Research Article

A Case Control Study on the Incidence and Prevalence of Hip Fracture in Association with Hypoglycemic Drugs Among Type II Diabetic Patients in a Major Trauma Care Center

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ABSTRACT

Background: Type II DM is a common metabolic disorder with increasing prevalence throughout the world. There is growing evidence indicating the effects of medications for diabetes on bone metabolism and fracture risk. More research is required to know the overall impact of these medications on bone health. **Aim:** To determine the incidence and prevalence of hip fracture in association with hypoglycemic drugs among Type II DM patients in major trauma care center. **Objectives:** To evaluate and compare the incidence and prevalence of hip fracture, the effect of hypoglycemic drugs on bone metabolism and fracture risk as well as the future probability of hip fracture risk in diabetes patients taking hypoglycemic drugs. **Methodology:** A case-control study was conducted with a sample size of 250 patients which included 95 cases and 155 control subjects enrolled for a period of 6 months in a major trauma care center. Subjects were assessed for future hip fracture risk within 10 years using WHO FRAX Score. Odds ratio (OR) were calculated using Fisher's Exact Test and statistical testing was performed at 0.05% level of significance with 95% CI. **Results:** Type II DM patients taking hypoglycemic drugs were associated with increased risk of hip fracture (odds ratio [OR] = 2.97). Incidence (19.2%) and prevalence (60%) of hip fractures was higher in patients taking hypoglycemic drugs than the incidence (14.8%) and prevalence (40%) of those who were not taking the drug. **Conclusion:** Hip fracture incidence in Type II DM patients taking hypoglycemic drug is higher than the patients who were not taking the drugs. FRAX tool has been proved to be helpful in preventing future incidents.

Key words: Type II DM, Hypoglycemic, Incidence, Prevalence, Hip fracture.

INTRODUCTION

Type II DM accounts for more than 90% of the cases of diabetes. Pharmacological treatment of Type II DM mainly includes insulin analogues and oral hypoglycemic drugs (secretagogues).[1] Hypoglycemic drugs may alter metabolism of bone and affect fracture risk affect bone metabolism and influence fracture risk in number of ways which includes bone turn over increase as well as fragility of skeletal bone along with causing deficit in insulin anabolic effects in insulin resistant conditions. It aids to the falling risk because of states and by augmenting the risk of falling due to hypoglycemic episodes.[2] Hip fracture or femoral fracture mainly affects the elderly people which comprise a population that is highly vulnerable to accidents and diseases and to falls in particular. In developed countries hip fracture is one of majorly faced health problems. There are two types of fractures called as neck of femur (intracapsular) and intertrochanteric fracture (extra capsular). Clinical features as for fractures of neck of femur, the patient is brought in with the history of a fall or road

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accident, followed by pain in the region of groin and inability to move their leg.[3]

Fractures associated with thiazolidinediones were first reported in 2006, as an adverse outcome in the ADOPT Trial, a large, double blind randomized controlled study comparing the glycemic durability in patients with Type II DM receiving monotherapy with rosiglitazone, metformin or glyburide.[4] Canagliflozin was showed to have the increased risk fractures among hypoglycemic drugs according to FDA. The health care providers were warned highly for this reason thereby to consider all the factors contributing to it even before initiating the medication.[5]

In recent years large number of oral and injectable medications has been made available for the treatment of Type II DM. Fracture risk is increased in Type II DM but there is a lack of good quality studies comparing effects on bone with hypoglycemic agents. Hypoglycemic drugs even then shows differences in their effects on bone heath. According to various randomized clinical trials it can be suggested that instead of glitazones, metformin and sulphonyl ureas could be chosen while considering bone health. In converse, metformin and sulphonyl ureas may encounter negative bone effects of diabetes since the patients treated with them are found to be in less risk than the others. Many interactions between bone and glucose metabolism have been reported which include osteocalcin, Wnt signaling and insulin growth factors. Osteocalcin is known to show a positive favorable effect on bone metabolism.[6] Hence more researches are necessary to elucidate the mechanism of hypoglycemic drugs on health of bone.[7] Women who are on hypoglycemic medication are found to be under less risk of hip fracture than those without having the disease.[8] In order to identify subjects who are prone to hip fracture risk, a web-based algorithm was designed to estimate the 10-year probability. It gives an idea of fractures which are either osteoporosis related or other hip fractures. This assessment tool is called FRAX through which fracture risk is assessed based on easily available clinical factors, bone mineral density and gender.[9-11] This tool was used in the study to find out the incidence and prevalence of fractures in hip region in those patients taking hypoglycemic drugs.

