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LETTER TO THE EDITOR

Nutritional Status in Agammaglobulinemia: An Italian Multicenter Study

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To the Editor,

Although primary antibody deficiencies may be associated with undernutrition, there is just one published study on the nutritional status of patients with primary immunodeficiencies [1]. Kouhkan et al. studied 38 patients with different primary immunodeficiencies and showed that 21 % of them were underweight, 8 % overweight and 3 % obese [1].

Between April 2012 and November 2014, we evaluated the nutritional status of 73 patients (71 males) with X-linked (XLA, n = 67) or autosomal recessive agammaglobulinemia

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(ARA, n= 6) followed at 14 Centers of the Italian Primary Immunodeficiency Network (IPINet). All patients were undergoing appropriate immunoglobulin replacement therapy according to international guidelines [2]. In ARA patients, mutations in genes encoding for μ heavy chain, Igα, Igβ and λ5 were evaluated. The 2 ARA girls had the same homozygous mutation for the μ heavy chain and the 4 ARA boys had no detectable mutation.

Weight, length (< 2 years of age) or height (≥ 2 years of age) were measured and body mass index (BMI) was calculated [3]. Standard deviations scores (SDS) of weight-for-age, length-for-age, height-for-age and BMI-for-age were calculated using the World Health Organization (WHO) reference data [4]. For patients aged 0 to 19 years, values of BMI SDS < −2.0, − 2.0 to 1.0, > 1.0 to 2.0, and >2.0 were used to diagnose underweight, normal weight, overweight and obesity, respectively. For patients aged >19 years, BMI was evaluated according to the WHO guidelines for adults [3]. Stunting was defined as a length or height < 2.0 SDS [4].

The anthropometric measurements of the patients at the study visit are given in Table 1. Blood samples were collected in order to evaluate IGF-1, prealbumin, albumin, transferrin, glucose, insulin, total cholesterol, HDL cholesterol, LDL cholesterol, apolipoprotein A, apolipoprotein B and triglycerides.

Among the 41 patients aged >19 years at the study visit, 3 (7 %) were underweight, 26 (63 %) had a normal weight, 11 (27 %) were overweight and 1 (2 %) was obese. The first undernourished patient had no complications. The second undernourished patient had chronic obstructive pulmonary disease (COPD) and chronic sinusitis. The third undernourished patient had severe thinness (BMI < 16.0 kg/m2), anemia and hypoalbuminemia (3.1 mg/dl), and was treated with parenteral nutrition. Evidence of a chronic inflammatory infiltrate at jejunal biopsy in this patient suggested infection with Microsporidium, which was treated following standard guidelines. The hypoalbuminemia of this patient was the only instance of an altered laboratory marker of nutritional status identified during the study. In fact all other nutritional indexes were within the normal limits according to the different laboratory settings. Among the 32 patients aged ≤19 years at the study visit,1 (3 %) was underweight, 15 (47 %) had a normal weight, 8 (25 %) were overweight and 8 (25 %) were obese. Moreover, 3 of them were (9 %) stunted. No other patient reported intestinal malabsorption and/or gastrointestinal problems. All patients had no evidence of endocrine or pubertal disease.

COPD, the most frequent complication of agammaglobulinemia, was present in 22 (30 %) of our 73 patients, mostly in those aged ≥19 years. Its appearance would be independent of nutritional status. For 44 patients, we were able to retrieve the anthropometric measurements performed when agammaglobulinemia was diagnosed and compared them with the anthropometric measurements performed at the study time. The median duration of follow-up for these 44 patients was 17 years.

Table 1 Anthropometric measurements at the study visit

	N	Level	Value
Age (years), mean (SD)	73		22 (11)
Weight (kg), mean (SD)	73		61.1 (21.2)
Weight-for-age (SDS WHO), mean (SD)	11		0.88 (0.95)
Height (m), mean (SD)	72		1.63 (0.21)
Height-for-age (SDS WHO), mean (SD)	31		0.08 (1.10)
Length (m), mean (SD)	1		0.86 (NA)
Length-for-age (SDS WHO), mean (SD)	1		0.5 (NA)
BMI (kg/m2), mean (SD)	73		22.5 (4.7)
BMI-for-age (SDS WHO)	32		0.90 (1.35)
BMI status (WHO), N (%)	73	Underweight	4 (5 %)
		Normal weight	41 (56 %)
		Overweight	19 (26 %)
		Obese	9 (12 %)

SDS of weight-for-age available from 0 to 10 years of age; SDS of length-for-age available from 0 to 2 years of age; SDS of height-for-age available from 2 to 19 years of age; SDS of BMI-for-age available from 0 to 19 years of age.

Abbreviations: SD = standard deviation; SDS = standard deviation scores: WHO = World Health Organization; NA = not available

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Among the 6 patients that were underweight at diagnosis, 1 was underweight, 3 were normal-weight, 2 were overweight and none was obese at the study time. Among the 18 patients who were normal-weight at diagnosis, 1 was underweight, 13 were normal-weight, 3 were overweight, and 1 was obese at the study time. Among the 17 patients who were overweight at diagnosis, 1 was underweight, 8 were normal-weight, 6 were overweight and 2 were obese at the study time. Among the 3 patients who were obese at diagnosis, none was underweight, 1 was normal-weight, 2 were overweight, and none was obese at the study time.

In this multi-center study of XLA and ARA patients, overweight and obesity (38 %) were much more common than undernutrition (5 %). The low frequency of undernutrition is at least partly attributable to the appropriate immunoglobulin replacement therapy, which is known to decrease the occurrence of infectious disease and to increase the life expectancy. The median age at the diagnosis of immunodeficiency was in fact 2 years, with 3 cases diagnosed prenatally. Early diagnosis is the gold standard for primary immunodeficiencies, with the aim to start therapy as soon as possible in order to reduce complications and improve quality of life. A limitation of the present study is the lack of a control group, due to the difficulty of finding healthy children similar to XLA and ARA patients for age and other features when many tertiary care centers are involved. Although a direct comparison with population data is unwarranted because our study was performed in subjects with a rare disease followed by tertiary care centers, it is certainly of interest that overweight and obesity were nearly as common in young and adult Italian patients with XLA and ARA as they are in the general Italian population [5, 6], but with a trend towards a higher rate of obesity in those patients aged less than 19 years.

In conclusion, the most interesting finding of this study is the unexpected high frequency of apparent overnutrition with excess body weight in a group of XLA and ARA patients. No one displayed enough features justifying the diagnosis of metabolic syndrome.

Low physical activity, partly motivated by an unsubstantiated fear of infection, together with a poor diet and the psychological burden of a chronic illness, may contribute to the risk of overweight and obesity in these patients. During follow-up of XLA and ARA patients a nutritional counseling may be recommended to keep under control the development of risk factors for cardiometabolic disease. Further surveys are needed to confirm our observations in order to better investigate the nutritional status (and the body composition, if possible) in patients with agammaglobulinemia and other primary immunodeficiencies with the aim of improving their quality of life.

Conflict of Interest The Authors declare that they have no conflict of interest.

Compliance with Ethical Standards This study was performed in accordance with the ethical standards of the institutional research committees and with the 1964 Helsinki declaration and its later amendments.

Informed Consent Informed consent was obtained from all individual participants included in the study.

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