

Ischemia-modified albumin must be evaluated as an oxidative stress marker together with albumin and bilirubin in individuals with acute appendicitis

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We recently read the article "Correlation between the serum and tissue levels of oxidative stress markers and the extent of inflammation in acute appendicitis" by Dumlu et al. with great interest (1). The study's primary objective was to determine serum and tissue levels of oxidative/antioxidative markers in acute appendicitis. The authors concluded that oxidative/antioxidative imbalance plays a pathological role in acute appendicitis. The authors should be praised for their study design, objectives, methodology and results. Nonetheless, we unearthed several interesting points during our reading of the article.

Ischemia-modified albumin (IMA) detection has generated a great deal of interest worldwide. Initially, IMA was examined as a promising but relatively nonspecific marker of myocardial ischemia (2). Recently, IMA has been widely accepted as a marker of oxidative stress in several pathological states, including acute appendicitis (1-3). Notably, Dumlu et al. measured IMA using an albumin cobalt binding (ACB) assay and reported the results in absorbance units (ABSU). In principle, the ACB assay involves the binding of cobalt to albumin protein. In cases involving oxidative stress, the ability of albumin to bind cobalt decreases; as a result, there are greater quantities of unbound free cobalt and therefore elevated IMA values (2). Thus, the ACB assay and the IMA results it produces are sensitive to changes in serum albumin concentrations. Interestingly, even within the physiological range of albumin levels (35–45 g/L), there is a strong negative association between albumin and IMA; in particular, a change of 1 g/L in albumin produces an opposite change of 2.6% in IMA (4). Importantly, appendicitis is associated with changes in serum albumin (5). Given prior evidence indicating that serum albumin changes in acute appendicitis (5-6) and that albumin levels can affect the estimation of IMA (4,7), it is extremely important to provide serum albumin levels and IMA values that are corrected for albumin interference, as previously reported (7). This evidence could strongly suggest the need to evaluate IMA as an oxidative stress marker in

combination with albumin in individuals with acute appendicitis.

Furthermore, albumin is known to bind with and transport bilirubin in circulation. Recently, a significant association between IMA and bilirubin has been reported (8). Literature findings have demonstrated that in cases of appendicitis and appendiceal perforation, serum bilirubin is significantly increased; thus, hyperbilirubinemia has been suggested as an independent marker of these conditions. Hyperbilirubinemia has exhibited better sensitivity for acute appendicitis than white cell count or C-reactive protein level, and it has been suggested that bilirubin evaluation should be included in the assessment of appendicitis patients (9). Therefore, we speculate that it is necessary to examine hyperbilirubinemia in appendicitis patients because elevated bilirubin levels could partially explain IMA differences among study groups.

Thus, it would have been interesting if Dumlu et al. had evaluated serum levels of albumin and bilirubin because it is highly plausible that changes in these levels could have influenced their IMA results. The following important reasons also support the need to study albumin and bilirubin. 1) Preoperative total bilirubin is positively associated with morbidity; in contrast, preoperative albumin is negatively associated with morbidity (10). 2) Preoperative hypoalbuminemia is an independent risk factor for the development of surgical site infection following gastrointestinal surgery (11). 3) Hypoalbuminemic patients have significantly longer hospital stays than other patients (12). 4) Serum albumin measurements are regarded as objective markers of nutritional status but also reflect ongoing acute inflammatory processes and immunological compromise (12). 5) Serum albumin serves as an important antioxidant (13). 6) Because albumin is an acute phase protein, albumin levels reflect the activity of inflammatory cytokines (5).

In their results section, Dumlu et al. reported that they had found no significant differences between the preoperative and postoperative levels of any serum parameters ($p > 0.05$ for all parameters). However, Table 3 indicates that there was a significant difference between the preoperative and postoperative levels of advanced oxidized protein products (AOPP) ($p = 0.039$). This apparent contradiction should have been clearly addressed. The authors used the Alvarado score as a diagnostic tool for acute appendicitis because this score can predict the presence and extent of appendicitis. Similarly, it has been suggested that oxidative/antioxidative



imbalances influence the degree of inflammation in acute appendicitis and that the Alvarado score can be used to predict the severity of inflammation. Although the authors did address correlations between serum and tissue parameters, we feel that an examination of the correlations between oxidative stress parameters and the Alvarado score would produce important findings.

Finally, a question that must be asked is if the authors considered determining whether the age difference between the control group (19–64 yrs) and the appendicitis group (17–73 yrs; mean \pm SD: 31.4 \pm 12.06 yrs) was significant. The mean age for the control group was not mentioned. This issue is important because age per se plays a significant role in the generation of oxidative stress. We believe that the aforementioned issues must be addressed in future studies of IMA in acute appendicitis.

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