} supplements, had the highest mean pre-treatment RA factor value and showed a decrease in RA factor after the treatment. Our result showed that supplements of Mg^{+2} have an effective role in lowering the level of RA factor. In light of these results, future prospects for research could focus on investigating the mechanisms by which Mg^{+2} and K^{+} supplements impact glycated hemoglobin levels and RA factor to optimize treatment strategies for individuals with diabetes and RA.

Introduction

Type 2 diabetes mellitus (T2DM) is described as a dysregulation of blood sugar levels, which is recognized as an international health problem. Prolonged elevation of blood sugar levels triggers an imbalance that results in sensitive oxidative stress and the release of pro-inflammatory cytokines.[1] The prevalence of diabetes mellitus (DM) is approximately 9% of the world's adult population, although there are large geographical variations from as low as 2.5% (Republic of Moldovia) to 17% (Egypt).[2] Diabetes can lead to various medical complications such as diabetic ketoacidosis and non-ketotic hyperosmolar coma. Additionally, there are other serious complications associated with DM, including creatine kinase

myocardial band, stroke, kidney failure, foot ulcers, and damage to the eye.[3] Diabetes can also affect the rates at which enzymes are generated and destroyed, as well as their enzymatic activity.[4] T2DM has a tremendous effect on the economy and health around the world; estimates show that by 2035, 592 million people will have diabetes.[5] Severe hypoglycemia is a powerful indicator of macrovascular events, negative clinical results, and mortality in individuals diagnosed with T2DM.[6]

Rheumatoid arthritis (RA) and T2DM have a common pathogenesis basis of inflammation,[7] which has been hypothesized to play a vital role in the improvement and propagation of atherosclerosis, cardiovascular diseases (CVD), and other associated inflammatory diseases. RA, a systemic and chronic inflammatory disease characterized by joint pain and synovial joint damage, may lead to functional disability and premature mortality.[8] RA is an autoimmune disease that is challenging to treat and lasts a lifetime, leading to various systemic complications, a diminished quality of life (QoL), and a reduced lifespan.[9] It is the most common inflammatory rheumatic disease and is, like DM, associated with an increased risk of CVD which is not fully explained by traditional CVD risk factors.[10] Concomitant DM among patients with RA is a serious health issue as these patients have more atherosclerotic CVD, depression, renal failure, and hospital stay compared with patients with RA without DM.[11] The prevalence of RA was calculated to be at 0.24% worldwide. While in China, the prevalence of RA may reach 1.02%.[12] Furthermore, the number of comorbidities in patients with RA was positively related to disease activity and severity.[13] Nevertheless, the management of those comorbidities is far from optimal. Since scheduling fewer sessions is easier for many people, the majority of clinical trials evaluating physical activity in T2DM patients have utilized a frequency of three sessions per week.[14] Patients with RA were found to have a diet lacking in potassium (K), and people with seropositive RA who took dietary K supplements reported less pain and improved arthritis symptoms.[15] RA affects more than 400,000 people in the UK, with an annual rate estimated at 3.8 cases per 10,000 people.[16] People with RA stop working within 2 years and a half are not able to work within 10 years (guideline NG100, N. I. C. E. 2018). Since there is presently no cure for RA, disease-modifying antirheumatic drugs must be used over an extended period of time to slow the disease's progression.[17] Additionally, patients with RA, particularly those with longstanding disease, face a high risk of undiagnosed diabetes.[18]

Magnesium (Mg) in the human body holds the position as the fourth most abundant element and is essential for various osteogenesis functions. The majority of Mg in the body is present in the bones (approximately 60%) and soft tissues (around 40%), with less than 1% found in the blood.[19] Mg is an essential mineral that plays a primary act in the functioning of more than 350 enzymes in the body, making it an essential nutrient for overall well-being.[20] Most of the studies suggest that the inclusion of Mg in one's diet, considering its status as the 4th prevalent mineral in the body, could potentially lead to a reduction in blood pressure.[21] Mg-based biomaterials are emerging as promising agents for bone repair and regeneration, addressing the rising demand for orthopedic implant materials due to various musculoskeletal injuries and defects caused by sports, trauma, inflammation, and aging.[22]

