

## Evaluation of Serum Magnesium Level Among Patients with Essential Hypertension in Erbil-Iraq

Salam Naser Zangana (MBChB, DM, MD, FRCP (Glasg), FRCP (Edin))<sup>1</sup> and  
Suhad Ali Khazaal (MBChB, HD/FM)<sup>2</sup>

<sup>1</sup> College of Medicine, Hawler Medical University , Erbil ,Iraq

<sup>2</sup> Specialist in family medicine, Ministry of Health-Directorate of Health, Erbil ,Iraq

Correspondence Address:

Dr. Salam Naser Zangana

College of Medicine, Hawler Medical University , Erbil ,Iraq

email: dr\_salam2003@yahoo.com

Received: 15 November 2020

Revised: 19 November 2020

Accepted: 20 December 2020

Published: 25 June 2021

Diyala Medical Journal 2021:20(2): 23- 30

### Abstract

**Background:** Hypertension is a well-established risk factor for cardiovascular diseases with an ongoing global increase in incidence. Low Magnesium may play a critical role in cardiovascular physiology. Although many reports have mentioned the correlation between low serum magnesium levels and hypertension, the results were conflicting.

**Objective:** To measure the levels of serum magnesium in hypertensive patients, and to evaluate the prevalence of hypomagnesemia among them.

**Patients and Methods:** A case-control study from June 2019 to December 2019 was carried out in Rizgary Teaching Hospital and Nawroz Health Center involving 100 adult patients with essential hypertension (group I ) and 100 normotensive age and gender-matched controls ( group II). The serum magnesium level was measured in all participants.

**Results:** Females constitute 64 % of both study groups. The means of the age of both study groups show no significant difference ( $p=0.82$ ). Although the means of Mg level in hypertensive and control groups were within the normal range, it was significantly lower in hypertensive patients ( $p=0.004$ ). Besides, 4 hypertensive patients (4%) had hypomagnesemia compared with zero in controls ( $p=0.043$ ).

**Conclusion:** There was a significantly lower mean magnesium level in hypertensives compared to controls. A relationship was assumed between serum magnesium level and hypertension. However; hypomagnesemia was not common in hypertensive patients.

**Keywords:** Hypertension; Magnesium; Hypomagnesemia

## Introduction

Magnesium (Mg) is the second most common intracellular cation in the human body [1]. Total body Mg is about 25 g, 60% of it is in the bones, 39% is intracellular (20% in skeletal muscle), and only 1% is in the extracellular fluid [2]. Mg is a participatory element in the build of nearly 300 enzymes in the body that adjust many biological and chemical reactions including blood pressure (BP) regulation [3]. Mg may play a pivotal role in BP regulation by many mechanisms. It can stimulate prostacyclin and nitric oxide formation [4], adjusting vasodilation [5, 6], decreasing vascular tone [7], and it can prohibit vascular injury through its antioxidant and anti-inflammatory functions [8, 9]. Considerable studies have linked between hypomagnesemia and hypertension [10].

When systolic blood pressure (SBP) is higher than 140mmHg and/or diastolic blood pressure (DBP) is higher than 90mmHg, hypertension is determined [11]. Hypertension is a common health problem worldwide. Approximately one billion adults or ~22% of the population of the world have hypertension [12]. Hypertension is regarded as an important cause of death in Iraq with a high prevalence (35.6% to 40%) [13], and a total number of nearly 7000 deaths occurred during 2015 [14].

Hypertension is considered remarkable risk factor for cardiovascular disease that can be modified [15]. Hypertension is an important accelerator of the atherosclerotic process and it frequently accompanies adult ischemic heart disease [16].

Many factors were involved in the pathogenesis of hypertension; one of them

was changed in intracellular concentrations of calcium, sodium, potassium, and magnesium with an opposite correlation between serum magnesium level and occurrence of cardiovascular events [17]. Many studies have shown a relationship between low dietary intakes of magnesium with hypertension suggesting a possible effect of magnesium in the pathogenesis of hypertension [18].

