



Research Article

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## Correlation of minerals and glycated hemoglobin (HbA1c) in renal dialysis patients of Hail, Saudi Arabia

Mohammed Kuddus, Nawaf OM Alhazmi, Mohammed RM Alshammari, Rasheed HR Alshortan, Ahmad F. Alhaysuni, Syed MA Shahid, Tariq Ginawi and Jamal M. Arif\*

Department of Biochemistry, College of Medicine, University of Hail, PO Box 2440, Hail, Saudi Arabia

\*Corresponding E-mail: [mkuddus@gmail.com](mailto:mkuddus@gmail.com)

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### ABSTRACT

Minerals play an important role in the glucose metabolism and energy production in the cells. Abnormalities of mineral metabolism have been associated with the increased mortality in patients of chronic kidney disease but their effects in renal dialysis patients are less characterized. In this study, we examined the associations between levels of minerals (serum calcium, phosphorus and magnesium) and HbA1c in diabetic and non-diabetic renal dialysis patients. Blood samples were collected from 76 Saudi renal dialysis patients with diabetic (age  $51.28 \pm 20.85$  years) and non-diabetic (age  $52.05 \pm 18.84$  years) subjects and biochemical analysis were performed using biochemical kits. Expectedly no significant relationship was observed ( $p > 0.05$ ) in baseline parameters such as age, sodium, potassium, bilirubin, creatinine, urea and glucose, in diabetic and non-diabetic renal dialysis patients. The study also showed that there was no significant relationship ( $p > 0.05$ ) between calcium and phosphorus, calcium and magnesium as well as magnesium and phosphorus in non-diabetic renal dialysis patients; however, in diabetic patients calcium and phosphorus have minor significant association ( $p = 0.057$ ) with increased levels of phosphorus, while calcium and magnesium showed strong significant relationship ( $p < 0.05$ ). Moreover, no significant relationship ( $p > 0.05$ ) was shown between magnesium and phosphorus even with increased level of phosphorus. Further, there was no significant relationship ( $p > 0.05$ ) between phosphorus and HbA1c in both types of renal dialysis patients. However, in diabetic renal dialysis patients there was significant relationship ( $p < 0.05$ ) between calcium and HbA1c as well as magnesium and HbA1c. These preliminary results prompted us to cautiously predict a supportive role of calcium, magnesium and HbA1c in better diagnosis and management of diabetes which could be helpful to alleviate some of the low energy associated weakness symptoms in the diabetic patients by calcium and magnesium supplementation.

**Key words:** HbA1c, renal dialysis, calcium, phosphorus, magnesium

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### INTRODUCTION

Dialysis is the process of removing the wastes and extra fluid from the blood that kidneys can no longer remove themselves. Renal failure is one of the leading terminal health problems in most of the patients with hypertension and uncontrolled diabetes. Therefore, abnormalities in serum calcium, phosphorus, magnesium and HbA1c concentrations are common in patients with chronic kidney disease (CKD) and have been associated with increased

morbidity and mortality (Kovesdy and Kalantar-Zadeh 2008, Schwarz et al 2006, Menon et al 2005). Glucose metabolism and its management in these patients is quite challenging due to imbalance in the mineral equilibrium. In addition to the pivotal role of vitamin D in calcium/phosphorus homeostasis and bone physiology (Holick 2009, Dusso et al 2005), several lines of evidence suggest that calcium/magnesium status may also have a significant role in cell's energy or glucose homeostasis in general (Flores 2005) and diabetes in particular (Thomas et al 2012). Magnesium is the second most abundant intracellular cation and has been established as a cofactor for over 300 metabolic reactions in the body. It plays an important role in insulin homeostasis and glucose metabolism. Some epidemiological studies demonstrated magnesium deficiency as a risk factor for diabetes (Phuong-Chi et al 2007). Another research has indicated that lower intake of magnesium and/or lower serum magnesium concentrations may lead to and are associated with the metabolic syndrome and/or type 2 diabetes mellitus (Volpe 2008). In diabetic hemodialysis patients, glycaemia control is also associated with improved outcomes for management of these patients. However, HbA1c in chronic kidney disease patients, and particularly those on hemodialysis, reflects much more than the changes in average blood glucose levels and therefore should be carefully interpreted (Coelho 2016). There is enough evidence that the prevalence and the incidence of renal dialysis patients and CKD in Saudi Arabia is increasing and showed rapid rise over the last 3 decades. The average percentage of annual increase of dialysis population in Saudi Arabia is 7.8% (www.scot.gov.sa). The disturbances in homeostasis of calcium, phosphorus, magnesium and HbA1c are frequently seen in chronic kidney disease patients. It is vital for physician to know the relationship among them for better management of renal failure patients. The main objective of the present study was to examine the relationship between calcium, phosphate, magnesium and HbA1c levels in Saudi dialysis patients. We hypothesized that the serum magnesium level is correlated with HbA1c in the renal failure diabetic patients and in combination could provide better management of diabetic and renal failure patients.

