Correlation between total and ionic magnesium concentration in human serum samples is independent of ethnicity or diabetic state

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Abstract. The relationship between total and ionic serum magnesium in health and chronic disease across different ethnicities has not been well studied. Accordingly, we have examined the interrelationship between total magnesium and ionic magnesium, as well as ionic calcium to ionic magnesium ratio, in 286 patients made up of indigenous and non-indigenous Australians, with or without diabetes. Significant correlations were noted between total and ionic magnesium in all groups (p < 0.001). Amongst people with diabetes, the correlation coefficient (r) was 0.81 whereas in non-diabetics, the r was 0.66. This relationship was independent of whether the sample was from indigenous (r = 0.71) or non-indigenous (r = 0.81) participants. Overall the correlation between total and ionic magnesium across all participants was 0.75. There was no correlation between serum total magnesium and serum ionic calcium (r = 0.07), and similarly none between serum ionic magnesium and serum ionic calcium (r = 0.26). There was, however, a significant negative correlation between the calcium: magnesium ratio and serum total magnesium (r = 0.80; p < 0.001) across all participants, irrespective of whether the sample was made up of indigenous (r = 0.83) or non-indigenous participants (r = 0.77), or of diabetics (r = 0.71) versus non-diabetics (r = 0.83). We conclude that total and ionic magnesium serum concentrations are strongly correlated, and that either gives an accurate assessment of magnesium status in health and chronic diabetes, irrespective of ethnicity.

Key words: indigenous, diabetes, ethnicity, ion-selective electrodes, clinical, pathology, blood

It is becoming increasingly accepted that optimal magnesium homeostasis is associated with clinical well-being, and numerous examples exist describing an association between altered magnesium status and disease states [1-3]. For example, chronic low magnesium levels have been associated with chronic diseases such as diabetes, hypertension, cardiovascular disorders, neurological disorders and osteoporosis whereas acute magnesium deficiency has been associated with hypocalcaemia and hypokalaemia as well as asthma, stroke, cardiac arrhythmias and neurological dysfunction [1, 2, 4-6].

While a variety of methods are now available to determine magnesium status, the most commonly used methods in a clinical setting are colorimetric methods and ion selective electrodes for the determination of total or ionic serum concentration, respectively [1, 7]. Since ionic magnesium is the biologically active form of magnesium, a number of studies have accordingly suggested that only the ionic magnesium pool accurately reflects magnesium status and have recommended the routine use of ionic magnesium analyzers for magnesium assessments in serum samples [8-10]. Few studies,
however, have examined the interrelationship between total and ionic serum magnesium concentration in health and chronic disease, especially across specific ethnic groups at high risk for chronic disease [11, 12], rendering the choice of appropriate assessment methodology difficult.

The current study therefore measured serum total and ionic magnesium concentration, as well as ionic calcium/ionic magnesium ratios, in a group of 286 participants made up of indigenous and non-indigenous Australians, with and without type 2 diabetes. Correlations between total and ionic magnesium were then described in each of the subgroups divided on the basis of ethnicity and diabetic status.

**Methods**

**Subjects and setting**

Townsville Aboriginal and Islander Health Services (TAIHS) is a community-controlled Aboriginal Medical Service located in a suburban area of Townsville, Queensland, Australia that serves a community of over 16,000 indigenous residents [13]. About 20% of the TAIHS patient population are non-indigenous, mostly pensioners from the immediate neighbourhood. Diabetes is the number one reason for TAIHS general practitioner (GP) consultations (11.3 times per 100 doctor consults) [14]. All Aboriginal and Torres Strait Islander people recruited for this study were TAIHS patients who presented for care and subsequently required fasting blood tests as part of routine care between August 2004 and February 2006. Additional non-indigenous people were recruited from five GP practices in the Townsville area. Inclusion criteria included persons over the age of 15 (Tanner Stage 5). Exclusion criteria included chronic diarrhoea, alcoholism or binge drinking in the past two weeks, use of diuretics, consumption of magnesium supplements, reduced renal function (urinary albumin to creatinine ratio exceeding > 2.5 mg/mmol in men and > 3.5 mg/mmol in women), severe mental illness, pregnancy, or breastfeeding.

Ethics approval was obtained from the Townsville Health Service District Ethics Committee and the TAIHS Board of Directors ethics sub-committee. Additional community consultation was obtained at community diabetes events and from small focus groups held at TAIHS. As part of ethics approval under indigenous community consultation, this cross-sectional study was restricted to a convenience sample, integrated as part of on-going medical care, and included non-indigenous subjects. All subjects gave informed consent for participation in the study. A brief survey was administered to all subjects to verify the exclusion criteria. Medical records were reviewed for all TAIHS patients in the study, and blood glucose and glycosylated hemoglobin (HbA1c) levels were requested from the GP records. The diagnostic standard for diabetes was a random (non-fasting) blood glucose > 11 mmol/L with confirmed symptoms of diabetes, or fasting plasma glucose ≥ 7.0 mmol/L, or a 2-hour plasma glucose > 11 mmol/L during an oral glucose tolerance test [15]. In total there were 286 participants, made up of 152 indigenous and 134 non-indigenous participants. Of these 139 were confirmed as having diabetes, leaving 147 non-diabetics.

