A Henry Ford Hospital study finds women with type 2 diabetes who take a commonly prescribed class of medications to treat insulin resistance may be at a higher risk for developing bone fractures.

After taking a thiazolidinedione (TZD) for one year, women are 50 percent more likely to have a bone fracture than patients not taking TZDs, according to study results. And those at the greatest risk for fractures from TZD use are women older than 65.

"Older women are already at a higher risk of osteoporosis and osteoporosis-related fractures, which might explain why they appeared to be the most affected by TZDs," says study senior author L. Keoki Williams, M.D., MPH, Center for Health Services Research and Department of Internal Medicine at Henry Ford Hospital.

The study - one of the largest groups to examine the longitudinal relationship between TZD use and fractures - appears in this month's issue of The Journal of Clinical Endocrinology & Metabolism.

TZDs such as pioglitazone and rosiglitazone help keep blood glucose levels on target by decreasing insulin resistance and making body tissues more sensitive to insulin's effects. TZDs also cut down on the amount of glucose made by the liver in patients with type 2 diabetes.

But in recent years, TZDs have been linked to bone loss and increasing fracture risk. Complicating matters, type 2 diabetes and insulin use are
also associated with an increased risk for fractures.

To determine the relationship between TZD use and fracture risk in patients with type 2 diabetes, Dr. Williams and his colleagues conducted a retrospective study from Jan. 2, 2000 to May 31, 2007 of 19,070 Henry Ford patients. Among the study group, 9,620 were women and 9,450 were men.

During the study period, 4,511 patients had at least one prescription fill for a TZD. The researchers used electronically maintained medical claims data to identify non-traumatic bone fractures. The increased risk in women appeared after approximately one year of TZD use.

The location of the fractures in this group also was unique. Typically, osteoporosis-related fractures involve the vertebra and hip. This study, however, found TZD use in women to be associated with fractures of the upper extremity and distal lower extremity. Similar findings were observed in treated women older than 65, who were shown to have a 70 percent increased risk for developing fractures. Men, regardless of age, were not at an increased risk for fractures.

"Although two recent studies suggest that men may also be at increased risk for fractures after TZD exposure, we did not observe this association for men, despite having nearly equal numbers of men and women in our study," says study co-author Zeina A. Habib, M.D.

African-American race-ethnicity was protective for fractures when compared with other race-ethnic groups, which were predominately Caucasian.

"Fractures are just one of a growing number of problems associated with these medications. Henry Ford and other researchers have previously found that this class of medications also can increase risk of congestive
heart failure hospitalization," says Dr. Williams.

Dr. Williams notes that there are other medication options available to treat insulin resistance in patients with type 2 diabetes.

"TZDs may put some patients at increased risk for other health issues, and I encourage patients to talk with their physician about other suitable options," says Dr. Williams. "If the physician feels the patient should be placed on a TZD, routine screening for bone loss and prophylactic therapy to prevent bone loss and fractures may also be needed."

**More information:** "Thiazolidinedione Use and the Longitudinal Risk of Fractures in Patients with Type 2 Diabetes Mellitus." The Journal of Clinical Endocrinology & Metabolism.

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