MATERIALS AND METHODS

Methodology

A case-control study was conducted to determine the incidence and prevalence of hip fracture in association with hypoglycemic drug among Type II DM patients. It included both male and female above 35 years of age, patients admitted for maximum seven days, either IT or NOF. Excluded criteria were pregnant women, road traffic accident cases and major trauma patients. Total sample (n=250) was enrolled for a period of 6 months from February 2017 – July 2017 in Ganga Medical Care and Hospital Pvt (Ltd) Coimbatore, Tamil Nadu. A well-structured data collection was used for the sampling which included Patient Demographics (Age, gender, BMI), diagnosis/ type of fracture, past medical and medication history, social status, menstrual status, laboratory findings, nature of fall, DM or Non DM patient and diabetic profile. Subjects were divided into case and control groups. Case group included subjects identified with hip fracture as the outcome whereas control included subjects without hip fracture as the outcome. Exposure for case as well as control groups included the presence and absence of Type II DM patients with and without taking hypoglycemic drugs, respectively. Both the groups were compared for their age, gender, body mass index, social habits, menstrual history, co morbidities and other drug use. Their risk in the hip fracture incidence was noted. Diabetic history such as duration of disease, anti-diabetic drug use, its dose and frequency were evaluated to determine its role in incidence and prevalence of hip fracture among Type II DM patients. Subjects were also assessed for future hip fracture risk within 10 years as part of clinical intervention to prevent secondary fracture by using WHO FRAX Score. Those who were at higher secondary fracture risk were provided with appropriate counseling regarding their disease state, lifestyle modification, fall prevention strategies and medication use.

Statistical Analysis

The information collected from case and control groups were entered in the MS Excel sheet. For the patients on risk of hip fracture and taking hypoglycemic drugs as well as not on hypoglycemic drugs among Type II DM group and non-Type II DM group were obtained using Fisher's Exact Test. Statistical testing was performed at 0.05% level of significance with 95% CI.

Incidence of hip fracture in patients takindg hypoglycemic drug was calculated by

$$= \frac{\text{Number of patients with new hip fracture}}{\text{Total number of patients}} \times 100$$

Prevalence of hip fracture in patients taking hypoglycemic drug was calculated by

$$= \frac{\text{Number of all cases with hip fracture}}{\text{Total number of patients}} \times 100$$

RESULTS AND DISCUSSION

Out of total patients (*n*=250), 95 (38%) were case (with hip fracture) while 55 (62%) were control (without hip fracture) subjects. The case group comprised of 60% diabetic subjects taking hypoglycemic drugs and 40% non-diabetic subjects without taking hypoglycemic drugs in case. The control group comprised of 33.54% diabetic subjects taking hypoglycemic drugs and 66.45% non-diabetic subjects without taking hypoglycemic drugs. It was demonstrated that the higher number of subjects was found between the age group of 66-80 years (43.15%) among subjected with hip fracture and in those subjects without hip fracture (40.64%) which highly matched with the Johnell *et al.*[12] Data showing that hip fractures occur commonly in older patients. It was revealed that the number of females (54.73%) was higher than the number of males (45.26%) among subjects with hip fracture. Thus, females had higher risk of hip fracture than males on comparing to the control group (Wallander *et al.*)[13] Increased rate of hip fracture is in women which could be because of osteoporosis found commonly after attaining the menopausal age because of hormonal changes.

Highest number of subjects had an increased HbA1c levels seen in the range of 6-8% among hip fracture (38.59%) and without hip fracture (36.53%). It showed that patients with glycated hemoglobin 6% had an increased risk to cause hip fracture which was similarly highlighted in the Tsai *et al.* and Starup Linde J *et al.*[14-15]

A higher usage of calcium channel blockers as well as anticonvulsants was found in both the subjects with hip fracture as well as without hip fracture to treat their co morbidities. It indicated that these drugs influenced in hip fracture risk through their detrimental effects over bone. Lee *et al.*[16] Showed high consistency in their findings that anti-convulsant drugs may induce hip fractures by decreasing bone mineral density.

Hip fracture was seen more in subjects taking Biguanides (33.3%) as well as combination of Biguanides and Sulphonyl urea (19.29%) because in this study Biguanides along with Sulphonyl ureas were observed to be used higher in subjects with Type II DM being the first line drugs. Vestergaard *et al.*[17] Reported a decreased fracture risk in Metformin and Sulfonylurea users as well as neutral outcomes with the use of Metformin and Sulfonylurea as in few other studies. In this study no effective conclusion was drawn with the use of TZDs but in contrast Bilik *et al.*[18] Confirmed that higher dose of TZD had higher risk and no variation was observed for the effects between Rosiglitazone and Pioglitazone. Thus, it suggests that TZDs show a class effect on fracture risk.