## MATERIALS AND METHODS

### 2.1 Selection of study subjects:

Total 76 renal dialysis patients were randomly selected for the study which was carried out between September 2015 and February 2016. These patients were admitted to the King Khalid Hospital dialysis unit (Hail, KSA). Patients having magnesium supplementation were excluded from the study.

### 2.2 Consent form and ethical consideration

The objective of the study was well explained to all participants in this study. All patients were informed by a written consent before sample collection. The anonymity of patient was maintained by coding the sample. Permission of this study was obtained from the hospital and college ethical committee.

### 2.3 Collection of sample:

Blood samples were collected in EDTA coated tube and serum vacutainers in morning after 12 h of fasting and the serum was separated within 30–45 min, aliquoted and stored at  $-20^{\circ}\text{C}$  for further analysis. The study was conducted at Biochemistry lab, University of Hail and in King Khalid Hospital, Hail, KSA.

### 2.4 Analytical methods:

Estimation of calcium, phosphate, magnesium and HbA1c levels in serum were measured by using respective assay kits (Human, Germany; UDI, KSA; Crescent, KSA). All the samples were analyzed according to the protocols of the assay kit manufacturers. Biochemical investigations (urea, creatinine, bilirubin, sodium and potassium) were carried out by commercially available kits using an auto-analyzer system in the King Khalid Hospital, Hail, Saudi Arabia.

### 2.5 Statistical analysis:

The appropriate statistical analysis was applied whenever required, for determination of correlation between calcium, phosphate, magnesium and HbA1c levels. The statistical analysis was conducted using SPSS program and  $p < 0.05$  was considered as significant.

## RESULTS AND DISCUSSION

### 3.1 Assessment of Anthropometric indices and Biochemical parameters

Total 76 renal dialysis patients were included in the study, and based on their HbA1c, 38 were diabetic ( $\text{HbA1c} > 6$ ) and 38 were non-diabetic ( $\text{HbA1c} < 6$ ). Baseline characteristics of the participants are summarized in Table 1. No

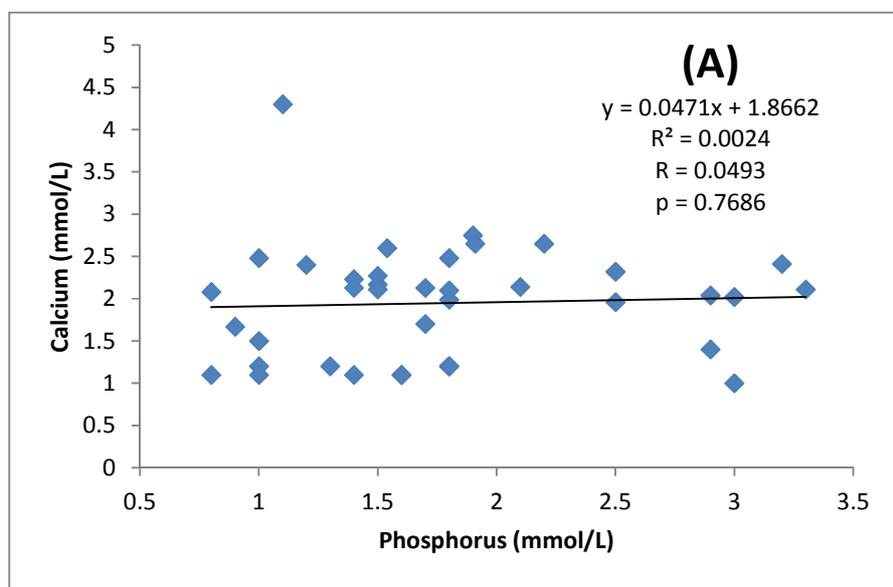
significant relationship was observed in age, sodium, potassium, bilirubin, creatinine and urea in diabetic and non-diabetic renal dialysis patients ( $p>0.05$ ) which was expected as all of these patients were renal failure patients.