No previous study was done in Erbil city concerning the same subject. Accordingly, the current study was done to estimate the levels of serum Mg in patients with essential hypertension and to evaluate the prevalence of hypomagnesemia among them, and find out any correlation between serum magnesium level and blood pressure. The present study was done among a sample of hypertensive patients versus controls in Erbil city, Iraq.

### Aims and objectives:

1. To detect the serum magnesium levels in hypertensive patients.
2. To evaluate the prevalence of hypomagnesemia among them.
3. To find out any correlation between serum magnesium level and blood pressure.

### Patients and Methods

This case-control study was conducted between June 2019 and December 2019 in Rizgary teaching hospital and Nawroz Health Center in Erbil city, Iraq, The study included 200 adults distributed as 100 patients with essential hypertension (group I) and 100 healthy normotensive age and gender-matched individuals as controls (group II). The inclusion criteria were adult patients

with essential hypertension, their age  $\geq 18$  years, and of both genders. Participants with any of the following conditions were excluded: patients with secondary hypertension (diabetic nephropathy, polycystic kidney disease, and renovascular hypertension), Cushing syndrome, thyroid disease, chronic renal failure, primary hyperparathyroidism, malabsorption, osteomalacia or osteoporosis, patients taking medications like diuretics, glucocorticoids and vitamin supplements.

According to the recommendations of the 2018 ESC/ESH Guidelines for the management of arterial hypertension [11], the definition of hypertension is established when systolic blood pressure is  $\geq 140$  mmHg and diastolic blood pressure is  $\geq 90$  mmHg for adults aged 18 years. Blood pressure measurements were taken with a mercury sphygmomanometer, in the sitting position with the arm supported. The average of two readings was taken with a 5-minute break.

The data included in this study were age, gender, and a suitable clinical examination. A sample of the venous blood was obtained after overnight fasting from all participants to measure serum Mg level. The estimation of serum magnesium was done by an enzyme-linked immunosorbent assay (ELISA) test. According to the laboratory values, the

reference range for total Mg level was 1.6-2.6 mg/dl in both male and female adults. Hypomagnesemia was considered when the magnesium level falls below 1.6 mg/dl.

### Questionnaire and data collection

The data were collected by designing a self-administered, close-ended questionnaire, prepared for this purpose by the researcher and was filled by direct interview.

### Statistical analysis

Data analysis was done using the statistical package for social sciences (SPSS) version 19. The results were analyzed using a t-test sample. An appropriate table was used for data representation. A P-value of  $\leq 0.05$  was considered statistically significant.

### Results

As shown in Table (1), females constitute 64 % of both groups with no statistically significant difference between both groups regarding gender. The means of the age of both groups show also no significant difference ( $p=0.82$ ). Although the means of Mg level in hypertensive and control groups were within the normal range, it was significantly lower in hypertensive patients ( $p=0.004$ ). In addition, four hypertensive patients (4%) had hypomagnesemia compared to 0% in the control group and it was statistically significant ( $p= 0.043$ ).

**Table (1):** Some demographics and magnesium (Mg) levels of both study groups

	Group I Hypertensive patients(n=100)		Group II Controls(n=100)		P value
	No.	%	No.	%	
Gender					NS
Male	36	36	36	36	
female	64	64	64	64	
Age (years) $\pm$ SD	46.68 $\pm$ 12.81		46.87 $\pm$ 11.64		0.82
Serum Mg (mg/dl)	1.99 $\pm$ 0.21		2.08 $\pm$ 0.22		0.004
Patients with hypomagnesaemia	4	4	0	0	0.043

## Discussion

In the present study, lower magnesium levels were detected in hypertensive patients compared to controls. Thus; this study suggests a relationship between serum magnesium levels and blood pressure in hypertensive patients. This result is in agreement with other old studies like the Uza [19] and Ma *et al* studies [20], as well as more recent studies done by Kanwar *et al* [10], Shaikh *et al* [21] and Champagne *et al* [22].

In the Uza study, which was done in 1987, serum magnesium was determined in 202 patients with essential arterial hypertension as well as in 38 normotensive control subjects. The mean value of serum magnesium was significantly lower in hypertensive patients. In 1995, Ma and his colleagues made a cross-sectional study in four US communities, in which 15,248 participants took part. The results showed that mean serum Mg levels were significantly lower in participants with hypertension. The serum Mg levels were also inversely associated with systolic blood pressure.