**Serum magnesium determinations**

Venous blood samples were collected in sterile blood separation tubes (Becton-Dickinson 5 mL vacutainer), refrigerated immediately, and analysed for total serum magnesium (Mg-s) in less than 24 hours using a colorimetric method with chlorophosphonazo III (COBAS INTEGRA 400®). Serum was then stored at -80°C before being analyzed for ionic magnesium (Mg-i) and ionic calcium (Ca-i) concentration using a NOVA-8 STAT analyzer equipped with ion selective electrodes.

**Statistical analysis**

Linear regression analysis was performed using Graph Pad Prism v. 5.01 (www.graphpad.com), with statistical significance being set at p < 0.05.

**Results**

The correlation between Mg-i and Mg-s in all participants was highly significant (figure 1; r = 0.75; p < 0.001). This relationship was independent of ethnicity (figure 2), with a strong correlation being observed between Mg-i and Mg-s in non-indigenous participants (figure 2A; r = 0.81; p < 0.001) as well as in indigenous participants (figure 2B; r = 0.71; p < 0.001). There was no effect of diabetes on these correlations. The correlation between Mg-i and Mg-s in non-diabetic participants was highly significant (figure 2C; r = 0.66; p < 0.001), with a similar strong correlation being observed between Mg-i and Mg-s in diabetic participants (figure 2D; r = 0.81; p < 0.001). There was no correlation between Mg-s and Ca-i (r = 0.07), and similarly none between Mg-i and Ca-i
There was, however, a significant negative correlation between Ca-I/Mg-I ratio and Mg-s (Figure 3; r = 0.80; p < 0.001) across all participants. This significant relationship was independent of ethnicity (r = 0.83 for non-indigenous and 0.77 for indigenous participants; p < 0.001) or diabetic status (r = 0.71 for non-diabetic and 0.83 for diabetic participants; p < 0.001).

**Figure 1.** Correlation between serum total magnesium and serum ionic magnesium across all participants. The correlation was highly significant (p < 0.001).

**Figure 2.** Correlation between serum total magnesium and serum ionic magnesium across (A) non-indigenous; (B) indigenous; (C) non-diabetic and (D) diabetic participants. In every sub-group, the correlation was highly significant (p < 0.001).

**Figure 3.** Correlation between serum total magnesium and serum ionic calcium/serum ionic magnesium ratio across all participants. The correlation was independent of diabetic status or ethnicity, and was highly significant (p < 0.001).
Discussion

In the current study, we have shown that serum ionic magnesium is strongly correlated to serum total magnesium concentration, with the relationship being apparent irrespective of either diabetic status or ethnicity. Similarly, serum ionic calcium/ionic magnesium ratio was also correlated to serum total magnesium irrespective of diabetic status or ethnicity. Notably, there was no correlation between serum total magnesium and serum ionic calcium suggesting that the change in ionic calcium/ionic magnesium ratio was dependent upon changes in total magnesium concentration, which were reflected in the ionic magnesium pool.

Although a number of reports have suggested that the total serum magnesium pool does not accurately reflect changes in the ionic Mg pool [4, 8, 16-18], and vice versa, several studies have now reported correlations between the two parameters in various disease states. In particular, the group of Saha et al. [9, 19] have published several reports showing strong correlations between total and ionic Mg concentration in serum taken from hemodialysis patients, patients with intestinal disease, alcoholic liver disease, and chronic renal disease. In contrast, a poor correlation was noted in critically ill patients in the study by Johansson and Whiss (r = 0.59) and the study by Barrera et al. (r = 0.57) [17, 18]. Although the reasons for these differences are unclear, the chronic or acute nature of the patients’ condition may be an important factor. In most chronic conditions, a generalized magnesium deficiency would manifest as both a decline in the total and ionic magnesium pools, with the interrelationship between the two maintained. Conditions affecting protein metabolism might impact the total magnesium fraction independent of the ionic unbound portion. In acute conditions that more commonly require critical care, the rapid onset of a condition that alters the binding status of serum ionic magnesium (e.g., hormonal changes, stress) may result in a dissociation of total and ionic magnesium. Thus, the chronic or acute nature of the condition should be considered when deciding whether to assess total or ionic magnesium in the assessment of magnesium status.

Diabetes is a chronic condition where a decline in serum total magnesium has been well described. In the present study, we have shown a strong correlation between serum total and ionic magnesium in diabetic participants, as well as in non-diabetic controls. This strong correlation was also apparent irrespective of the participants’ ethnicity. Our findings are similar to a previous report by Mikhail and Ehsanipoor [20] who also report a correlation between the total and ionic Mg, although their study reported that serum ionic but not serum total magnesium declined in diabetes. This is in contrast with the widely reported phenomenon of decreased serum total Mg in diabetes, which has been reported by a number of different laboratories [21-23].

In conclusion, our results suggest that serum total magnesium determination is sufficient for the assessment of magnesium status in diabetic and non-diabetic patients, and that ethnicity does not play a significant factor. While serum ionic magnesium determination may be a better indicator of magnesium status in acute disease states, the correlation between serum ionic magnesium and total magnesium in more stable chronic states may not require such assessment.

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References