Table 1. Anthropometric and biochemical parameters in renal dialysis patients

Parameters (T=76)	Diabetic dialysis patients (N=38) (Mean $\pm$ SD)	Non-diabetic dialysis patients (N=38) (Mean $\pm$ SD)	p value
Age (year)	51.28 $\pm$ 20.85	52.05 $\pm$ 18.84	$p>0.05$
Sodium (mmol/L)	136.87 $\pm$ 4.09	137.29 $\pm$ 3.56	$p>0.05$
Potassium (mmol/L)	4.32 $\pm$ 1.09	4.37 $\pm$ 0.89	$p>0.05$
Bilirubin (mmol/L)	7.66 $\pm$ 4.29	8.47 $\pm$ 10.00	$p>0.05$
Creatinine (mmol/L)	523.25 $\pm$ 355.56	479.84 $\pm$ 274.02	$p>0.05$
Urea (mmol/L)	15.17 $\pm$ 10.64	13.22 $\pm$ 7.24	$p>0.05$
Fasting glucose (mmol/L)	7.43 $\pm$ 4.46	7.3 $\pm$ 3.00	$p>0.05$

### 3.2 Association among calcium, phosphorus, magnesium and glycated hemoglobin levels

It is well known that calcium, magnesium, and phosphate are multivalent cations that are essential for various biologic and cellular functions (Blaine et al 2015). Kidneys play a significant role in the homeostasis of these ions. Hence, the concentration of calcium, magnesium, and phosphate are going to disturb in patients suffering from renal failure. Moreover, mineral homeostasis is quite important in maintaining cellular health but several clinical problems including CKD could potentially disturb this equilibrium. Normally, it is reported that there is inverse correlation between calcium and phosphorus levels in the normal healthy individuals (Peacock 2010). Further, calcium absorption is affected by the parathyroid hormone (PTH), vitamin D and calcitonin levels. In the renal failure patients, vitamin D activation will be severely affected which subsequently may lead to hypocalcaemia. The results showed that there was no significant relationship between calcium and phosphorus ( $p>0.05$ ) in non-diabetic renal dialysis patients, though in diabetic renal failure patients calcium and phosphorus have minor significant association ( $p=0.057$ ) with increased level of phosphorus (Figure 1). Further, there was insignificant relationship between magnesium and phosphorus ( $p>0.05$ ) in renal dialysis patients, whether they are diabetic or non-diabetic but the level of phosphorus relatively increased in the diabetic patients (Figure 2). In contrast, other researchers reported significant correlation between magnesium and phosphorus in diabetic renal dialysis patients (Assimina et al 2014, Khatami et al 2013). Moreover, there was no significant relationship observed between calcium and magnesium ( $p>0.05$ ) in non-diabetic renal dialysis patients, whereas they are strongly correlated ( $p<0.05$ ) in diabetic renal patients (Figure 3). Assimina et al (2014) also showed positive correlation between calcium and magnesium in diabetic renal patients.