Kanwar and coworkers in 2011 reported a significant correlation between serum magnesium levels and hypertensive Indian patients. They mentioned that most of the hypertensive patients had low serum Mg levels. Shaikh *et al* found a relation between serum magnesium and blood pressure in the Pakistan population. A study by Champagne *et al* had shown that patients with hypertension have a marked increase in the prevalence of hypercholesterolemia, diabetes, insulin resistance and hypomagnesaemia. On the contrary, Khan *et al* [23], Ravi *et al* [24],

and Maheri *et al* [25] studies revealed no relationship between low Mg level and hypertension.

In Khan *et al* study, which depends mainly on The Framingham Heart offspring cohort study, and after eight years of follow up, found no association between baseline serum magnesium and the development of hypertension, CVD, or all-cause mortality. In Ravi *et al* study, were 80 subjects with different grades of hypertension and 20 normotensive controls included, no significant difference was observed in serum magnesium levels between cases and controls. Maheri and colleagues reported non-significant difference was found regarding serum Mg levels when both groups were compared statistically. They concluded that there was no relation between serum magnesium level and hypertension.

Although in the current study hypomagnesemia was present in hypertensives but not in controls, it was not common. The prevalence was 4%. To the best of our knowledge, this is the first study that estimates the prevalence of Mg level in a hypertensive population in Erbil city. Our results are not compatible with the prior studies, which reported higher rates of prevalence [10, 19, 21]. In Uza study, the prevalence of hypomagnesemia detected in hypertensives was 27.72%, while it was higher in Kanwar *et al* study (61.25%) and in Shaikh *et al* study (62%). There are several causes for a lack of magnesium in the body. The main two sources for magnesium deficiency are through the gastrointestinal tract and kidneys. Causes for hypomagnesemia include low dietary intake, diarrhea, increased urinary loss, and poor absorption

from the intestines [26]. We excluded many causes for low Mg level in our study, yet the exact cause of hypomagnesaemia in our hypertensive patients is not well explained. We think it may be multi-factorial. It may be related to low magnesium intake, or increased urinary loss of magnesium, or it may be genetically determined. Numerous experimental studies showed that low dietary intake of Mg may increase the risk of acquiring hypertension [27]. The kidneys are very efficient at maintaining body levels of Mg. However, if the diet is deficient, levels may drop. Ronghua et al, in 2009, mentioned that a mutation in mitochondrial tRNA is the cause for the hypomagnesemia linked with hypertension and dyslipidemia [28].

The magnesium levels in serum do not usually represent the precise body magnesium levels. There may be a low intracellular magnesium level even if the serum magnesium level is normal. A 24-hour urine excretion of magnesium reflects intestinal absorption and is also of value in determining whether magnesium wasting is occurring by the renal route [29]. New researches propose that urinary magnesium excretion is inversely correlated with the risk of developing hypertension [30]. The magnesium tolerance test has been used for many years and it appears to be an accurate means of assessing magnesium status. This test is a very sensitive method to detect magnesium deficiency [31, 32].

## Conclusions

The mean Mg level was significantly lower in hypertensives compared to controls. An association is observed between serum magnesium levels and hypertension.

However; hypomagnesemia is not common in hypertensive patients.

## Recommendations

1. It is suggested that further clinical studies are proposed to clear ideas about serum magnesium levels in hypertensive patients.
2. There are controversial results regarding the effects of dietary magnesium intake and the risk of hypertension. Hence, further studies are needed before recommending this mineral supplement within the antihypertensive treatment.
3. We need to search for new and accurate methods to assess magnesium status. It has been proposed that the measurement of serum total magnesium and the magnesium tolerance test are the simplest, most useful and readily available tests to detect hypomagnesemia.

**Source of funding:** The author stated that no financial support has been received.

**Ethical clearance:** An ethical approval was obtained from the Ethics Committee of the College of Medicine at Hawler Medical University. A verbal consent was obtained from all participants in this study. The aim of the study was illustrated to the patients.