K^+ is a vital element found in the human body, with approximately 140g present in an adult.[23] K plays an important role in maintaining the electrical balance of cell membranes, and any deviation from the normal K level can disrupt the electrical activity of the heart, leading to negative effects.[24] K^+ is a vital positively charged ion found within cells, K^+ plays a vital role in the functioning of resting and action potentials.[25] Several chronic conditions, including advanced chronic kidney disease, heart failure, T2DM, and hypertension, are known to raise the risk of developing HK.[24] This study aimed to investigate the effects of Mg and/or K^+ supplementation on RA factor and QoL in patients with T2DM.

Materials and Methods

The study was conducted following the Basic & Clinical Pharmacology & Toxicology policy for experimental and clinical studies.[26] This was a randomized controlled trial (single-blinded) conducted at Lahore Garrison University and Lahore Medical Research Center. The trial registration number of this study is: NCT04642313. After obtaining written informed consent, 10 cc of blood was collected from subjects in a gel blood tube using a BD sterilized syringe (Asto Life Sciences Pvt. Ltd., Lahore, Pakistan) by venipuncture in Akhuwat Foundation with written consent (Becton, Dickinson and Company, Nebraska, USA). Samples were collected from 80 T2DM patients and frozen in a biology research laboratory at Lahore Garrison University. DM diagnosis was based on the World Health Organization criteria using random blood glucose. Samples were centrifuged at 3000 rpm for 5 minutes after 30 minutes of blood collection, to separate plasma and serum. Glucose estimation was done in the plasma sample and electrolytes were processed in a serum sample. All the assays were performed according to the standard international procedures on an automated chemistry and electrolytes analyzer. For glycated hemoglobin (HbA1C), a whole blood sample was used in an ethylenediaminetetraacetic acid vial and directly analyzed, but for blood glucose, Mg, K, and RA factor estimation, the Cobas 6000 Roche automation electrolyte analyzer (Roche Diagnostics International, Rotkreuz, Switzerland) was used. The accuracy and precision of the values were ensured by internal and external quality control measures. Demographic data was collected through a proforma and body mass index was calculated using the standard formula (kg/m^2). Questions about medical history, family history, diet, and physical activity were also asked. Four groups were formed. Group I (T1) consisted of a control or placebo group (Calsip D); group II (T2) contained patients to whom Mg supplements (Ostin) were administered; group III (T3) received K^+ supplements (Paravit); and group IV (T4) received both to test the effects of K^+ and Mg supplements (Bionta) on RA factor level in diabetic patients. Different tests were performed to evaluate the levels of sugar, HBA1C, K, Mg, and RA factor. Samples were taken before the use of Mg and K^+ supplements and after 8 weeks of supplements taken. Every group comprises 20 patients.

The sample size was estimated using the prevalence of T2DM (16.98%) at an 8% margin of error and a 95% confidence level using Eq. 1:

$$n = \frac{z^2 - \underline{a}\,(1-p)}{\frac{2}{d^2}} \qquad \text{[Eq. 1]}$$

Where, p is the proportion of poor knowledge (0.1698), d is the marginal error set at 8%, α=0.05, Z is the standard normal deviation for a 95% confidence interval, n is the number of respondents (80) (Aamir *et al.*, 2019).

Doses per day

Doses were as follows: T1 – placebo (starch 250 × 2 mg); T2 – Mg (250 × 2 mg); T3 – K (250 × 2 mg); and T4 – Mg + K (250+250 × 2 mg).

