

Serum Albumin Levels: A Simple Answer to a Complex Problem? Are We on the Right Track of Assessing Metabolic Syndrome?

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Serum albumin makes up a major portion of circulating proteins in our body. Serum albumin level is closely linked to the body's nutritional (malnutrition/overnutrition) and inflammatory status. Insulin resistance is the main pathogenetic mechanism underlying metabolic syndrome, a condition that is associated with obesity and chronic vascular inflammation [1]. Several studies have focused on the association between serum albumin level and factors/diseases related to metabolic syndrome (insulin resistance, diabetes, and cardiovascular disease).

In this issue, Bae et al. [2] reported that a high serum albumin level is associated with insulin resistance, but they failed to show a significant correlation between serum albumin level and the development of diabetes in a longitudinal follow-up. The authors analyzed data for a large cohort from a health promotion center located in an urban area, Seoul, South Korea. Cho et al. [3] also reported a positive relationship between serum albumin level and metabolic syndrome, although they studied a healthy adult population located in a rural area.

Bae et al. [2] explained that the positive association between serum albumin level and insulin resistance might be a consequence of increased albumin production in the liver under insulin-resistant conditions. Insulin resistance goes hand-in-hand with increased insulin levels and insulin is known to

stimulate albumin production in hepatocytes [4]. On the other hand, some reports have shown that albumin has a cardioprotective effect [5,6] that may be due to albumin acting as an antioxidant and a protective protein against chronic inflammation [1,7]. Albumin is a main constituent of serum proteins and, owing to its presence in vast amounts, it accounts for approximately 80% of thiol's antioxidant effect in the body [8]. The free ³⁴cysteine (³⁴Cys) residue of albumin reacts with reactive oxygen species, generating two reversible intermediate derivatives, and finally sulfonic-albumin, which is susceptible to enzymatic digestion compared with the nonoxidized counter molecule [9]. Therefore, serum albumin seems to have complicated effects on metabolic syndrome and related factors/diseases.

Several reports have shown a negative correlation between serum albumin level and cardiovascular risk factors, as well as cardiovascular disease [10,11]. However, there have also been conflicting reports that serum albumin level is not associated with atherosclerosis as evaluated by carotid intima media thickness [12]. To make matters even more difficult to interpret, there are also papers demonstrating positive relationships between serum albumin level and vascular dysfunction as measured by pulse wave velocity [6], as well as early carotid atherosclerosis [5]. These differences in findings between pa-

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pers demonstrate a possible complex mechanism that underlies the interaction between albumin's antioxidant capacities. More specifically, the antioxidant effect of albumin is not solely dependent on the amount of serum albumin *per se*, but also on the oxidative status of albumin. Previous papers have demonstrated that the antioxidant capacity of albumin is decreased in various disease conditions, such as diabetes [13], and in patients on hemodialysis [14]. Furthermore, insulin signaling is altered under insulin-resistant conditions and insulin levels decrease in the later stages of diabetes. Therefore, the answer may lie in the total antioxidant capacity of serum albumin and not the total amount of albumin itself. In this context, a plausible explanation of the findings by Bae et al. [2] in this issue of the journal would be that the increase in serum albumin level may be because of a compensatory increase in albumin production that is due to a decrease in the antioxidant effects of albumin in an insulin-resistant state.

What, then, is the main message of the study by Bae et al. [2]? Serum albumin is relatively simple to measure and is included in every admission panel throughout Korea. Testing is inexpensive and does not need fasting for proper measurement, which certainly makes it more comfortable for patients visiting the hospital. Therefore, Bae et al. [2] are to be congratulated for re-emphasizing the clinical utility of a simple biomarker in evaluating a patient's complex metabolic status under stable metabolic conditions. Although the study fails to show a positive correlation between the development of diabetes and serum albumin level, a larger population or a longer follow-up period may be all that is needed. The medical society certainly awaits the results of such investigations.

And what remains to be investigated? First, the findings urge a large-scale population analysis on whether albumin level in a healthy population may serve as a good surrogate marker for future cardiovascular events. Because there are data in Western countries demonstrating that serum albumin level is associated with cardiovascular outcomes [10,15], a separate study in Asia, and particularly Korea, is definitely needed. This is important, especially considering that the pathogenetic mechanism leading to diabetes may be influenced by several factors, including genetic factors. Second, the total amount of albumin may not accurately reflect the total antioxidant capability, as discussed earlier. The data of Bae et al. [2] should also be supported by a thorough, mechanistic, *in vitro* analysis. Third, is the antioxidant property of albumin reversed with the improvement of a patient's metabolic status? This remains a crucial step to providing a definite answer as to whether albumin

is really a good marker.

In conclusion, Bae et al. [2] have reinforced an important positive association between serum albumin level and parameters of insulin resistance in healthy Korean adults. In addition, even though they did not show a significant association between albumin level and diabetes development, the report is one of the first longitudinal studies to evaluate this issue. Further investigations are needed to demonstrate whether albumin is indeed 'the' important antioxidant in the body and whether it is linked to clinical outcomes. The medical society awaits the answers to these questions.

CONFLICTS OF INTEREST

No potential conflict of interest relevant to this article was reported.

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