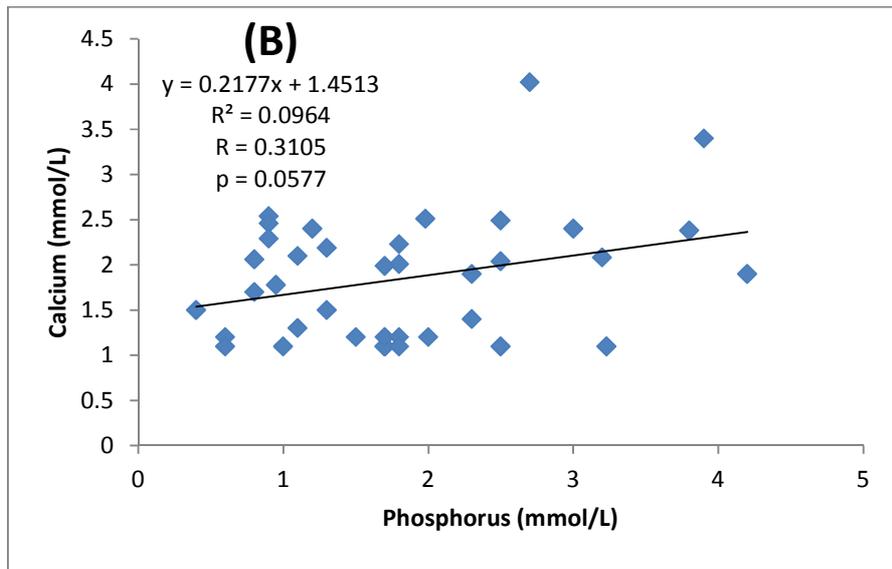
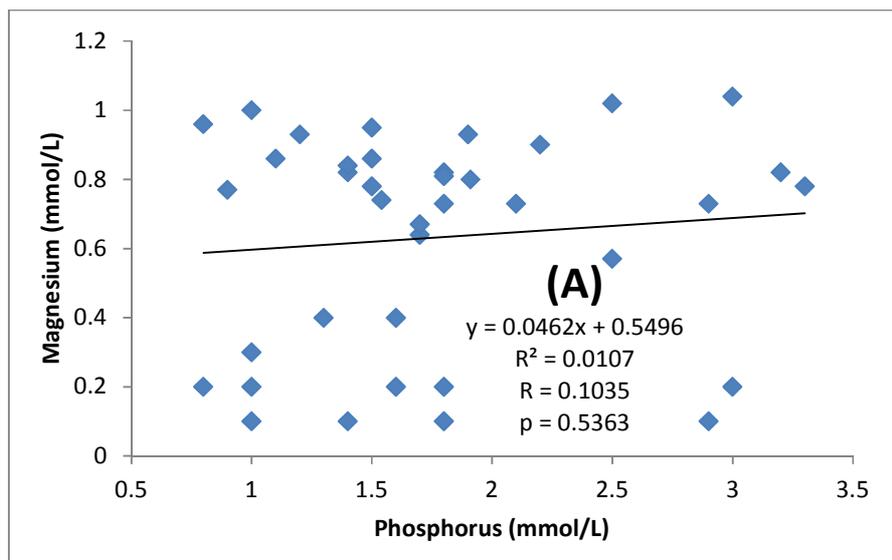


Fig. 1 Association of calcium with phosphorus in non-diabetic (A) and diabetic (B) renal dialysis patients



