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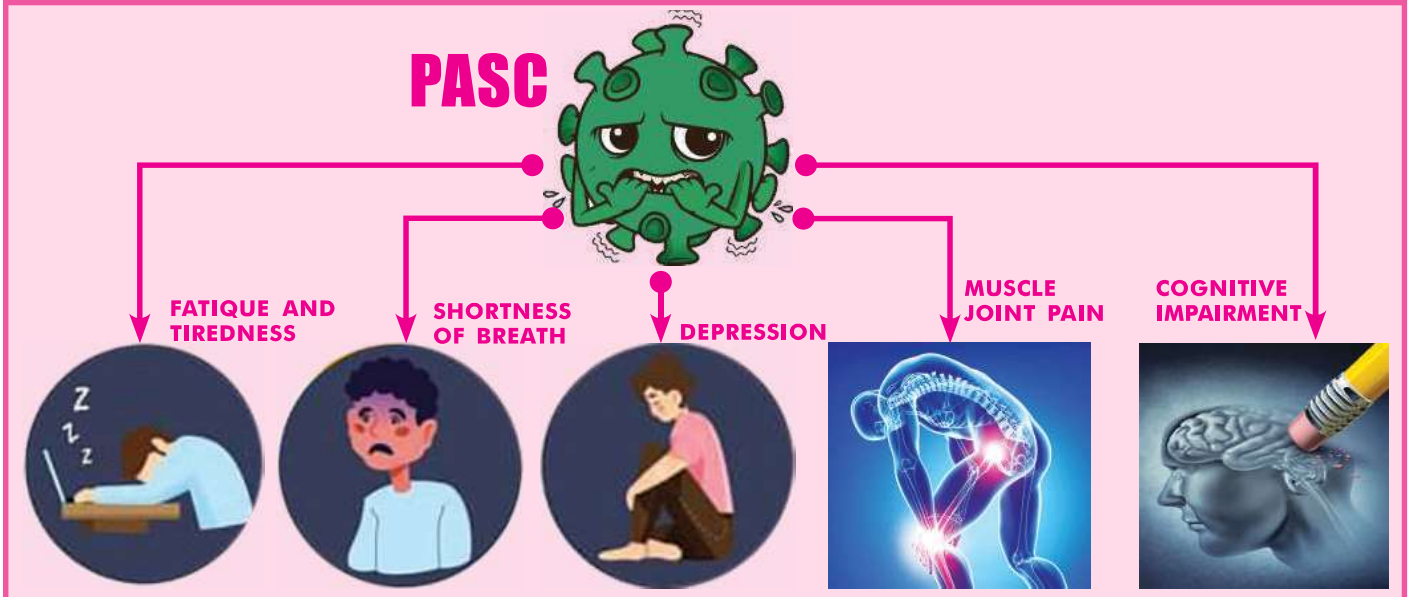

