Association of cell blood counts and cardiometabolic risk factors among young obese children

To the Editor

I would like to comment on the outstanding extensive study by Kelishadi et al[1] on the association of cell blood counts and cardiometabolic risk factors among young obese children.

First, metabolic syndrome (MS) is not only a serious problem for adults, but it is also afflicting an increasing number of children and adolescents. This syndrome is a predictive risk factor for type 2 diabetes mellitus and cardiovascular diseases. Since there is a familial aggregation of the MS among Iranian families, it is anticipated that pediatric MS will impose a significant health threat, in term of future burden of diabetes mellitus and cardiovascular diseases. Efforts, therefore, must be targeted to minimize that burden.

Second, Kelishadi et al[1] applied the National Cholesterol Education Program Third Adult Treatment Panel (ATP III) modified for age diagnostic criteria to diagnose MS. Some concerns exist considering the precision of that protocol in diagnosing MS in children. The concept of ATP III protocol commonly applied in adults, which is now beginning to be applied to children, differs in terms of the cutoff points used, whether it employs body mass index or waist circumference to define obesity, and the substantial instability of pediatric MS in the short and long term.[2] According to my knowledge, no standardized age and gender Iranian children specific charts are present considering various components of MS, particularly waist circumference and systolic blood pressure. This ultimately will bias the selection of obese children who might fill the required criteria of MS. There is, therefore, a need to standardize eligible criteria for diagnosing MS in children to identify those at greatest risk of future sequelae.

Third, adults with coronary heart diseases were found to have markers of low grade inflammation that are strongly related to MR variables independently of obesity. Such observation has triggered a similar concern for pediatric MS where the conclusion by Kelishadi et al[1] of pro-inflammatory state of MS in obese Iranian children could be reliably added to the same context recently addressed. In a recent Turkish study,[3] the levels of acute phase reactants, as an indicator of inflammation in patients with MS, were assessed. The number of MS components was strongly correlated with serum levels of high sensitivity C-reactive protein, interleukin-6, fibrinogen, uric acid, and leukocyte count. It could be, therefore, postulated that the estimation of serum inflammatory markers in obese children with MS might be regarded as a biochemical screening tool as it could be of help in anticipating cardiovascular risks and in assessing the efficacy of treatment. This definitely necessitates further studies to consider its implication in the clinical settings.

Fourth, though the age group of the studied obese children was 6-12 years, the assumption by Kelishadi et al[1] that most of the studied obese children were prepubertal and, therefore, obviates the effect of puberty on the results and conclusion of their study seems questionable for 2 reasons: 1) The exact age distribution of the studied obese children was not fully addressed by Kelishadi et al.[1] However, the mean age of 8.8±2.7 years in the studied children (**Table 1**) perpetuates the concern that those near puberty could constitute a significant proportion of the total studied children. 2) Puberty generally begins between age 8 and 14 years. Various studies have disclosed that sex hormones play a pivotal role in the modulation of insulin resistance and MS. In a recent Turkish study,[4] the relation between puberty, sex hormones, insulin resistance, and lipid levels in children was assessed in prepubertal versus adolescent girls and boys. Among prepubertal boys, estradiol was significantly associated with increased log homeostasis model assessment-estimated insulin resistance (HOMA-IR) and insulin levels. Testosterone was associated with increased high density lipoprotein-cholesterol (HDL-C) levels among prepubertal boys. Among adolescent girls, sex hormone binding globulin (SHBG) was significantly associated with decreased HOMA-IR and insulin levels. SHBG was also related to the increased HDL-C levels among prepubertal and adolescent girls. The study concluded that sex hormone levels and SHBG have important effects on HDL-C and insulin resistance among children and adolescents. Thus, the role of puberty in modulating the results and conclusion installed by Kelishadi et al[1] must not be overlooked.

Fifth, efforts are continuously directed to find a simple clinical tool for assessing the risk of MS during routine health checkups. Kelishadi et al[1] addressed that with the exception of the waist to height ratio (WHR), the anthropometric measurements of body mass index (BMI), waist circumference (WC), and hip circumference (HC) had statistically significant correlations with the components of MS (p<0.001) (Table 3), thus, indicating their reliabilities to be considered as important clinical tools for assessing the risk of MS in obese Iranian children. This obviously requires construction of age and gender specific anthropometric charts considering various genetic, ethnic, nutritional, and cultural

backgrounds of Iranian community. There is nowadays an increasing interest that WHR could be a better and more sensitive clinical marker to evaluate the clustering of coronary risk factors in children.[5]

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Reply from the Author

In reply to the comments of Prof. Mahmood D. Al-Mendalawi to our paper entitled "Association of cell blood counts and cardiometabolic risk factors among young obese children".[1] First of all I should forward my sincere thanks to his kind interest to this paper.

Some items should be clarified in response to his valuable comments: 1) He referred to the importance of the metabolic syndrome (MetS) in the pediatric age group; this is exactly the message of our paper, we highlighted the importance of MetS and its complications, as the pro-inflammatory state, from early life. The crucial importance of the pediatric MetS for developing countries is underscored.[6] 2) He emphasized on the high prevalence of MetS in Iranian adults and children; I totally agree with his valuable comment, as I have previously described it in the first national reports from Iran about the high prevalence of MetS in Iranian adults[7] and children.[8] 3) He pointed to the use of the modified ATP III definition in this study; his comment is well respected, however as the definition provided by the International Diabetes Federation for the pediatric MetS[5] does not include children with less than 10 years of age, we used this definition as used in many previous studies.[8,10] 4) He pointed that "According to my knowledge, no standardized age and gender Iranian children specific charts are present considering various components of MS, particularly waist circumference and systolic blood pressure." The age- and gender- specific percentiles are published for waist circumference,[11] blood pressure[12] and lipid profile.[13] These values are also compared with other countries.[14,15] 5) He explained about the association of low grade inflammation with the components of the metabolic syndrome, independent of obesity. I totally agree with him, our recent trial is a confirmatory evidence.[16] 6) He stated about the influence of puberty on the findings, he also referred to the mean age of participants (8.8±2.7 years), consistent with his suggestion, we have acknowledged the influence of puberty in the study limitations (before the final conclusion). However, as many studies in Iran, including our study in Isfahan city[17] puberty have shown the mean age of puberty is higher than the mean age of the participants of the current study. 7) He suggested about the use of waist-to-height ratio, and referred once more about the necessity of constructing reference curves for anthropometric indices of Iranian children. As stated above, we have provided specific reference curves for Iranian children; moreover we have documented the appropriateness of the waist-to-height ratio for Iranian children and adolescents.[18]

Once more, I forward my gratitude for the interest of Prof. Mahmood Dhahir Al-Mendalawi to our study.

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