EDITORIAL

Vitamin D in Critical Illness: Not a Panacea for All Ills!

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India has abundant sunshine, and we would have expected the population to be vitamin D replete. However, that is not the case, and the prevalence of vitamin D deficiency in children documented in several studies is as high as 75-90% [1]. Most of these studies have assessed the vitamin D status of infants, adolescents, pregnant and lactating women. Status of vitamin D levels in children between infancy and adolescence is not well studied, though we could expect the same degree of deficiency in them as well. Skin pigmentation and clothing habits along with poor nutrition and atmospheric pollution are thought to account for this deficiency. Recent attention has focused on the myriad actions of vitamin D on cardiovascular and respiratory health, inflammation, innate immunity and neuromuscular function; hence deficiency is expected to have multiple effects. The adverse effects of this deficiency are hypocalcemic seizures and increased risk of lower respiratory tract infections, apart from the well known effects on bone health.

When on one hand children who are otherwise healthy are found to be vitamin D-deficient, it is not surprising that critically ill children are deficient in vitamin D. Studies in sick Indian children are scarce [2,3]. However, there are some studies showing vitamin D deficiency in critically ill adult patients [4]. Critically ill patients with vitamin D deficiency have been found in some studies to have a worse outcome [5]. A higher requirement of vasoactive drugs, higher severity of illness scores, longer duration of intensive care unit stay, and higher mortality have all been attributed to vitamin D deficiency. However, the results are very varied, and no adverse effects can be firmly attributed to vitamin D deficiency. While vitamin D supplementation has not been found to be beneficial in most critically ill patients, children with congestive cardiac failure fared better with vitamin D supplementation in one study [6]. Results of ongoing studies on vitamin D supplementation in critically ill children are still awaited.

In the current issue of *Indian Pediatrics*, Shah, *et al.* [7] present the findings of their study of the calcium-parathyroid hormone-vitamin D axis in a cohort of critically ill children. They assessed the prevalence of vitamin D deficiency in this population and further studied whether the presence or absence of a parathyroid hormone (PTH) response in the setting of vitamin D deficiency influenced the outcome. The authors justified parathyroid hormone assessment as they speculated that critical illness may impair the calcium-PTH-vitamin D axis rather than affecting vitamin D alone. Vitamin D deficiency (defined as 25-hydroxy vitamin D level <20 ng/mL) was found in 83% of the children, which is similar to the prevalence in otherwise healthy children. The median level of vitamin D in the cohort was 11.7 ng/mL (a seriously low level), with 13.6% having levels <5 ng/mL. Vitamin D-deficient children were hypocalcemic more often than those who were vitamin D replete, as expected. Vitamin D deficiency was not associated with any increase in morbidity or mortality. Considering that the median level of 25-(OH)D was 11.7 ng/mL, it would have been interesting to note if children with levels ≤10 ng/mL fared worse than those with higher levels. Since children with congestive cardiac failure have been shown to have a worse outcome if vitamin D-deficient, this is a subgroup in which further study was warranted; however, the number of children in this subgroup was too small. The expected rise in PTH was seen in only around 20% of the children who were either vitamin D-deficient or hypocalcemic. It is rather contradictory that vitamin D-deficient children, who showed an appropriate PTH response, had higher severity of illness scores at admission! The explanation offered by the authors that lack of PTH response indicates better utilization of tissue vitamin D is not very convincing. A large proportion of children were malnourished, and hence this could affect the PTH response. Similar paradoxical results of sicker patients having a more appropriate PTH response to hypovitaminosis D have been found in earlier studies of adult critically ill patients [8].

To summarize, this study adds to the growing body of literature on vitamin D deficiency in critically ill children. Unfortunately, the clinician is left wondering whether

routine assessment and/or supplementation of vitamin D in this population of children is necessary. Intervention studies of supplementation of vitamin D would perhaps solve this question. Meanwhile, we should not forget our preventive role, and should continue to encourage a healthy diet and lifestyle to prevent vitamin D deficiency in the community.