Patients were advised to have monthly follow-ups so that treatment/supplement was provided again for the next month. During the collection of the data, patients were informed to have weekly on-call follow-ups through their provided contact numbers. On-call follow-up took place after 7-10 days to determine the follow-up/dropout rate or any side effects, during the second month as well. After 8 weeks, the physician advised the patient to give a blood sample (in fasting) the next morning or on the spot (if in fasting condition) to the pathology of Akhuwat Foundation.

Statistical data analysis

SPSS 25.0 (UBM, Armonk, NY, USA) was used to analyze the results from patients. Mean ± standard deviation was used for quantitative variables while frequency and percentage were used to define qualitative variables. Comparison among groups was conducted by applying an analysis of variance test. A p-value of <0.05 was considered significant.

Ethical considerations

Ethical approval (IRB-UOL-FAHS/760/2020) was gained from the Institutional review board (IRB), Faculty of Allied Health Sciences, The University of Lahore.

Results

Table 1 shows descriptive statistics for the variables of age and gender. A total of 80 patients of both genders with T2DM were enrolled in this study. There were 32 (40%) males and 48 (60%) females among 80 patients. The average age of male and female participants was 49.0625±10.38279 and 51.3750±10.55407, respectively (Table 1).

A total of 80 patients were divided into four groups. 22 (27.5%) patients in T1 (control), 10 (12.5%) patients in T2, 24 (30%) patients in T3 and 24 (30%) patients in T4. Supplements such as Calsip-D, Ostin (Mg), Paravit (K), and Bionta (Mg, K) were given to T1, T2, T3, and T4, respectively. The pre-treatment mean values for RA factor were 6.3436±4.36140 in T1, 6.2980±6.65330 in T2, 3.9433±1.08861 in T3, and 3.9642±2.46964 in T4. Post-treatment mean values for RA factor were 5.5136±4.24579 in T1, 6.5860 ±8.16516 in T2, 3.7675 ±1.66240 in T3, and 5.1900 ±3.69619 in T4. Levels of RA factor were found to be statistically non-significant in all groups. The overall RA factor of all groups before drug intervention was statistically non-significant, as shown in Table 2.

The pre-treatment mean values for Mg were 2.0727±0.27976 in T1, 1.7600±0.10750 in T2, 2.0333±0.45556 in T3, and 2.1250±0.26085 in T4. Post-treatment mean values for Mg were 2.1000±0.17995 in T1, 2.2200±0.21499 in T2, 2.0917±0.20624 in T3, and 2.1500±0.33232 in T4, shown in Table 3. Mg levels were

Table 1. Descriptive statistics of age and gender.

Variables	Male	Female
n (%)	32 (40)	48 (60)
Age	49.0625±10.38279	51.3750±10.55407

Table 2. Rheumatoid arthritis factor levels before and after drug intervention.

Groups	n (%)	RA factor I	RA factor II	p
T1	22 (27.5)	6.3436±4.36140	5.5136±4.24579	0.5259
T2	10 (12.5)	6.2980±6.65330	6.5860±8.16516	0.9320
T3	24 (30)	3.9433±1.08861	3.7675±1.66240	0.6667
T4	24 (30)	3.9642±2.46964	5.1900±3.69619	0.1833
Overall	80(100)	4.9040±3.68674	5.0268±4.24651	0.8454
p	-	0.0432*	0.2893	-

RA, rheumatoid arthritis; T1, placebo group; T2, group that received magnesium (Mg) supplements; T3, group that received potassium (K) supplements; T4, group that received K and Mg supplements.

Table 3. Serum magnesium level before and after drug intervention.