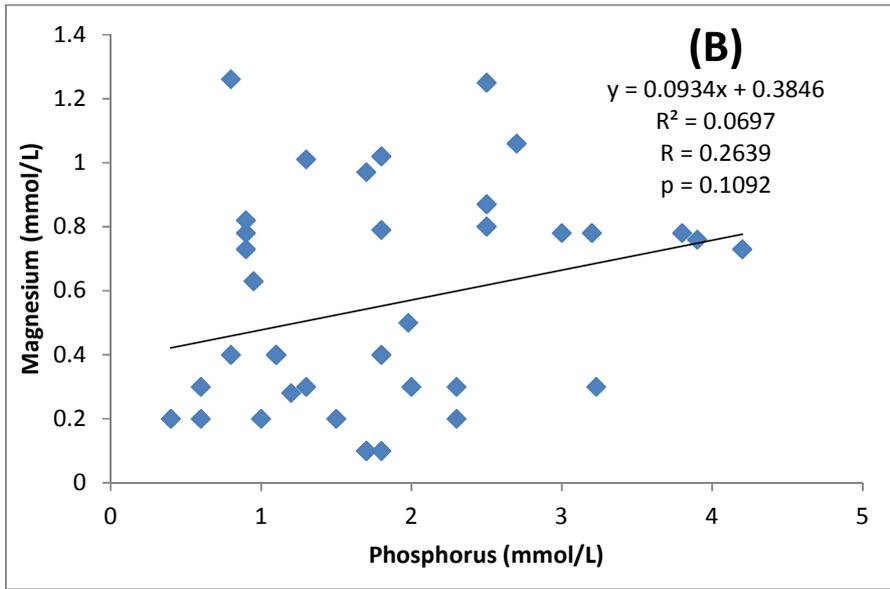
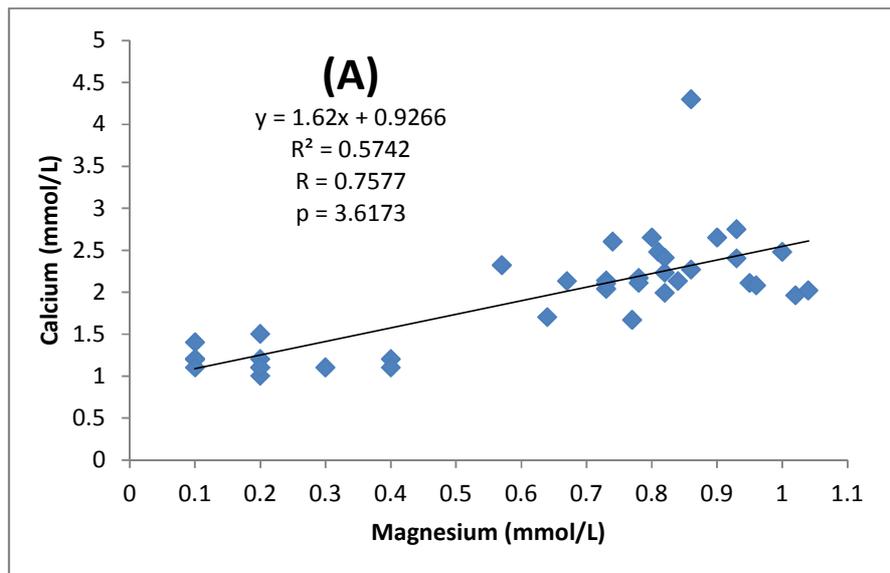
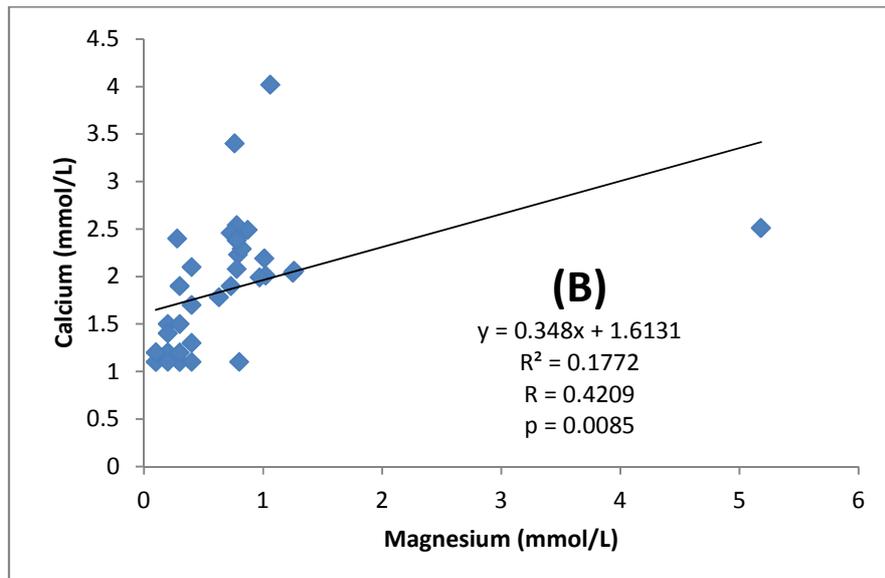


Fig. 2 Association of magnesium with phosphorus in non-diabetic (A) and diabetic (B) renal dialysis patients





**Fig. 3** Association of calcium with magnesium in non-diabetic (A) and diabetic (B) renal dialysis patients

Further, we explored the relationship between these minerals and HbA1c to see if in combination they could predict diabetes. Our results showed insignificant relationships between phosphorus and HbA1c (Figure 4) in both diabetic and non-diabetic renal dialysis patient. Surprisingly, in diabetic renal dialysis patients, there was significant relationship ( $p < 0.05$ ) between calcium and HbA1c (Figure 5B) and magnesium and HbA1c (Figure 6B). In both cases HbA1c level is inversely proportional to calcium and magnesium level. Khubchandani and Sanghani (2013) also reported significant relationship between HbA1c and magnesium in diabetic patients. Other researchers also concluded strong negative correlation between the plasma levels of magnesium and HbA1c levels in diabetic patients (Assimina et al 2014, Ahmed and Ahmed 2013). Reduction in the level of serum magnesium in diabetic renal dialysis patients may suggest hypomagnesemia as a possible risk factor for progress of renal failure in diabetic renal dialysis patient. However, there was no significant relationship between calcium and HbA1c, and magnesium and HbA1c in non-diabetic renal dialysis patient (Figure 5A and 6A, respectively) and HbA1c was directly related to calcium and magnesium level.