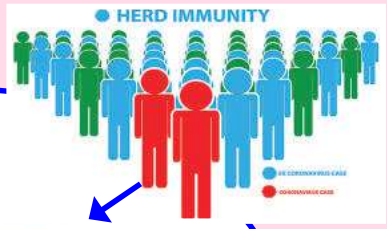

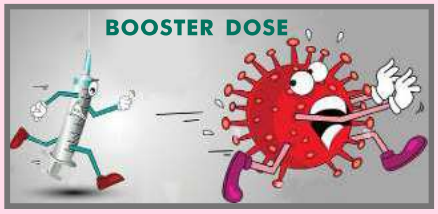

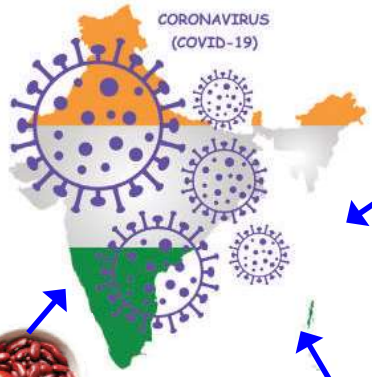

The long and the short of COVID in India

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CoVLP

GENERAL

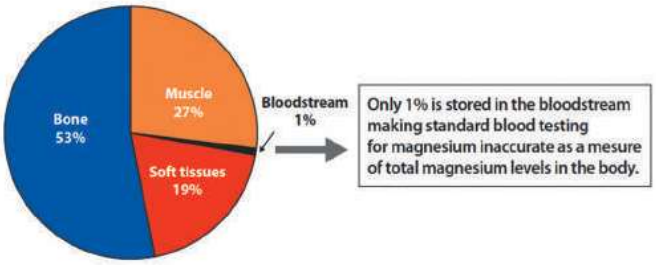
Magnesium and Type 2 Diabetes

SANJAY AGARWAL, MANDARA M.S.

Magnesium- the master cation

Magnesium is the fourth most common mineral in the human body after calcium, sodium, and potassium. It is also the second most common intracellular cation after potassium.

In a 70 kg individual, there is an average of 25 grams of magnesium in reserve.Of total body Mg2+, ~99% is intracellular, with 53% in bone, 27% in muscle, 19% in soft tissues, and less than 1% in the serum[1]



Magnesium homeostasis

Roughly 30% of ingested magnesium through food or drinking water is absorbed by the intestine, although the extent of absorption depends on the body magnesium status (increased in case of Mg2+ deficiency). Magnesium homeostasis is further regulated through the secretion and reabsorption in the kidneys, where about 95% of the filtered magnesium is reabsorbed.

Figure 1

Physiological functions of magnesium

Magnesium (Mg2+) is a critical micronutrient. Magnesium is implicated in over 80% of metabolic functions. Mg2+ is an essential cofactor in the activation of hundreds of enzymatic processes regulating diverse biochemical reactions, including energy production, protein synthesis, muscle and nerve function, blood glucose, and blood pressure control[2]

Figure 2

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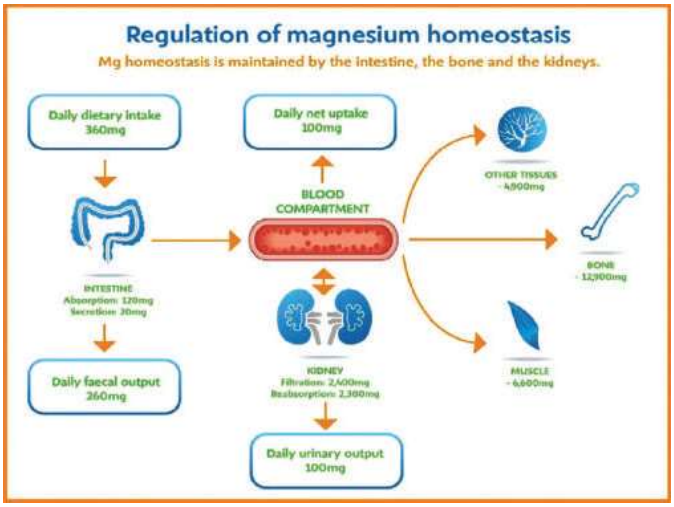

