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► **To cite this version:**

Thi-Phuong-Thao Pham, Didier Raoult, Matthieu Million. IGF1 levels in children with severe acute malnutrition after nutritional recovery: A good predictor for children's long-term health status. *EBioMedicine*, 2019, 45, pp.9-10. 10.1016/j.ebiom.2019.07.011 . hal-02504557

**HAL Id: hal-02504557**

**<https://amu.hal.science/hal-02504557>**

Submitted on 25 Oct 2021

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## **IGF1 levels in children with Severe Acute Malnutrition after Nutritional Recovery: a Good Predictor for Children's Long-term Health Status**

Thi-Phuong-Thao PHAM<sup>1,2</sup>, Didier RAOULT<sup>1,2</sup>, Matthieu MILLION<sup>1,2,\*</sup>

<sup>1</sup>IHU-Méditerranée Infection, Marseille, France

<sup>2</sup>Aix Marseille Univ, IRD, APHM, MEPHI, Marseille, France

\*Corresponding author

**E-mail:** matthieumillion@gmail.com

The use of ready-to-use therapeutic foods (RUTF) have successfully reduced mortality in children with severe acute malnutrition (SAM), but the incomplete restoration including growth retardation (or stunting) and persistent immaturity of gut microbiota (1) and the long-term consequences such as increased risk of developing obesity, type 2 diabetes, cardiopathies (2) remain a major challenge for children's health worldwide.

The metabolomics study of Bourdon C, et al. (2) reported in *EBioMedicine* has characterized the metabolite profiles of SAM survivors from the "ChroSAM cohort" (3) and showed that children who survived from early childhood SAM had a similar profile to control groups 7 years after treatment. This is the first quantitative metabolomics study of long-term consequences in SAM survivors. They indicated that early childhood SAM could mainly impact on growth and muscle mass, rather than inducing persistent metabolic derangement.

In addition, Bourdon et al. (2) also marked the association between stunting and low levels of circulating IGF1 (Insulin-like Growth Factor 1). The stunted SAM survivors had even lower circulating IGF1 levels than other stunted children from similar low socio-economic communities (2). The findings are consistent with those of previous studies that observed the low levels of IGF1 in hospitalized children suffering from protein and energy malnutrition; the values were even lower in marasmus than in kwashiorkor children (4). After

the nutritional rehabilitation, IGF1 increased significantly in both children with kwashiorkor and marasmus but the values were still lower than in healthy children 14 days post-treatment (4). Moreover, low levels of IGF1 in early life is known to be associated with late risk of NCDs (Non-Communicable Diseases), particularly diabetes (2). It has recently been shown that IGF1 was modulated by microbiota, especially gut resident-bacteria-derived SCFAs (acetate, butyrate and propionate) (5). Indeed, numerous bacterial species can produce SCFAs such as *Akkermansia muciniphila*, *Faecalibacterium prausnitzii*, *Ruminococcus* spp., *Roseburia* spp., *Eubacterium* spp. This suggests that these bacteria could be useful in the treatment of SAM as potential probiotics (6). Strikingly, loss of fecal butyrate has been associated with mortality among children with SAM suggesting the global collapse of gut microbiota mutualism in such a situation (7).

Several studies, including ours (1,6,8,9,10) have demonstrated the link between microbiota alteration (including bacterial diversity depletion, increased gut redox, a massive invasion of pathogens and the missing of benefit taxa) with SAM. Undoubtedly, diet components have a strong influence in shaping the gut microbiota and conversely, the gut microbiota contributes to nutrients uptake. Thus, the transient or persisting alteration of gut microbiota during and perhaps after SAM may induce persisting low levels of IGF1, and the physical growth retardation (or stunting), even after nutritional recovery. However, the mechanisms by which microbiota induces IGF-1 production and whether microbiota-mediated IGF-1 production is dependent on growth hormone is still under investigation (5).

In the study, Bourdon et al. (2) choose the control group as children from similar low socio-economic communities, who were also stunted and have a history of poor health. In relation to the selection of control children, further sub-group analysis or exploration of interactions could be limited. Another limitation of the study is the lack of birth weight record which is also known as a risk factor for developing NCDs in later life.

Overall, Bourdon et al.'s exhaustive work through the period of 7 years follow-up children after admission, the minimal loss-to-follow-up, and the use of both sibling and community controls make this study particularly interesting. Their results not only provided a more comprehensive view of metabolic changes in long-term SAM survivors but also generated new directions for effective treatment response and for preventive medicine (potential marker IGF1 and its relationship with gut microbiota). Elucidating this relationship may contribute to the improvement of long-term care of SAM survivors.

## **Disclosure**

The authors declared no conflicts of interest.

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