Maintenance of normal calcium, phosphorus, and magnesium homeostasis largely depends on a complex interplay between absorption from the gut and renal regulation. However, in renal failure, abnormalities of calcium, phosphorus, and magnesium levels are very common clinical findings (Blaine et al 2015). Magnesium is involved in many cell functions specially energy metabolism where it is acting as preferential cofactor for many kinases. Serum magnesium concentration is maintained within a narrow range by the kidney and digestive tract. Patients with chronic renal failure have increased body magnesium content. In subjects on hemodialysis and peritoneal dialysis the serum magnesium concentration parallels the dialysate magnesium level (Navarro-González 1998). In our study, most of the patients showed lower or normal range of magnesium except few patients which showed higher than the normal range. In addition, research has to be conducted with glycolytic enzymes specially kinases to clarify the role of magnesium in cellular energy metabolism in these patients.

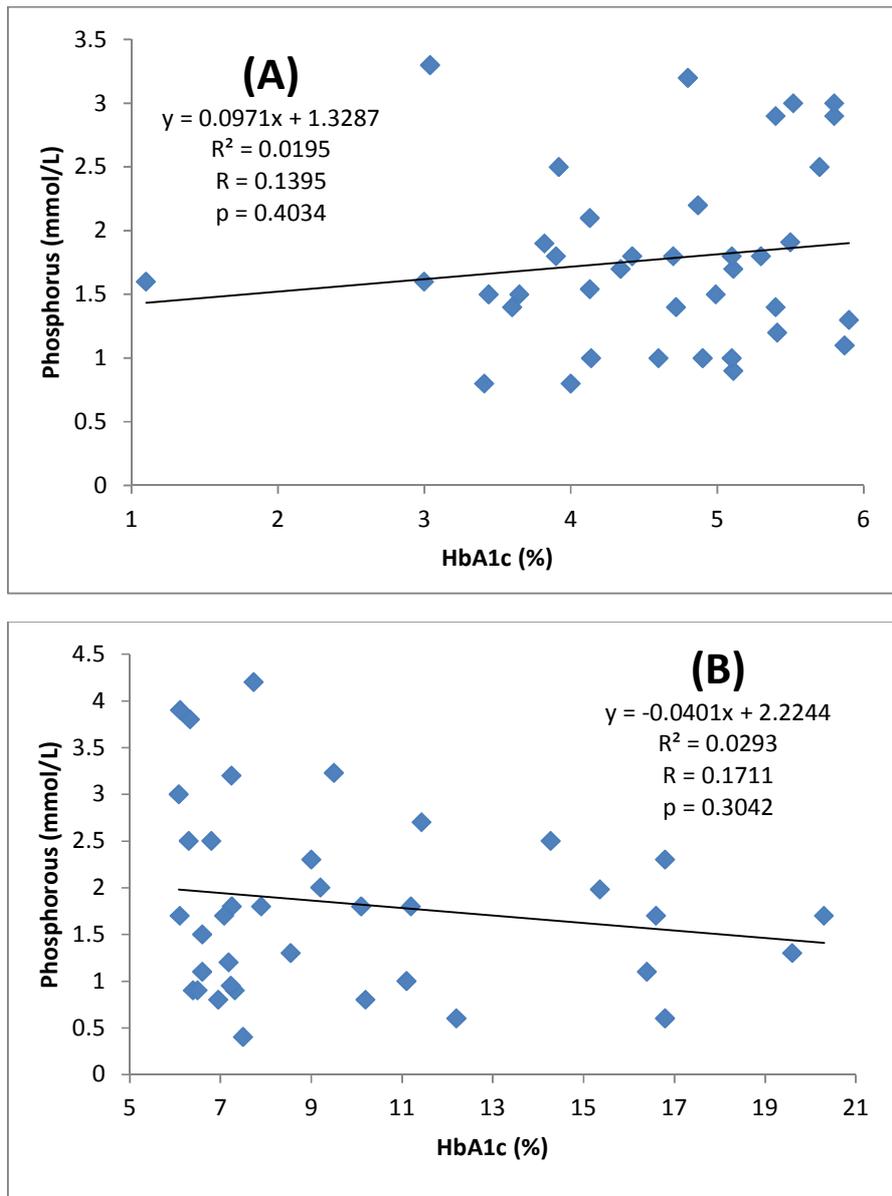


Fig. 4 Association of phosphorus with HbA1c in non-diabetic (A) and diabetic (B) renal dialysis patients