**Conflict of interest:** The author stated no opposition of interest.

## Limitations

1. The small sample size was one of the limitations of this study. Therefore, a larger sample size would help clarify a more statistically precise conclusion.
2. Since Magnesium is an intracellular ion, normal serum Mg levels do not reveal intracellular magnesium deficiency. As a result, intracellular Mg concentration is more significant than serum Mg concentration. As

intracellular electrolyte estimation tests are costly, they are not easily obtainable and difficult for clinical application. Accordingly, serum Mg levels are used for detecting changes in body Mg concentration.

## References

- [1]"Dietary Supplement Fact Sheet: Magnesium". Office of Dietary Supplements, US National Institutes of Health. 11 February 2016. Retrieved 13 October 2016.
- [2] Volpe SL. Magnesium. In: Erdman JW, Macdonald IA, Zeisel SH, eds. *Present Knowledge in Nutrition*. 10th ed. Ames, Iowa; John Wiley & Sons, 2012:459-74.
- [3]Rude RK. Magnesium. In: Ross AC, Caballero B, Cousins RJ, Tucker KL, Ziegler TR, eds. *Modern Nutrition in Health and Disease*. 11th ed. Baltimore, Mass: Lippincott Williams & Wilkins; 2012:159-75.
- [4] Satake K, Lee JD, Shimizu H, Uzui H, Mitsuke Y, Yue H, et al. Effects of magnesium on prostacyclin synthesis and intracellular free calcium concentration in vascular cells. *Magnes Res*. 2004; 17:20–27.
- [5]Landau R, Scott JA, Smiley RM. Magnesium-induced vasodilation in the dorsal hand vein. *BJOG*. 2004; 111:446–451.
- [6]Soltani N, Keshavarz M, Sohanaki H, Zahedi A S, Dehpour AR. Relaxatory effect of magnesium on mesenteric vascular beds differs from normal and streptozotocin induced diabetic rats. *Eur J Pharmacol*. 2005; 508:177–181.
- [7]Touyz RM, Yao G. Inhibitors of Na<sup>+</sup>/Mg<sup>2+</sup> exchange activity attenuate the development of hypertension in angiotensin II-induced hypertensive rats. *J Hypertens*. 2003; 21:337–344.
- [8] Blache D, Devaux S, Joubert O, Loreau N, Schneider M, Durand P, et al. Long-term moderate magnesium-deficient diet shows relationships between blood pressure, inflammation and oxidant stress defense in aging rats. *Free Radic Biol Med*. 2006; 41:277–284.
- [9] Iglarz M, Touyz RM, Amiri F, Lavoie MF, Diep QN, Schiffrin EL. Effect of peroxisome proliferator-activated receptor- $\alpha$  and - $\gamma$  activators on vascular remodeling in endothelin dependent hypertension. *Arterioscler Thromb Vasc Biol* 2003;23:45-51.
- [10] Kanwar G, . kirad S, . chawala L, Yadav M, . jain K b. Study of serum magnesium and fasting blood glucose in hypertension. *IOSR Journal of Biotechnology and Biochemistry (IOSR-JBB)* .2015, Volume 1, Issue 6, PP 55-57.
- [11]2018ESC/ESH Guidelines for the management of arterial hypertension .The Task Force for the management of arterial hypertension of the European Society of Cardiology and the European Society of Hypertension. *Journal of Hypertension* 2018, 36:1953–2041.
- [12] "Raised blood pressure". World Health Organization. Global Health Observatory (GHO) data. Archived from the original on 8 August 2016.
- [13]WHO. National Multiple indicator cluster survey (MICS), Baghdad: MOH Iraq, MOP Iraq & WHO, 2016.
- [14]Ministry of Health. Statistical annual report of Ministry of Health Iraq. Baghdad: Ministry of Health, 2015.
- [15]"Global health risks: mortality and burden of disease attributable to selected major risks". World Health Organization.