Figure 1: Magnesium homeostasis

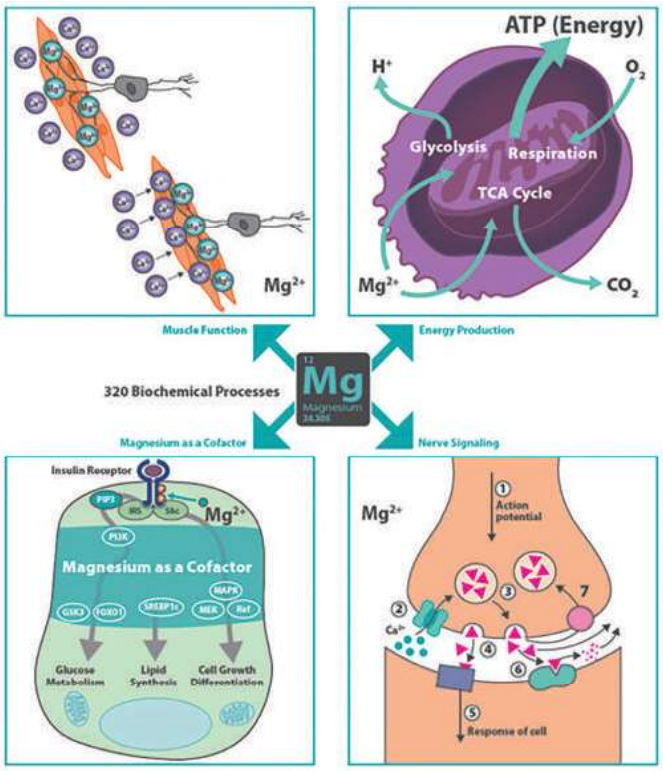

Figure 2: Physiological functions of Magnesium

Magnesium and carbohydrate metabolism

Magnesium acts as an insulin sensitizer by inducing autophosphorylation of insulin receptors and by regulating tyrosine kinase activity on these receptors[3]. In addition, magnesium may directly affect the activity of the glucose transporter - 4

(GLUT4) and help to regulate glucose uptake by the cell[4].

Magnesium and the cardiovascular system

Magnesium plays an important role in maintaining normal physiological functions of the cardiovascular system. It influences myocardial metabolism, Ca2+ homeostasis, and endothelium-dependent vasodilation. It also acts as an antihypertensive, antiarrhythmic, anti-inflammatory, and anticoagulant agent[5]

Magnesium is a physiological calcium antagonist. Through this action it produces vasodilation and reduces vascular resistance, improving blood circulation. It also maintains the electrical property of the myocardium, and also has anti-inflammatory activity.[6]

Magnesium also inhibits platelet adhesion and platelet aggregation. It is reported that magnesium deficiency can induce oxidative stress, which in turn activates the inflammatory process mediated via activation of nuclear factor kappa-B. This condition ultimately results in various pathological conditions like atherosclerosis, thrombus formation, and vascular calcification[7]

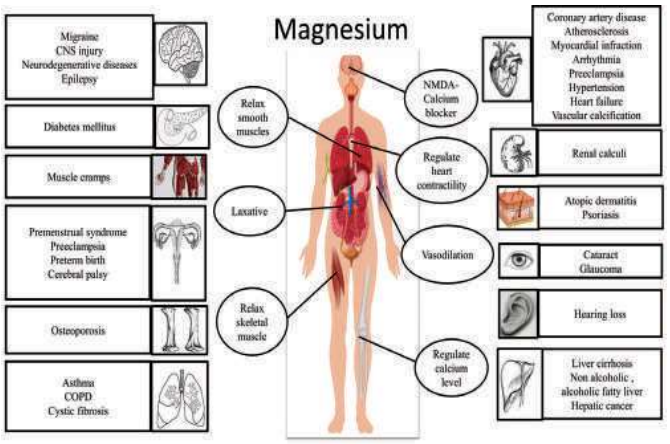

Figure 3: Physiological role of magnesium in vital systems. Text in the circle represents the physiological role of Mg in various vital organs. Text in the rectangle indicate the disorders associated with magnesium deficiency

Magnesium: Recommended Dietary Allowance (RDA)

The current RDA of magnesium for males ranges from 240 mg/day (range, 9–13 year of age) to 420 mg/day (31–70 year of age and older). For females, it ranges from 240 mg/day (9–13 year of age) to 360 mg/day (14–18 year of age). The RDA for females 31–70 year of age and older is 320 mg/day[8].

Many nutritional experts feel the ideal intake for magnesium should be based on the body weight (e.g.4–6 mg per kg/day).