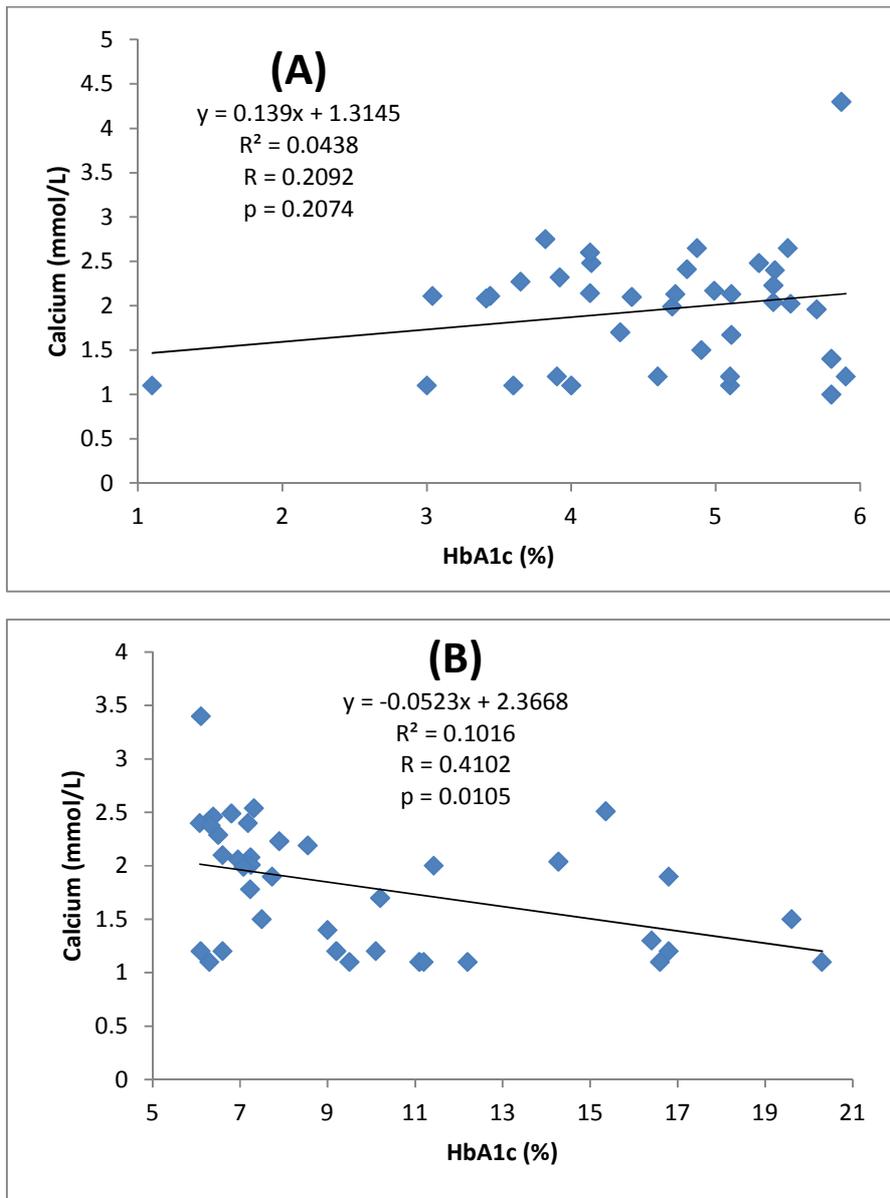


Fig. 5 Association of calcium with HbA1c in non-diabetic (A) and diabetic (B) renal dialysis patients