2009. Archived from the original on 14 February 2012. Retrieved 10 February 2012.
- [16] Lewington S, Clarke R, Qizilbash N, Peto R, Collins R. "Age-specific relevance of usual blood pressure to vascular mortality: a meta-analysis of individual data for one million adults in 61 prospective studies". December 2002 *Lancet*. 360 (9349): 1903–13.
- [17] Cunha AR, Umbelino B, Correia ML, Neves MF. Magnesium and vascular changes in hypertension. *Int J Hypertens* 2012; 2012:754250.
- [18] Touyz RM, Pu Q, He G, Chen X, Yao G, Neves MF, et al. Effects of low dietary magnesium intake on development of hypertension in stroke-prone spontaneously hypertensive rats: role of reactive oxygen species. *J Hypertension* 2002; 20:2221-32.
- [19] Uza G., Pavel O, Uza D., Vlaicu R. :Hypomagnesemia in patients with essential arterial hypertension.,” *Magnesium Bulletin* 1987, vol. 9, pp. 177–180.
- [20] Ma J, Folsom A R, Melnick S L, Eckfeldt J H, Sharrett A R, Nabulsi A A , et al: Associations of serum and dietary magnesium with cardiovascular disease, hypertension, diabetes, insulin, and carotid arterial wall thickness: the ARIC study. *Atherosclerosis Risk in Communities Study. J Clin Epidemiol* 1995 Jul;48(7):927-40.
- [21] Shaikh M K, Samo J A, Mangrio G M, Fazlani K, Devrajani B R, Ali Shah S et al: Fasting Blood Glucose and Serum Magnesium Levels in Patients with Hypertension. *World Applied Sciences Journal* 2012.17 (10): 1261-1264.
- [22] Champagne, C.M. Magnesium in hypertension, cardiovascular disease, metabolic syndrome, and other conditions: a review. *Nutr. Clin. Pract.*, 2008.23(2): 142-51.
- [23] Khan AM, Sullivan L, McCabe E, Levy D, Vasani RS, Wang TJ. Lack of association between serum magnesium and the risks of hypertension and cardiovascular disease. *Am Heart J* 2010; 160:715-20.
- [24] Ravi B.V., Usha S.M.R. Serum magnesium levels in patients with hypertension. *J Clin Sci Res* 2014; 4:282-5.
- [25] Maheri W M, Akhund I A, Ujjan I, Shaikh I A, Memon R A, Farooq M, et al. Serum Magnesium Level in Hypertensive Patients. *P J M H S .APR – JUN 2007 , Vol. 1 No.2 ,62.*
- [26] de Baaij JHF, Hoenderop JGJ, Bindels RJM. Regulation of magnesium balance: lessons learned from human genetic disease. *Clin Kidney J* 2012; 5 (Suppl 1): i15–i24.
- [27] Song Y, Sesso HD, Manson JE, Cook NR, Buring JE, Liu S , et al. Dietary magnesium intake and risk of incident hypertension among middle-aged and older US women in a 10-year follow-up study. *Am J Cardiol* 2006; 98:1616–1621.
- [28] Ronghua, L., L. Yuqi, L. Zongbin, Y. Li, W. Shiwen, and G. Min-Xin, 2009. Failures in Mitochondrial tRNA and tRNA Metabolism Caused by the Novel 4401A>G Mutation Are Involved in Essential Hypertension in a Han Chinese Family, *Hypertension*. 2009., 54(2): 329-337.
- [29] Swaminathan R .Magnesium Metabolism and its Disorders. *Clin Biochem Rev*. May 2003, Vol 24, pp 47-66.
- [30] Joosten MM, Gansevoort RT, Mukamal KJ, Kootstra Ros JE, Feskens EJ, Geleijnse JM, et al. Urinary magnesium excretion and risk of hypertension: the prevention of renal

and vascular end-stage disease study.  
Hypertension 2013; 61:1161-7.

[31] Rude RK. Magnesium metabolism and deficiency. *Endocrinol Metab Clin North Am* 1993; 22: 377-395.

[32]Nadler JL, Rude RK. Disorders of magnesium metabolism. *Endocrinol Metab Clin North Am* 1995; 24: 623-641.