

Depression linked to bone-thinning in premenopausal women

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Premenopausal women with even mild depression have less bone mass than do their nondepressed peers, a study funded in part by the National Institute of Mental Health (NIMH), part of the National Institutes of Health (NIH), shows. The level of bone loss is at least as high as that associated with recognized risk factors for osteoporosis, including smoking, low calcium intake, and lack of physical activity.

Hip bones, the site of frequent fractures among older people, were among those showing the most thinning in depressed premenopausal women. The reduced bone mass puts them at higher risk of these costly, sometimes fatal fractures and others as they age, the researchers note in the November 26 issue of the *Archives of Internal Medicine*. The report was submitted by Giovanni Cizza, MD, PhD, MHSc, of NIMH and the NIH National Institute of Digestive Disorders and Kidney Diseases (NIDDK); Farideh Eskandari, MD, MHSc, of NIMH; and colleagues.

“Osteoporosis is a silent disease. Too often, the first symptom a clinician sees is when a patient shows up with a broken bone. Now we know that depression can serve as a red flag – that depressed women are more likely than other women to approach menopause already at higher risk of fractures,” said NIMH Deputy Director Richard Nakamura, PhD.

After bone mass reaches its peak in youth, bone-thinning continues throughout life, accelerating after menopause. Preliminary studies had suggested that depression may be a risk factor for lower-than-average bone mass even in young, premenopausal women. Results of the current

study lend considerable weight to those earlier findings. The study's design reduced the possibility that the lower bone mass was linked to factors other than depression.

Study participants included 89 depressed women and 44 nondepressed women, for comparison. All were between 21 and 45 years old and were premenopausal. Except for depression, the two groups were similar in risk factors, including calcium, caffeine, and alcohol intake; smoking; level of physical fitness; use of oral contraceptives; and age of first menstrual period. Both groups were of relatively high socioeconomic status and were well nourished.

One difference was that the depressed women were taking antidepressant medications. A previous study suggested that older adults taking antidepressants called selective serotonin reuptake inhibitors had more bone fractures than others. However, the current study showed that these medications were not linked to low bone mass in premenopausal women.

The researchers found that 17 percent of the depressed women had thinner bone in a vulnerable part of the hip called the femoral neck, compared with 2 percent of those who were not depressed. Low bone mass in the lumbar spine, in the lower back, was found in 20 percent of depressed women, but in only 9 percent of nondepressed women. Bone mass was measured via an X-ray technique called DXA scanning.

There was no significant link between the degree of bone loss and the severity of depression or the cumulative number of depressive episodes, the researchers found. The depressed women had been diagnosed with mild depression and were having, or had recently had, a depressive episode.

“Depression generally isn't on clinicians' radar screens as a major risk

factor for osteoporosis, particularly for premenopausal women. It should be,” said Cizza.

Blood and urine samples also showed that depressed women have imbalances in immune-system substances, including those that produce inflammation, compared to their healthy peers. This additional finding strengthens the case for a suspected link between depression-induced imbalances in the immune system and accelerated bone loss. The blood and urine samples were taken every hour for a full day, providing a truer picture than does less frequent testing, as had been done in previous studies.

The immune-system imbalances may be tied to excess adrenalin, since the part of the nervous system that produces adrenalin is over-active in depressed people. Increased adrenalin can over-stimulate the immune system. Compared to the others, the depressed women in this study had higher levels of immune-system proteins that promote inflammation, and lower levels of those that prevent it.

One of these inflammation-promoting proteins, IL-6, is known to promote bone loss. At the molecular level, bones routinely break down, and their minerals, notably calcium, are reabsorbed into the blood, where they travel throughout the body to perform crucial functions in cells. At the same time, the body builds the bone back up. Imbalances in this normal loop of bone re-absorption and build-up, such as high levels of IL-6, could promote bone loss, the researchers suggest.

Source: National Institute of Mental Health

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