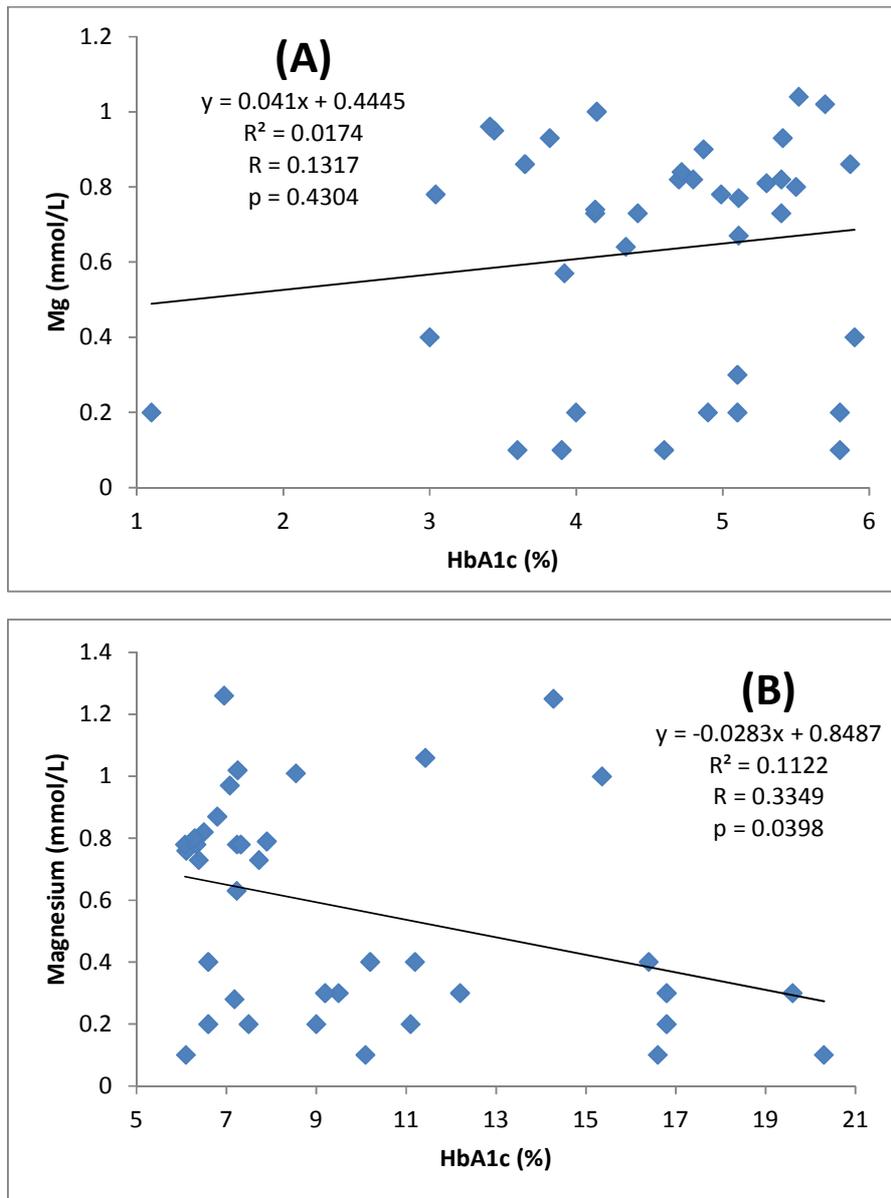


Fig. 6 Association of magnesium with HbA1c in non-diabetic (A) and diabetic (B) renal dialysis patients

### CONCLUSION

Our study shows that there is a possible correlation between serum calcium, magnesium and HbA1c in diabetic renal dialysis patients of Hail, Saudi Arabia. It can also be used to predict the status of diabetes also. Calcium being an important cation in both the extracellular and intracellular spaces plays a vital role in nerve impulse transmission, blood coagulation and hormone secretion. Therefore, hypocalcemia in diabetic renal patient may be due to defective calcium metabolism in kidney failure. Magnesium is essential to the glucose metabolism which needs to be maintained to improve proper energy level in the diabetic renal failure patients as these patients are suffering from hypomagnesemia. Although such an association seems reasonable, future research will have to be conducted to clarify the role of calcium, magnesium and HbA1c to assess mineral and energy metabolism of the cell that would be helpful in management of diabetic renal dialysis patients.

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