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COVID DEATHS

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GENERAL

Magnesium supplementation in pregnancy

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Introduction

Diet with adequate and balanced intakes of macronutrients such as carbohydrates, proteins and fats and micronutrients such as vitamins and minerals, before, during and after pregnancy, is essential for healthy growth and development of foetus.[1] Optimal nutritional status of the mother reduces the risk of complications, birth defects and future diseases in off springs during adult hood.

Magnesium and pregnancy

Apart from iron, iodine, calcium and zinc, magnesium is a micronutrient of great importance during pregnancy and lactation.

The US recommended dietary allowance (RDA) for magnesium is 310 mg/day and 320 mg/day for females aged 19–30 years and 31–50 years, respectively. In pregnant women, it is 350-360 mg/day and during lactation it is about 310-320 mg/day[2]. The increased magnesium requirement during pregnancy is due to altered tissue distribution, increased renal excretion of magnesium and increased foetal requirement.[3]

Given that the majority of women of childbearing age do not meet the US RDA for magnesium, it is unlikely that the increased demand for magnesium during pregnancy or lactation is being met. A study conducted among pregnant women in India reported that the incidence of hypomagnesemia was as high as 43.6%[4].

Recent studies suggest that magnesium deficiency during pregnancy may be associated with adverse maternal and fetal outcomes such as preeclampsia and preterm birth[5]. Magnesium deficiency is also implicated in the occurrence of gestational diabetes mellitus and intrauterine growth restriction (IUGR)[6].

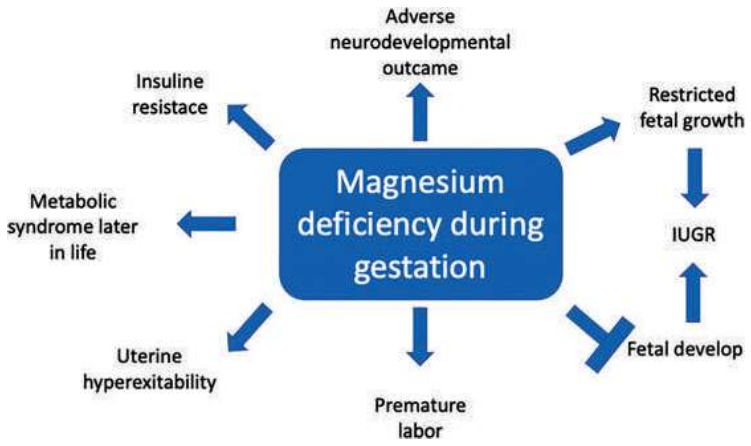

Figure: Consequences of magnesium deficiency during pregnancy

Magnesium, Pre-eclampsia, and Eclampsia

The association of a low dietary magnesium intake and an increased risk of preeclampsia has been confirmed in a meta-analysis studying the effects of various dietary factors on the risk of pregnancy-induced high Blood Pressure[7]. In a small cohort study (n=20 cases, n=20 controls), a significant decrease in red cell magnesium was observed in women with preeclampsia compared with controls (0.98 mmol/L vs 1.35 mmol/L, P<0.001)[8].

Magnesium sulfate has been shown to have vasodilatory action via inhibition of angiotensin II and endothelin I[9]. In addition, it may have an immunomodulatory role in preeclampsia[10]. Administration of magnesium sulfate decreases the risk of eclampsia and maternal death by 50%[11]. The American College of Obstetricians also recommends magnesium sulfate for the treatment of severe preclampsia[12].

In a recent double-blind randomized controlled trial, 300mg of magnesium citrate was found to prevent an increase in diastolic blood pressure during the last weeks of pregnancy, with the average diastolic reading being significantly lower in the magnesium-supplemented group at week 37 (72mmHg vs 77mmHg, P = 0.031)[13].

Clinical trials with oral magnesium supplementation have shown that it is associated with significantly fewer babies with an Apgar score of less than 7 at 5 min (RR, 0.34; 95%CI, 0.15 to 0.80; four trials, 1083 infants), with meconium-stained liquor (RR, 0.79; 95% CI, 0.63 to 0.99; one trial, 4082 infants),

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late fetal bradycardia (RR, 0.68; 95% CI, 0.53 to 0.88; one trial, 4082 infants), and mild hypoxic-ischemic encephalopathy (RR, 0.38; 95% CI, 0.15 to 0.98; one trial,4082 infants). Moreover, women receiving oral magnesium were significantly less likely to require hospitalization during pregnancy (RR, 0.65; 95% CI, 0.48 to 0.86; three trials, 1158 women)[14].