Groups	n (%)	Pre-Mg level	Post-Mg level	p
T1	22 (27.5)	2.0727±0.27976	2.1000±0.17995	0.7022
T2	10 (12.5)	1.7600±0.10750	2.2200±0.21499	<0.0001*
T3	24 (30)	2.0333±0.45556	2.0917±0.20624	0.5700
T4	24 (30)	2.1250±0.26085	2.1500±0.33232	0.7732
Overall	80(100)	2.0375±0.33879	2.1275±0.24545	0.0561
p		0.0326*	0.4995	

T1, placebo group; T2, group that received magnesium (Mg) supplements; T3, group that received potassium (K) supplements; T4, group that received K and Mg supplements.

statistically significant only in T2, while Mg levels in T1, T3, and T4 remained relatively unchanged. These findings suggest that Mg supplementation (T2) had a positive impact on Mg levels compared with the other groups. It demonstrated the potential efficacy of Mg supplementation in improving Mg status. This increase in Mg level in T2 has an impact on HBA1C level and results in a slightly reduced blood sugar level. The overall Mg level of all groups before drug intervention was statistically significant, as shown in Table 3.

The pre-treatment mean values for K were 4.1182±0.35137 in T1, 4.3200±1.39108 in T2, 4.2333±0.48871 in T3, and 4.1583±0.61214 in T4. Post-treatment mean values for K were 5.1364±1.78900 in T1, 3.9600±0.57581 in T2, 4.1250±0.55502 in T3, and 4.7250±0.62987 in T4, as shown in Table 3. K level was statistically significant in T1 and T4, and the difference was non-significant in T2 and T3. The overall serum K level of all groups after drug intervention was statistically significant, as shown in Table 4.

Table 5 shows the association of QoL in terms of physical, psychological, environmental, social, and overall symptoms with respect to RA factor before and after drug intervention. Out of 80 patients, 16 (20%) patients identified their physical symptom-related QoL as neither poor nor good, showing no significant difference with their mean RA factor value of 5.8287±5.16720 before drug intervention and 6.3800±6.34308 after drug intervention. Other 64 (80%) patients reported good QoL with respect to physical symptoms, with RA factor mean values from 4.6728±3.22728 before drug intervention to 4.6884±3.52869 after drug intervention, showing non-significant difference. The level of RA factor in physical symptom-related QoL before drug intervention and after drug intervention was non-significant.

QoL in terms of environmental symptoms and RA factors was observed both before and after drug intervention. 56 (70%) patients out of 80 showed neither poor nor good QoL (environmental symptoms) with no significant change in RA factor with a mean value of RA 4.7214±3.19933 before drug intervention and 5.1675±4.33064 after drug intervention. 22 (27.5%) patients reported no significant change in RA factor with good QoL (environmental symptoms), with a mean value of 4.5082±3.94174 before drug intervention and 3.9255±3.32170 after drug intervention. 2 (2.5%) patients showed no significant difference in the mean value of RA factor with very good QoL (environmental symptoms). RA factor in all groups was statistically significant in environmental symptom-related QoL both before and after medication.

Out of 80 patients, 14 (17.5%) showed QoL in terms of psychological symptoms as neither poor nor good with no significant change in RA factor, with a mean value of RA of 6.2200±5.43036 before drug intervention and 6.9057±

Table 4. Serum potassium level before and after drug intervention.

Groups	n (%)	Pre-K level	Post-K level	p
T1	22 (27.5)	4.1182±0.35137	5.1364±1.78900	0.0122*
T2	10 (12.5)	4.3200±1.39108	3.9600±0.57581	0.4593
T3	24 (30)	4.2333±0.48871	4.1250±0.55502	0.4767
T4	24 (30)	4.1583±0.61214	4.7250±0.62987	0.0028*
Overall	80(100)	4.1900±0.66057	4.5625±1.13911	0.0124*
p		0.8533	0.0045*	

T1, placebo group; T2, group that received magnesium (Mg) supplements; T3, group that received potassium (K) supplements; T4, group that received K and Mg supplements.

Table 5. Association of rheumatoid arthritis factor with quality of life symptoms before and after drug intervention.