Magnesium deficiency and diabetes

Chronic magnesium deficiency is often under-recognized and under-diagnosed because the commonly used serum magnesium levels often falls within the reference range and it is usually associated with non-specific symptoms. Over the last three decades, several experimental, clinical, and epidemiological studies have shown that chronic magnesium deficiency is associated with and/or amplifies many chronic diseases such as cardiovascular disease, osteoporosis, diabetes and hypertension[9].

Type 2 diabetes is frequently associated with both extracellular and intracellular Mg depletion. Several epidemiologic studies have recognized a high prevalence of hypomagnesaemia in subjectswith type 2 diabetes, especially in those with poor glycemic control, with longer duration of the disease and with the presence of micro and/or macrovascular complications of diabetes[10].The incidence of hypomagnesemia in patients with type 2 diabetes varies from 13.5– 47.7%[11]

Low intracellular magnesium impairs cell responsiveness to insulin, because it alters the tyrosine-kinase activity of the insulin receptor (INSR), leading to the development of post-receptor insulin resistance and decreased cellular glucose uptake and utilization[12]. Several studies have reported that a reduced intracellular magnesium level can lead to increased insulin resistance[13]

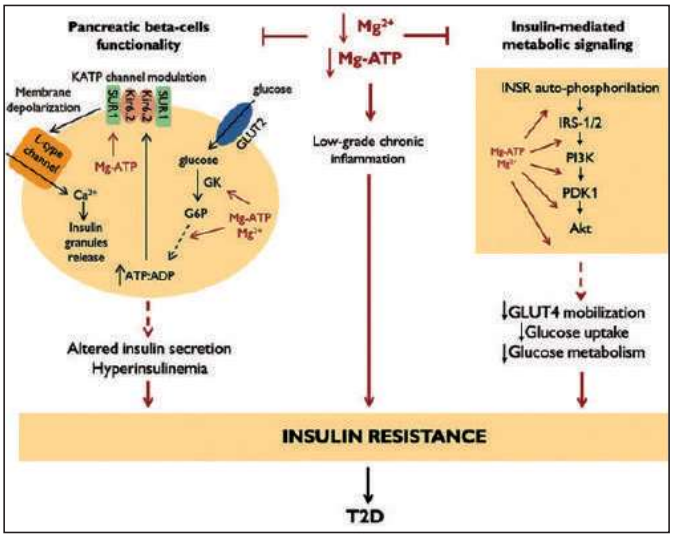

Figure 4: Link between magnesium and insulin signalling

Magnesium deficiency and risk of diabetes

Various epidemiological studies have confirmed

a clear and direct relationship between the dietary magnesium intake, type 2 diabetes and metabolic syndrome, suggesting that the higher consumption of magnesium is associated with a reduced incidence of diabetes.Two meta-analyses of prospective studies concluded that magnesium intake is inversely associated with type 2 diabetes [14].

Increased magnesium intake is associated with increased insulin sensitivity[15] and a decreased risk of developing type 2 diabetes[16].

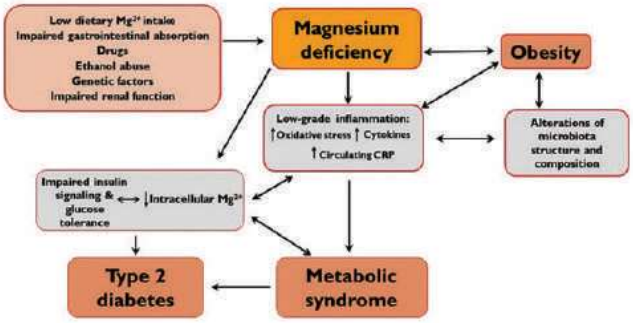

Figure 5: Patho-physiology of magnesium deficiency and type 2 diabetes, metabolic syndrome and obesity

Magnesium deficiency and chronic complications of diabetes

Endothelial dysfunction, vascular inflammation and oxidative stress are known to promote vasoconstriction, atherosclerosis and increase the risk of thrombus formation, which may lead to myocardial infarction or stroke[17].