Magnesium and preterm birth

Studies indicate that magnesium deficiency is associated with hyperactivity of uterine muscle cells, which may consequently increase the risk of spontaneous abortion,preeclampsia, and preterm birth.[15] Two prospective cohort studies recruited 150 women (75 each in the hypomagnesemia or normal group) and 160 women (80 each in the hypomagnesemia or normal group), respectively, who had begun the second trimester of pregnancy and for whom serum magnesium concentrations were measured at baseline[16]. Both studies found, after controlling for potential confounding variables (eg, age, parity, social class, and body mass index), that the rate of preterm birth in the hypomagnesemia group was significantly higher than that in the normal magnesium group. 8 cross-sectional studies, conducted in developing countries (India, Bangladesh, Iran, Iraq, and Nigeria), consistently demonstrated lower serum magnesium levels in the preterm birth group as compared to the full-term birth group ($P<0.05$)[17]. Results of 6 different randomized, controlled trials reported that magnesium supplementation significantly reduced rate of preterm birth. When intention-to-treat analysis was performed, the pooled RR was 0.58 (95% CI, 0.35 – 0.96), indicating a beneficial effect of magnesium supplementation on preterm birth[18].

Magnesium and Intrauterine Growth Restriction (IUGR)

Trace elements, including magnesium, are an essential nutritional component for humans, particularly in the intrauterine life when foetal development occurs, and inadequate tissue concentrations of magnesium may have significant adverse effects on foetal weight at birth[19].

The hypothesis that magnesium deficiency might be responsible for IUGR has been confirmed in a study aimed to correlate magnesium levels in umbilical vein and in maternal peripheral blood with foetal weight at birth[20]. In this study, newborns of pregnant women supplemented with magnesium sulfate (25% magnesium sulfate 20 ml in 5% glucose 500 ml i.v.) were characterized by a birth weight significantly higher than that of unsupplemented women with low serum magnesium levels.

Magnesium and gestational diabetes mellitus

Gestational diabetes mellitus (GDM) is reported in 1%–14% of pregnant women.Magnesium is involved in multiple steps of the insulin-signaling pathways such as secretion, binding, and receptor activity[21].

Magnesium supplementation has been shown to significantly improve insulin sensitivity in both hypo-and normomagnesemia[22] and to improve glucose status in paediatric patients with hypomagnesemia[23].

In a controlled double-blind randomized trial, women with magnesium deficiency and GDM were given 250 mg of magnesium oxide or placebo for 6 weeks. After 6 weeks, women in the treatment group showed significant improvement in glucose control and insulin secretion, whereas values for women in the placebo group worsened over time (fasting plasma glucose, -9.7 vs +1.8 mg/dL, $P<0.001$; serum insulin concentration, -2.1 vs +5.7mIU/mL, $P=0.001$; homeostasis model of assessment-estimated insulin resistance, -0.5 vs +1.4, $P<0.001$). In addition, newborns of supplemented mothers experienced a significant reduction in hyperbilirubinemia and hospitalization (8.8% vs 29.4%, $P=0.03$, and 5.9% vs 26.5%, $P=0.02$) respectively.[24].

Magnesium and pregnancy-induced leg cramps

About 30%–50% of pregnant women experience leg cramps at least twice a week during the third trimester[25]. The possible mechanisms for the use of magnesium supplementation in A leg cramps might be related to numerous processes that affect muscle function including oxygen uptake, energy production, and electrolyte balance[26].

Multiple randomized controlled trials have compared the efficacy of magnesium with other treatments in the treatment of nocturnal leg cramps.The meta-analysis of these studies concluded that magnesium supplementation is beneficial in the treatment of legcramps in pregnant women[27]. Another study,conducted on the basis of these data, reported that oral administration of magnesium decreased the frequency and intensity of leg cramps in pregnant women, suggesting magnesium supplementation as a treatment of choice for pregnancy-induced leg cramps[28].

To summarize, evidence from the current scientific literature suggests that optimum magnesium

levels are essential for the health of the mother and the foetus during pregnancy and for the health of the child postpartum. Hence it is advisable that pregnant women consume more magnesium rich foods prior to and during pregnancy and lactation. Magnesium supplementation may be considered in women with a history of hypertension or with other risk factors for preeclampsia, such as obesity or insulin resistance.

As per recommendation of Society for Magnesium Research e.g. every pregnant woman should be supplemented with 240-480 mg (10-20 mmol) of magnesium daily. Magnesium supplementation should start as soon as possible, continue until birth, and be continued post natally, since the magnesium requirement of the body also increases during breast-feeding[29].

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In 1998, Haissaguerre, et.al., demonstrated that 94% of atrial ectopic foci initiating AFib were localized to the pulmonary veins (PVs), and focal ablation of these foci eliminated AFib in a majority of patients. **- Cardiology**