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The magnesium global network (MaGNet) to promote research on magnesium in diseases focusing on covid-19

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Dear Editor,

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When the current SARS-CoV-2 pandemic began in early 2020, the global magnesium researcher community came together and noted the striking similarities between COVID-19 risk factors and conditions associated with magnesium deficit state in humans, reasoning that magnesium deficiency could worsen the course of COVID-19 [1–4]. This prompted establishment of a worldwide collaborative network with regular virtual meetings to brainstorm the associations between magnesium and COVID-19. We hypothesize that magnesium deficiency, a common but mostly unrecognized state in modern global societies, could be an important component of the susceptibility to SARS-CoV-2 infection. Consequently, restoring the magnesium deficit may be a putative therapeutic strategy to possibly ameliorate or prevent COVID-19.

Magnesium deficiencies, measured by both dietary and blood parameters, have been associated with many chronic diseases afflicting our modern world including cardiovascular diseases, *diabetes mellitus*, hypertension, dyslipidaemia, immune dysfunction, cancer and aging [5–8]. In addition, magnesium requirement increases with rising BMI, making obesity a risk factor for magnesium deficit and chronic diseases [9].

The low-magnesium state, long established in Western Societies consuming a modern processed food diet, can be exacerbated by certain long-term prescribed medicines [5], and is spreading worldwide as a consequence of globalization of lifestyles. As the world increases in wealth, consumption of processed, low-magnesium containing food is expanding, and along with it the chronic diseases associated with low magnesium state, probably also due to decrease of magnesium content in soil and water [10].

Sars-CoV-2 pandemic is a global concern due to the enormous number of infected persons and deaths worldwide (to date 144,099,374 and 3,061,912, respectively [11]), and no disease-specific treatments available.

There are at least two different domains where magnesium could be directly involved. First, nearly all the co-morbidities that exacerbate the risk of infection and the severity of symptoms are associated with magnesium status imbalance (e.g. immunological disorders, *diabetes*, hypertension, cardiovascular diseases, metabolic syndrome, obesity/adiposity, cancer and aging) [5–9].

Second, considering the critical role of magnesium in cellular function, inflammation and immune responses to stress and infection, it is possible that perturbed magnesium status impacts the pathogenesis of SARS-COV2 infection and associated immune and inflammatory responses [12]. Moreover, magnesium may be involved in processes related to the function of ACE2, the receptor through which SARS-CoV-2 mediates host cell effects [13].

These provocative considerations sparked important discussion in our magnesium network, with other important topics under consideration in COVID-19 and beyond, including:

- identification of the most appropriate approaches to evaluate body magnesium status;
- definition of the ideal reference range for serum magnesium levels;

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- census of ongoing clinical studies and trials specifically dedicated to disclosing the role of magnesium in COVID-19, and design of further research projects;
- elucidation of the potential correlation between magnesium imbalance and severity of COVID-19.

To date we have had 13 virtual meetings. The original group included "veterans", i.e. magnesium researchers who, up to 2008, used to meet at the dedicated Gordon Research Conferences. The network continues to grow as more researchers and clinicians interested in magnesium worldwide are identified. We welcome all those who were informed of the meetings through the SDRM website (International Society for the Development of Magnesium Research, www.sdrmsociety.org), where we post news, relevant references and recordings of our meetings.

Currently we are pursuing two projects:

- The collection of institutional or national serum magnesium reference ranges routinely used in hospitals around the globe, to discuss differences and propose standardized "normal" values.
- An accurate analysis of the relationship between magnesium status perturbations and COVID-19 pandemic based on upcoming data from ongoing clinical studies.

Our goal is to promote research on magnesium, the clinically still poorly acknowledged cation.

We hope to provide the scientific community with expert and up-to-date information and viewpoints on the role of magnesium in health and disease, especially related to COVID-19, the most urgent global challenge at this time.

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