Hypomagnesemia has been associated with inflammation and increased production of free oxygen radicals. Magnesium deficiency may trigger the development of a proinflammatory state both by causing excessive production and release of interleukins and by elevating circulating concentrations of proinflammatory neuropeptides that trigger activation of low-grade chronic inflammation[18].

A recent systematic review identified six randomized controlled trials that examined the effect of pharmacologic doses of oral magnesium on vascular endothelial function[19]. Three out of six trials, which included individuals with coronary artery disease, diabetes mellitus or hypertension, reported an improvement in flow-mediated dilation (FMD)with supplemental magnesium compared to control.

The measurement of the carotid intima-media thickness (CIMT) is sometimes used as a surrogate marker of atherosclerosis. Higher serum magnesium concentrations were associated with reduced carotid intima-media thickness (CIMT) in all women and in Caucasian men participating in the Atherosclerosis Risk in Communities (ARIC) study[20].

A meta-analysis of seven prospective trials with a total of 241,378 participants observed a modest but statistically significant inverse association between magnesium intake and risk of stroke. An intake increment of 100 mg magnesium/day was associated with a 8% reduction in risk of total stroke(combined RR: 0.92; 95% CI: 0.88, 0.97). Magnesium intake was inversely associated with risk of ischemic stroke (RR: 0.91; 95% CI: 0.87, 0.96)[21].

Low circulating magnesium levels have been associated a with a more rapid decline of renal function in diabetics. Hypomagnesaemia is currently considered an accurate predictor of progression to end stage renal disease and death and in patients with diabetic nephropathy[22].

Magnesium supplementation in diabetes mellitus

A randomized, double-blind, placebo-controlled study in 63 individuals with type 2 diabetes mellitus and hypomagnesemia found that those taking an oral magnesium supplement (638 mg/day of elemental magnesium) for 16 weeks had improved insulin sensitivity and better glycemic control compared to those taking a placebo [23]

A recent meta-analysis of nine randomized, double- blind, controlled trials concluded that oral supplemental magnesium lowered fasting plasma glucose concentrations in individuals with diabetes[24] Another meta-analysis of trials that included participants either at-risk of diabetes mellitus or with diabetes mellitus, suggested that evidence to support a benefit of magnesium supplementation on measures of insulin resistance was stronger in subjects who were magnesium deficient than in those with normal serum concentrations of magnesium[25]

According to the recent guidelines of the Association for Magnesium Research, patients with diabetes benefit from four effects of magnesium supplementation: insulin sensitizing effect, calcium antagonism, stress regulating, and endothelium stabilizing effects. In diabetics, the Association for Magnesium Research recommends a daily magnesium supplementation between 240 and 480 mg (10–20 mmol)[26]

To summarise, evidence from the scientific and medical literature suggests that maintenance of magnesium sufficiency can have a profound impact in management of diabetes. Magnesium supplementation

has been suggested as a possible complementary, economic and safe treatment option for improving outcomes in type 2 diabetes.

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Splenomegaly - Causes of splenomegaly can be divided into multiple mechanistic categories. Spleen enlargement can be due to congestion caused by portal hypertension, a condition characteristically encountered in patients with hepatic cirrhosis that may result in sequestration of leukocytes, erythrocytes, and platelets, with resultant cytopenias.

Spleen enlargement can also result from infiltrative processes, such as amyloidosis and sarcoidosis: myeloproliferative processes arising from cell lineages that commonly reside in the spleen, such as chronic leukemias, lymphomas, and other hematologic cancers, various infections, such as those caused by Epstein – Barr virus, human immunodeficiency virus, and mycobacteria, including tuberculosis; and auto-immune processes, such as rheumatoid arthritis and systemic lupus erythematosus.

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