

### **Evidence before this study**

Earlier and more reliable conditions (i.e. heart defects, vision problems, hearing loss, infections, hypothyroidism, blood disorders, hypotonia, Alzheimer's disease) in Down's syndrome (DS) have a direct impact on the design of relative preventive trials, which are impeded by the wide range in severity of the intellectual disability and the difficulty in standardising the onset of symptomatic diseases in this population. However, there is a paucity of standardised assessment protocols with established validity. Sensitive and specific biomarkers of associated diseases would improve its early diagnosis in those individuals. This makes early diagnosis of diseases in children with DS a major diagnostic challenge that could be improved by defining new specific disease biomarkers. Additionally, the targeted approach to nutritional intervention is expected to affect the results obtained. Hence, we searched PubMed on January 7, 2020, for research studies on established biomarkers in people with DS using the search terms “biomarker” AND “Down's syndrome” “biochemical” AND (“minerals” or “diagnosis”).

For decades, nutritional interventions have been popular but controversial treatments for DS. Clinical trials of nutritional supplements have had methodological problems and have shown no efficacy. Theoretically, antioxidants and some minerals may improve some of the clinical problems associated with DS. The medication that has received the most interest for the treatment of cognitive problems in DS is piracetam. The goal was to screen the biochemistry of children with Down syndrome and their foods.

### **Added value of this study**

Can nutritional supplements benefit individuals with Down syndrome? Novel advances in nutritional science and how those innovations are used to positively impact the biochemistry of DS has been investigated.

This is, to our knowledge, the first study to assess the relationship between the nutritional system consumed by those individuals and biomarkers which have superior sensitivity and

specificity. Besides, the biochemical concentrations in biofluids were weakly correlated. The current demonstration showed that nutritional deficiencies in DS children were originated from biochemical imbalances in their physiology and that not always food fortification, supplementation, or/and unplanned food with DS are proper strategies. We reached to an important conclusion that DS patients need to take away foods that are initiating intestinal permeability and heal and seal the gut lining since they are in need to ensure that the body and brain are protected from inflammation and excessive mucus production. Besides, body composition is an essential indicator of DS child's nutritional status.

### **Implications of all the available evidence**

The most clinically relevant finding of this study is the excellent diagnostic performance of nutrients participation in metabolism which might enable a shift in the management of diagnosing symptomatic diseases in people with DS, because they support a biological-based diagnosis. Such an outcome would be of paramount importance in clinical practice and for the development of specific therapeutic intervention. Therefore, biological-based diagnosis could be used for earlier and more reliable diagnosis considering the design of preventive trials in preclinical phases.