Results indicated that non-diabetes patients had more chances of secondary fractures compared to diabetes patients using FRAX tool. This gives a statement that FRAX tool underestimated major osteoporotic and hip fracture risk in diabetes patients but illustrated good concordance with observed fractures for patients not having diabetes. Study report highly agrees with the data from Kanis J *et al.*[11] Thus, common markers of bone frailty seem unable to detect and predict fractures in diabetes patients.

The overall incidence of hip fracture was found to be 34 per 100 patients. The incidence of hip fracture among diabetes subjects was found to be 19.2 per 100 patients whereas incidence of hip fracture among non-diabetes subjects was found to be 14.8 per 100 patients. (Figure 1)

The study showed that the incidence rate of hip fractures was more in patients on hypoglycemic medication than with those who are not on medication. Further, the overall prevalence of hip fracture was found to be 38%.

The study demonstrated that the higher rate of prevalence of hip fracture was found in subjects taking hypoglycemic drugs (60%) than in subjects not taking hypoglycemic drugs (40%). (Figure 2) The relative risk among subjects taking hypoglycemic drugs and without taking hypoglycemic drugs to cause hip fracture was estimated using Odds Ratio which was found to be significant with P value within the level of significance 0.05. (Table 1)

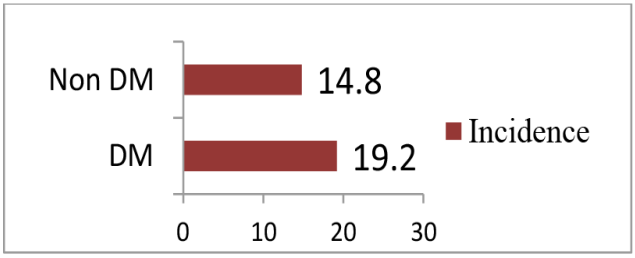

Figure 1: Incidence of hip fracture in patient taking hypoglycemic drugs and not taking hypoglycemic drugs.

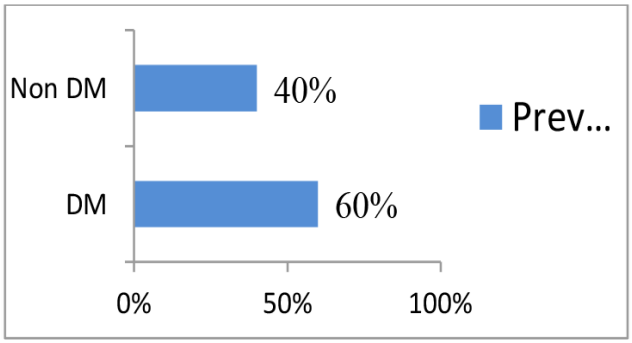

Figure 2: Prevalence of hip fracture in patient taking hypoglycemic drugs and not taking hypoglycemic drugs.

Table 1: Odds ratio for the risk of hip fracture in patients.

	OUTCOME		
EXPOSURE	**YES**	**NO**	**TOTAL**
YES	57	52	109
NO	38	103	141
TOTAL	95	155	250
ODD's RATIO	2.971		
P–VALUE	<0.0001****		
LEVEL OF SIGNIFICANCE	< 0.05		

CONCLUSION

The study finds a conclusion that incidence and prevalence of hip fractures in Type II DM patients taking hypoglycemic medication is higher than those who are not taking the medication. Hypoglycemic drugs used in Type II DM subjects are observed to be highly linked with the hip fracture risks. Therefore it was concluded that hypoglycemic medications are to be prescribed and used with good alert especially in older patients with Type II DM who have high risk for fracture. In this study, FRAX tool helped in evaluating the future probability of hip fracture risk. This assessment technique has also helped to bring awareness in high risk patients thereby preventing fractures.

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CONFLICT OF INTEREST

The authors declare no conflict of interest.

ABBREVIATIONS

FRAX: Fracture Risk Assessment Tool; **T2DM:** Type 2 Diabetes Mellitus; **TZD:** Thiazolidinediones; **IT:** Intertrochanter; **NOF:** Neck of Femur; **FDA:** Food and Drug Administration; **ADOPT:** A Diabetes Outcome Progression Trial; **WHO:** World Health Organization.

SUMMARY

A case-control study was conducted with a sample size of 250 patients. It was found that the incidence and prevalence of hip fractures in Type II DM patients taking hypoglycemic drug is higher than those without taking hypoglycemic drug. Hence concluded that hypoglycemic drugs should be used with caution especially in older patients with Type II DM who have high risk for fracture.

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