QoL	n (%)	RA I	RA II	p	
Environmental	Neither poor nor good	56 (70)	4.7214±3.19933	5.1675±4.33064	0.5365
	Good	22 (27.5)	4.5082±3.94174	3.9255±3.32170	0.5988
	Very good	2 (2.5)	14.3700±0.00000	13.2000±0.00000	--
p			0.0007***	0.0098**	
Social	Neither poor nor good	10 (12.5)	6.8780±6.39486	8.1880± 7.55731	0.6806
	Good	58 (72.5)	4.4914±2.80183	4.4759±3.31437	0.9783
	Very Good	12 (15)	5.2533±4.3479	5.0550±3.89507	0.9074
p			0.1577	0.0363*	
Psychological	Neither poor nor good	14 (17.5)	6.2200±5.43036	6.9057±6.63653	0.7672
	Good	46 (57.5)	4.1420±1.84179	4.3902±3.07822	0.6400
	Very Good	20 (25)	5.7355±4.9893	5.1755±4.33546	0.7069
p			0.0911	0.1500	
Physical	Neither poor nor good	16 (20)	5.8287±5.16720	6.3800±6.34308	0.7894
	Good	64 (80)	4.6728 ±3.22728	4.6884±3.52869	0.9792
p		0.2646	0.1554		
Overall	Neither poor nor good	12 (15)	6.5267±5.8422	7.5233±7.0098	0.7088
	Good	68 (85)	4.6176±3.14131	4.5862±3.44700	0.9558
p			0.0984	0.0262*	

QoL, quality of life; RA, rheumatoid arthritis.

6.63653 after drug intervention. 46 (57.5%) patients showed good QoL and 20 (25%) patients showed very good QoL in terms of psychological symptoms, indicating no significant change in the mean value of RA factor before and after drug intervention. RA factor in all groups were statistically non-significant in psychological symptom-related QoL both before and after medication.

Out of 80 patients, 10 (12.5%) patients showed neither poor nor good QoL in terms of social symptoms with no significant change in the mean value of RA factor (6.8780±6.39486 before drug intervention and 8.1880±7.55731 after drug intervention). 58 (72.5%) patients with social symptom-related QoL as good showed no significant change in RA factor with a mean value of 4.4914±2.80183 before drug intervention to 4.4759±3.31437 after drug intervention. The remaining 12 (15%) patients showed very good QoL in terms of social symptoms with no significant change in the mean value of RA factor. RA factor was statistically significant in social symptom-related QoL in all groups after drug intervention. 12 (15%) patients showed neither poor nor good QoL and 68 (85%) showed good QoL. No significant difference was observed in RA factor before and after drug intervention. RA factor was statistically significant in QoL overall symptoms in all groups after drug intervention.

The pre-treatment mean values for QoL were 71.6500±20.31664 in T1, 68.23±12.34 in T2, 67.2±7.96 in T3, and 65.7±5.44 in T4. The post-treatment mean values for QoL were 53.1000±16.24775 in T1, 58.3±9.18 in T2, 59.9±5.91 in T3, and 55.0±8.39 in T4. All groups showed significant results except the placebo group (T1) (Figure 1).

Discussion

The present study compared the effect of Mg and K on RA factors in T2DM patients. The present study included descriptive statistics for various variables such as age, gender, and biomarkers like Mg levels, K levels, and RA factor before and after treatment. There were 32 (40%) males and 48 (60%) females among the 80 patients. The average age of male and female participants was 49.0625±10.38279 and 51.3750±10.55407, respectively.

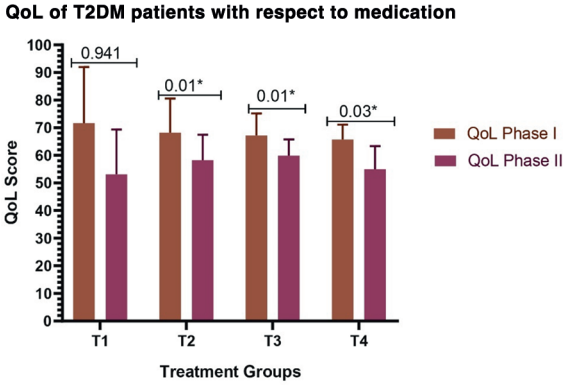

Figure 1. Quality of life after magnesium and potassium treatment in diabetic patients in relation to rheumatoid arthritis factor. QoL, quality of life; T2DM, type 2 diabetes mellitus; T1, placebo group; T2, group that received magnesium (Mg) supplements; T3, group that received potassium (K) supplements; T4, group that received K and Mg supplements.

