Dear Editor,

Enclosed please find the pre-submission inquiry manuscript entitled as “**Circulating serum amyloid A, hs-CRP and Vitamin D levels in postmenopausal osteoporosis**” for publication in your prestigious journal. Osteoporosis and its related fractures are global health issues. Women in menopausal phase are at a greater risk (1). Vitamin D deficiency has worldwide prevalence. Recently, its diagnosis and treatment have become a global concern (2, 3).

Although there are growing number of studies, indicating vitamin D deficiency as a risk factor for osteoporosis (4-6), the association between vitamin D serum level and bone mineral density as the most reliable diagnostic criteria for osteoporosis remains to be confirmed (7). Even though some studies have stated the association between low serum 25-OH vitamin D level and low BMD (8, 9), others failed to exhibit this association (10-12). Association between inflammatory biomarkers and osteoporosis is another contradiction that needs to be addressed (13), where some results are supportive (14, 15) while others are against it (16, 17). It still remains to be answered whether or not inflammation is a define etiology for osteoporosis or is it in association with other etiologies (18).

There are also inadequate data about the association of vitamin D level and BMD in postmenopausal osteoporosis (19). Considering the high prevalence of vitamin D deficiency in Iran, a few studies have investigated this association in our population (20), especially in postmenopausal women. Results of Hosseinpanah et al study revealed any association between 25(OH)D and BMD in 245 healthy free-living Iranian postmenopausal women(which can be considered to be in accordance with our results) ([10](#_ENREF_10)). The association between inflammatory biomarkers, vitamin D status and BMD should also be defined in this population.

High-sensitivity CRP (hs-CRP) has the advantage to detect the minimal rise in CRP level, even under 10 mg/L, which is not usually detectable by CRP (21). Recently, serum amyloid A (SAA) is suggested to have great advantage in quantitative assessment of inflammatory responses. In addition, new experimental studies have revealed bone regulatory effects for this member of apoprotein family (saa3) by modulating osteoblasts and osteoclasts function (22). There are merely a few human studies (saa1) that have mainly worked on gene polymorphisms of SAA in special population (23).

In the current study, we compared 25(OH)D, hs-CRP and SAA levels plus their association with BMD in post-menopausal osteoporotic patients in comparison with healthy gender matched controls to evaluate the protective effect of vitamin D and its inflammatory related mechanisms in postmenopausal osteoporosis.

Our results did not confirm the significant role of inflammatory biomarkers in postmenopausal osteoporosis. Beneficial effect of Vitamin D (as shown by Hosseinpanah et al in a larger study (10)), particularly due to its immune-regulatory mechanisms was not proven in the current study. Hence, it can be a hot article for your journal.

 One of our major limitations was to find a postmenopausal population with the exclusion of the above-mentioned confounding factors. Finding non osteoporotic women with the above mentioned criteria was even more complicated. In one hand, wide range of exclusion criteria might have increased the reliability of the results, but it led to a small sample size. Another advantage of this study was considering a control group (to compare the results).

The manuscript has no figure but three tables. The authors have no relevant affiliations with any organization or entity with financial interest in or conflict of interest with subject matters discussed in manuscript. This study was founded by Shiraz University of Medical Sciences (grant No#14345).

 Would you please be kind enough to consider this manuscript for publication in your journal as an “original article? Please do not hesitate to write me should any question arise. We are looking forward to hearing you soon. Thanks in advance for your kindness and support.

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