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Editorial

Do We Need Changes in Management Strategies of COVID-19 Pandemic? Vitamin D as a Balance Key for Health-Economy Dilemma

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Current COVID-19 pandemic represents one of the most challenging outbreaks over centuries. These challenges are attributed to its highly infectious rate to the edge that it overwhelms the capacity of national health systems worldwide. In addition, short and long-term economic consequences complicate existing health care challenges.
Accordingly, the medical community over the globe is in hurry for finding out a solution and increasing numbers of different clinical and laboratory studies investigating various treatment modalities are conducted. However till now, no current evidence-based curative medications or effective vaccinations are at hand and employed social distancing measures are not strictly followed in many situations; leading to rapidly rising curve of infection spread with its sequelae of unacceptable mortality rate.

1. WHY DO WE NEED CHANGES IN MANAGEMENT STRATEGIES?

- Time is a critically-pressing factor; e.g. emerging published reports herald expectations of 12-18 months duration before having globally-available effective vaccines or drugs. This long duration is to definitely perpetuate medical and economic crises.
- Widespread social distancing measures have drastically-negative economic repercussions.
- Currently investigated drugs have well-known side effects. For example, high doses of Hydroxychloroquine cause retinal damage. These side effects are to worsen clinical outcomes (e.g. morbidity and mortality rates) of those critically-ill patients of COVID-19 [1, 2].
- Mode of acquired immunity following COVID-19 infection and consequently vulnerability of cured patient for re-infection (i.e. relapse) have not yet been well-established.
- Another point is versatility of currently-investigated drugs to conquer highly possible mutations of COVID-19 in near future.
- Recent reports have emphasized role of immunity

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as a significant prognostic factor of COVID-19 infection; i.e. significantly poorer outcomes are linked to elderly and immunocompromised patients [3-5].

2. HOW CAN WE CHANGE MANAGEMENT STRATEGIES?

Current clinical efforts should be directed towards fortifying the immune system of both infected patients and healthy populations; so that COVID-19 is overcome by the innate immune response. *The mainstay step for this is to maintain serum active vitamin-D within normal levels (>50 nmol/L) by high doses of vitamin-D supplementation* [6].

3. WHAT ARE THE SUPPORTIVE CLINICAL SCIENTIFIC EVIDENCES?

- When reviewing literature and maps for geographic distribution of vitamin-D deficiency; a possible correlation can be clued between low serum levels of vitamin-D and high rates of infection spread [6-8].
- Interestingly, Wuhan where COVID-19 have begun and spread; is one of Chinese territories well-recognized for vitamin-D deficiency [8].
- Reviewing literature for demographic distribution of vitamin-D deficiency points out another possible correlation which can be clued between low serum levels of vitamin-D and high rates of COVID-19-related complications; e.g. highest mortality rates in geriatric population group [7].
- Historically, an integrated step of T.B. patients' management protocol was sun exposure in sanatorium. This was explained dry aeration-related factors. However another factor was increased sun-induced endogenous synthesis of vitamin-D.
- Different clinical studies have correlated vitamin-D deficiency with higher rates and more severe cases of respiratory tract infection. For example, a recent randomized trial of vitamin D supplementation demonstrated significant 42% prevention of seasonal influenza-A in schoolchildren [9].

4. WHAT IS THE BACKGROUND IMMUNOLOGICAL ROLE OF VITAMIN-D?

- Role of vitamin-D in modulating both innate and adaptive immunity mechanisms has been extensively investigated through various clinical and laboratory studies [10-14].
- It has been well-demonstrated that 1, 25 (OH) vitamin-D3 is the direct inducer of the genes for antimicrobial peptides (i.e. cathelocidin and beta defensing 4) transcription [10].
- Vitamin-D modulatory effects on functions of different immunological cells have been thoroughly studied with conclusion that vitamin-D is to results in an increased cellular production of anti-inflammatory cytokines and simultaneous decreased levels of inflammatory mediators. These effects are to offer adequate damage-control of cytokine storm currently reported in COVID-19 patients [3, 11, 12].

5. WHAT ARE THE ADVANTAGES OF VITAMIN-D SUPPLEMENTATIONS IN COVID-19 MANAGEMENT?

- It is readily available; i.e. its use as a part of standard COVID-19 management can be immediately commenced.
- It is relatively cheap so adding a minimal cost to the economic burden of the current economic crisis.
- It has a high safety profile.
- It has well-documented immunological role.

6. WHAT ARE THE RECOMMENDED SCIENTIFIC RESEARCHES?

The current health crisis might offer a golden chance for more detailed investigation of immunological role of vitamin-D; this chance can be exploited by a number of clinical and laboratory researches such as:

- Measurements of serum levels of vitamin-D in COVID-19 infected patients
- A randomized controlled trial of COVID-19 infected patients comparing clinical outcomes following vitamin-D supplementation.
- A randomized controlled trial of COVID-19 infected patients comparing laboratory parameters (i.e. cytokines) following vitamin-D supplementation.
- Laboratory animal studies:
    - Risk of COVID-19 infection in groups of healthy mice according to initial serum levels (i.e. low versus normal) of vitamin-D
    - Clinical outcomes and mortality rates in groups of COVID-19 infected mice following vitamin-D supplementation.

7. CONCLUSIONS

Current management strategies of COVID-19 infection

should be subjected to a number of modifications. Firstly; vitamin-D supplementation should be an integral part of medications protocol of COVID-19 infected patients. Secondly, healthy population should be screened and administered vitamin-D supplementation; thus keeping serum level of vitamin-D within normal which is an essential prophylactic action in conjunction with others as social distancing measures. And by extension, this second step is to allow governments to follow (Herd Immunity) policy especially among young-demographic populations which in turn is to ameliorate the economic consequences. Isolation should be confined to high-risk and old-age population, and already infected patients.

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