All four groups have shown no significant effect in the level of RA factor after drug intervention. The results showed that the mean value of RA factor levels before drug intervention varied among the groups. T1 and T3 both groups showed a decrease in the post-treatment mean value of RA factor. T3, which received K^+ supplements, showed a decrease in the post-treatment mean value of RA factor (3.7675±1.66240). Very few studies have been done to determine the relationship between RA and dietary K intake. Low K level was observed in RA patients.[27] Rastmanesh *et al.* observed a reduction in inflammatory arthritis and pain in RA patients when they were administered with K^+ supplements orally.[28] Uptake of K^+ results in a decrease in RA factor in T3. In the study by Toktam *et al.*, 38 RA patients participated in a randomized controlled trial that showed a daily high-dose K^+ chloride regimen given for 28 days when combined with grape juice significantly reduced joint pain.

The current randomized controlled study's main goal was to investigate any additional therapeutic advantages of oral K^+ in RA. The main assumption was that K^+ supplementation would reduce RA patients' joint pain.[9] In our study, we also observed that T4, which received both Mg and K^+ supplements, had a low pre-treatment mean RA factor value but an increased post-treatment mean RA factor value.

It was evident that all treatment groups experienced a reduction in HbA1c levels compared to their respective pre-treatment values. However, the magnitude of improvement varied among the groups. T2, which received Mg supplements, showed the smallest reduction in HbA1c levels, with a post-treatment mean value of 8.588±0.68684. T3, receiving K^+ supplements, showed a very significant reduction in the post-treatment mean value of HBA1C level, as compared to other groups. This study has shown the profound impact on HBA1C level after treatment with a post-treatment mean value of 8.3625±1.4666 in T3. T4, which received both Mg and K^+ supplements, demonstrated the smallest reduction in the post-treatment mean value of HBA1C level (8.635±1.75229), as compared to T3 (8.3625±1.4666), which received only K^+. According to the research by Li *et al.,* Mg and K^+ dietary consumption may be significant modifiable risk factors in the management of T2DM in rural China.[29] However, our study indicates that the combined supplement intervention did not yield the desired effect in reducing blood sugar levels as effectively as individual K^+ supplements (T3). In addition, another study showed that the K^+ and Mg intake was predictive of a decrease in HbA1C levels.[1] Low K^+ was found to be associated with diabetes.[30] This evidence supports our results that more reduction in HBA1C level was observed in T3 receiving K^+.

We found that QoL has a positive impact on diabetes management and control of micronutrients. In T1 (placebo group), the p-value was insignificant, but in Y2, T3, and T4, the p-value showed significant results after improvement of the QoL in RA factor with diabetic patients.

It was observed with the results that QoL is very important for reducing complications regarding diabetes and RA factor. This study noticed that neither poor nor good QoL among diabetic patients, as indicated by environmental, physical, psychological, and social symptoms, had a negative ef-

fect on RA factor levels. Good QoL as indicated by physical symptoms did not influence RA factor but had a negative effect on RA factor in the case of psychological symptoms. Good QoL among diabetic patients as indicated by environmental symptoms had a more positive effect on RA factor level and also a little positive effect was observed on RA factor in the case of social symptoms. It was also found that very good QoL as indicated by environmental, psychological, and social symptoms had a positive effect on RA factor among diabetic patients.