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EDITORIAL

Improving Access and Reducing Childhood Deaths due to Pneumonia

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Child health has been the cornerstone of global public health agenda for a long time, and the focus has ever been increasing with implementation of various evidence-based interventions and programs. But unfortunately, these efforts have not materialized fully, and we are still far from reaching the goals that we set ourselves. It becomes highly unacceptable provided that these targets were never overambitious. Global under-five child mortality – though, has declined by more than half since the year 1990, and was pegged at 5.9 million deaths per year in 2015 [1] – is still very high considering that most of these deaths were preventable by implementation of existing cost-effective, evidence-based interventions. This existing burden of under-five mortality is vastly unevenly distributed with countries and regions with the most impoverished bearing the brunt.

Achieving substantial progress and accelerating the current progress would require a focused, determined approach on the most common causes of under-five mortality. Infectious diseases and neonatal complications encompass a vast majority of these deaths globally. Half of these under-five deaths are due to infectious diseases and conditions, including pneumonia, diarrhea, malaria, meningitis, tetanus, HIV and measles [1]. Pneumonia alone accounts for 17% of all global under-five deaths [2], and is the single most common infection-related cause. It is critical to intensify efforts to improve the coverage of proven preventive and therapeutic strategies to tackle pneumonia. World Health Organization (WHO) and United Nations Children's fund (UNICEF), in 2013, launched an integrated 'Global Action Plan for the Prevention and Control of Pneumonia and Diarrhea' to create greater emphasis on countries to control these most common causes of child mortality [3].

The strategies for prevention of pneumonia are of unequivocal importance, including improved immunization, and better water, sanitation and environment, but adequate and timely diagnosis and management also holds unparalleled importance. Although most of these interventions are within the present health systems of many countries, their coverage and availability to poor and marginalized populations varies greatly. Majority of childhood pneumonia deaths are due to severe pneumonia, and management of these severe cases requires early identification, prompt referral and availability of good-quality care [4]. Previous guidelines developed by the WHO recommended that children, who have fast breathing with lower chest wall indrawing (severe pneumonia), be admitted and given parenteral antibiotics. But in underprivileged settings, failure to identify cases early is recognized as a major barrier and acknowledged to be the common determinant of mortality due to childhood pneumonia [5]. In many developing areas, even early identification and referral might not lead to optimum care for a number of reasons, including poor transportation systems, costs, distance, lack of skilled care providers and cultural perceptions [5].

Due to these existing inherent realities of the developing world, scientists across the world designed trials probing the possibilities of alternative management strategies, and multiple trials were designed to test the effectiveness of oral antibiotics for management of severe pneumonia. Oral amoxicillin was primarily tested, and proved as effective as injectable penicillin in the treatment of severe pneumonia. This provided an opportunity for substantial improvements in access to appropriate care, reduced nosocomial complications and iatrogenic infections, and reduced need for supplies, specialized care and costs. Trials also tested the feasibility of safe community-based treatment alternatives, and the authors documented that properly trained community health workers were able to satisfactorily diagnose and treat pneumonia associated with chest-indrawing [6]. This strategy could effectively increase access to care for pneumonia in settings where referral is difficult, and could become a key component of community detection and management strategies for childhood pneumonia, and substantially increase the number of children who can receive effective care.

These findings encouraged the WHO to revise the guidelines in 2014; all children with fast breathing and/or chest-indrawing are classified as having 'pneumonia' and treated with oral amoxicillin; the recommended dosage is 80 mg/kg for five days (40 mg/kg twice a day); in settings of low HIV prevalence, the duration of treatment for 'fast breathing pneumonia' can be reduced to three days [7]. The current systematic review, by Lodha, *et al.* [8], on oral antibiotics for community-acquired pneumonia with chest-indrawing in children below five years of age is a comprehensive synthesis of the existing evidence, and reaffirms that oral amoxicillin is effective for treating these cases in both the outpatient and community settings. These strategies, if implemented at scale in countries with a high pneumonia burden, will result in higher proportion of children receiving care at the outpatient or community levels, and a reduced number of pneumonia-related deaths.

The Lancet series on childhood pneumonia and diarrhea [9], has mapped the pathway of reducing under-five deaths due to these two conditions, but this will require a concerted effort using a systematic approach of sharpening evidence-based planning and implementation at all levels (communities, clinics and hospitals), and ensuring quality of care and effective systems of monitoring and accountability. Though, we as global community have missed the targets of child health in 'Millennium Development Goals' but let us aim to achieve the same in 'Sustainable Development Goals' targets.

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