The study by Afridi *et al.* also analyzed K levels in diabetic patients; they found K levels significantly higher ($p=0.05$) than normal levels in diabetic patients of both genders.[28] However, in our study, the group treated with both Mg and K^+ (T4) demonstrated an increase in K levels, indicating a combined effect of both supplements. Mg and K^+ are electrolytes that work together to maintain a proper fluid balance in the body. Imbalances in these electrolytes, particularly low K levels (hypokalemia), can lead to complications in patients with diabetes. Supplementing with Mg and K^+ may help prevent imbalances and maintain electrolyte homeostasis.

Conclusions

This study concluded that the association of T2DM and serum electrolytes was crucial for maintaining RA factor. Serum electrolytes such as Mg and K played a significant role in maintaining, stabilizing, and reducing the risk of RA factor in T2DM patients. All patients in the study were aged between 26 and 80, and a noticeable effect was observed on HBA1C reduction. The treatment had a substantial effect on HBA1C in T1, T3, and T4. A more significant difference was observed in T3. The study demonstrated that treatment with Mg and K^+ supplements resulted in a decrease in HbA1c levels across all four groups, although notable differences were observed among the groups. The results of the study showed that T3, which received K^+ supplements, showed a decrease in RA factor after the treatment. Further studies with larger sample sizes and longer durations may provide additional insights into the effectiveness of these supplements and their potential role in improving patient outcomes. Moreover, it would be beneficial to investigate the optimal dose and duration of supplementation to achieve the best outcomes.

References

1. Brandão-Lima PN, de Carvalho GB , Fonseca Santos RK, et al. Intakes of zinc, potassium, calcium, and magnesium of individuals with type 2 diabetes mellitus and the relationship with glycemic control. Nutrients 2018;10:1948.
2. Timmis A, Vardas P, Townsend N, et al. European Society of Cardiology: cardiovascular disease statistics 2021. EurHeart J 2022;43:716-99. Erratum in: Eur Heart J 2022;43:799.
3. Anwar A, Khan HA, Hafeez S, Firdous K. A comparative study of creatine kinase-MB and Troponin levels among diabetic and non-diabetic patients with acute MI. Pak J Med Health Sci 2016;10:296-7.
4. Evliyaoğlu O, Kibrisli E, Yildirim Y, et al. Routine enzymes in the monitoring of type 2 diabetes mellitus. Cell Biochem Funct 2011;29:506-12.
5. Esser N, Paquot N, Scheen AJ. Anti-inflammatory agents to treat or prevent type 2 diabetes, metabolic syndrome and cardiovascular disease. Expert Opin Investig Drugs 2015;24:283-307.
6. Pistrosch F, Ganz X, Bornstein SR, et al. Risk of and risk factors for hypoglycemia and associated arrhythmias in patients with type 2 diabetes and cardiovascular disease: a cohort study under real-world conditions. Acta Diabetol 2015;52:889-95.
7. Liu XZ, Gao Y, Fan J, et al. Metabolic abnormalities in rheumatoid arthritis patients with comorbid diabetes mellitus. Clin Rheumatol 2018;37:219-26.
8. Uhlig T, Moe RH, Kvien TK. The burden of disease in rheumatoid arthritis. Pharmacoeconomics 2014;32: 841-51.
9. Kianifard T, Saluja M, Sarmukaddam S, et al. An adjunct role of potassium rich vegetarian diet and a novel potassium food supplement to improve pain in chronic rheumatoid arthritis on supervised standard care: a randomized controlled study. BMJ Nutr Prev Health 2024;7:14-25.
10. Fohse FK, Rollefstad S, Ikdahl E, et al. Degree of arterial stiffness is comparable across inflammatory joint disease entities. Scand J Rheumatol 2022;51:186-95.
11. Ramos AL, Redeker I, Hoffmann F, et al. Comorbidities in patients with rheumatoid arthritis and their association with patient reported outcomes: results of claims data linked to questionnaire survey. J Rheumatol 2019;46: 564-71.
12. Hu H, Luan L, Yang K, Li SC. Burden of rheumatoid arthritis from a societal perspective: a prevalence-based study on cost of this illness for patients in China. Int J Rheum Dis 2018; 21:1572-80.
13. Radner H, Yoshida K, Hmamouchi I, et al. Treatment patterns of multimorbid patients with rheumatoid arthritis: results from an international cross-sectional study. J Rheumatol 2015;42:1099-104.
14. Cannata F, Vadalà G, Russo F, et al. Beneficial effects of physical activity in diabetic patients. J Funct Morphol Kinesiol 2020;5:70.
15. Kianifard T, Chopra A. A therapeutic role for potassium (K) to reduce pain and complications related to the cardiovascular system and bone in rheumatoid arthritis (RA): a clinical research perspective. Rheumatol Res 2018;3:1-12.
16. Abhishek A, Doherty M, Kuo CF, et al. Rheumatoid arthritis is getting less frequent - results of a nationwide population-based cohort study. Rheumatology 2017;56: 736-44.
17. Nagy G, Roodenrijs NM, Welsing PM, et al. EULAR definition of difficult-to-treat rheumatoid arthritis. Ann Rheum Dis 2021;80:31-5.
18. Ursini F, Russo E, D'Angelo S, et al. Prevalence of undiagnosed diabetes in rheumatoid arthritis: an OGTT study. Medicine 2016;95:e2552.
19. Barbagallo M, Veronese N, Dominguez LJ. Magnesium in aging, health and diseases. Nutrients 2021;13:463.
20. Dibaba DT, Xun P, He K. Dietary magnesium intake is inversely associated with serum C- reactive protein levels: meta-analysis and systematic review. Eur J Clin Nutr 2014;68:510-6.
21. Asbaghi O, Hosseini R, Boozari B, et al. The effects of magnesium supplementation on blood pressure and obesity measure among type 2 diabetes patient: a systematic

review and meta-analysis of randomized controlled trials. Biol Trace Elem Res 2021;199:413-24.
22. Zhou H, Liang B, Jiang H, et al. Magnesium-based biomaterials as emerging agents for bone repair and regeneration: from mechanism to application. J Magnes Alloy 2021;9:779-804.
23. Zoroddu MA, Aaseth J, Crisponi G, et al. The essential metals for humans: a brief overview. J Inorg Biochem 2019;195:120-9.
24. Palaka E, Grandy S, Darlington O, et al. Associations between serum potassium and adverse clinical outcomes: a systematic literature review. Int J Clin Pract 2020;74: e13421.
25. Kaya A, Keskin M, Tatlisu MA, Kayapinar O. Effect of dynamic potassium change on in- hospital mortality, ventricular arrhythmias, and long-term mortality in STEMI. Angiology 2019;70:69-77.
26. Tveden-Nyborg P, Bergmann TK, Jessen N, et al. BCPT 2023 policy for experimental and clinical studies. Basic Clin Pharmacol Toxicol 2023;133:391-6.
27. Syrjänen S, Lappalainen R, Markkanen H. Salivary and serum levels of electrolytes and immunomarkers in edentulous healthy subjects and in those with rheumatoid arthritis. Clin Rheumatol 1986;5:49-55.
28. Rastmanesh R, Abargouei AS, Shadman Z, et al. A pilot study of potassium supplementation in the treatment of hypokalemic patients with rheumatoid arthritis: a randomized, double-blinded, placebo-controlled trial. J Pain 2008;9:722-31.
29. Li J, Li Y, Wang C, et al. Dietary potassium and magnesium intake with risk of type 2 diabetes mellitus among rural china: the henan rural cohort study. Biol Trace Elem Res 2024;202:3932-44.
30. Chatterjee R, Colangelo LA, Yeh HC, et al. Potassium intake and risk of incident type 2 diabetes mellitus: the coronary artery risk development in young adults (CARDIA) study. Diabetologia 2012;55:1295-303.