Anadolu Psikiyatri Dergisi || ISSN: 1302-6631 || Volume 25; Number 2
https://doi.org/10.5281/zenodo.13309118

Incidence of Drug Induced Osteoporosis in a Tertiary Care Hospital

Taqui Mohammed, Dr. Abdul Ajeed Mohathasim Billah, Dr. M. Swamivelmanickam

Department of Pharmacy, Annamalai University; Department of Pharmacy Practice, Sri Ramachandra Institute of Higher Education and Research (DU); Department of Pharmacy, Annamalai University

Abstract*— Drug-induced osteoporosis is prevalent and has an impact on the prognosis of patients suffering from chronic diseases. The introduction of drugs (Glucocorticoids, Anti-epileptics, Loop diuretics, Anti-depressants, PPI) has changed pharmacological treatment drastically and increase in the adverse events, so drug safety has become increasingly relevant over the past few years. The goal of this study was to determine the prevalence of drug-induced osteoporosis at a tertiary care hospital. 950 patients among those visited to Hospital both outpatient and inpatient departments of General medicine, General surgery, Orthopaedics, Nephrology, Neurology, Psychiatry, Dermatology who meet the inclusion criteria were recruited in the study. Patients prescribed with Glucocorticoids, Anti-depressants, Anti-epileptics, Loop Diuretics and PPI for a minimum duration of 3 months after initiation of therapy were identified and followed (Ia). Patients receiving same class of drugs but along with the prophylactic therapy were identified and followed (Ib). Patients undergone treatment to with drugs such as Glucocorticoids, Anti-epileptics, Anti-depressants, Diuretics, and PPI (Group Ia) had a higher risk of osteoporosis than those who were not (Group Ib). This was confirmed by calculating the relative risk which found to be 1.9 (95% CI=1.2036 to 3.1113) with a P value of <0.001. According to statistical analysis, patients using preventative medication (calcium) together with medicines including corticosteroids, anti-epileptics, anti-depressants, diuretics, and PPI had a much lower incidence of drug-induced osteoporosis. Drug-induced osteoporosis is most typically related with glucocorticoids (GCs), followed by furosemide and carbamazepine. In current study, we conclude that the Patients exposed to drugs such as Glucocorticoids, Anti-epileptics, Anti- depressants, Diuretics and PPI have an increased chance of developing osteoporosis when compared to individuals who had not been exposed to them.

***Keywords*— Drug induced osteoporosis, Glucocorticoids, BMD, Adverse drug reaction, Incidence**

INTRODUCTION

Osteoporosis is characterized by low bone mineral density (BMD) and the loss of structural and biomechanical traits that are needed to preserve bone homeostasis.[1] Physicians have to be aware of the relationship between osteoporosis and age, post - menopausal status, and contributing factors such as lifestyle modifications and chronic disorders.[2] Many commonly prescribed medicines, however, have been found to lower BMD and increase fractures which many clinicians are unaware of the side effects.[3]

According to the National Osteoporosis Foundation(NOF), osteoporosis causes more than 1.5 million fractures in the U. S. each year.[4] Osteoporosis can affect men and women of all ages, although it is more prevalent in elderly women.[5] In the early stages of osteoporosis, there are no visible symptoms., patients may feel height loss, a change in posture, or discomfort as a result of a fracture in the later stages.[6] Osteoporosis is generally caused by an imbalance between osteoblasts (cells that produce bone mass) and osteoclasts (cells that break down bone mass) (cells that remove old bone).[7]

Drug-induced osteoporosis is a serious health issue that many doctors are unaware of tue multitude of routinely prescribed drugs can cause severe bone loss and fractures.[8] Preliminary studies can identify medications that put people at risk for drug-induced osteoporosis.[9] While glucocorticoids (GC) were the most likely source of drug-induced osteoporosis, a range of other drugs can cause significant bone loss and fractures. Selective serotonin receptor inhibitors, heparin, calcineurin inhibitors, proton pump inhibitors, anticonvulsants, thiazolidinediones, aromatase inhibitors, medroxyprogesterone acetate, and certain chemotherapy all have detrimental bone health effects.[10] Furthermore, many patients are given a combination of these medications, thereby exacerbating their adverse effects.

MATERIALS AND METHODS

A. Study Setting

This study was conducted who visited outpatient and inpatient departments of General medicine, General surgery, Orthopaedics, Nephrology, Neurology, Psychiatry and Dermatology

B. Study Place

Shadan Hospital, Peerancheruvu, Hyderabad. and Shadan Urban Health Centres and Shadan Rural Health Centres

C. Study Design

Prospective cohort study

D. Study Duration

March 2021 to February 2022

E. Sample Size

950 patients who were prescribed with Glucocorticoids, Anti- depressants, Anti-epileptics, Loop Diuretics, and PPIs for a minimum duration of 3 months were identified and enrolled.

All the patients taking Glucocorticoids, Antidepressants, Antiepileptics, Loop Diuretics and PPI for a minimum duration of 3 months after initiation of therapy was considered as Group (Ia). Patients receiving same class of drugs but along with the prophylactic therapy were identified and followed was considered as Group Ib. On the other hand patient who had not visited the outpatient and inpatient department but they visited the General Hospital was considered as the Control Group (II).

F. Inclusion Criteria

- Patients of either gender who were prescribed and treated with long term (not less than 3 months) Glucocorticoids, PPI, anti-epileptic, anti-depressants, loop diuretics for their respective clinical condition.
- Patient age of ≥30 years.
- Samples were selected from the respective departments where cases were collected.

G. Exclusion Criteria

- The patients not adherent to the prescribed medications for a time period of 3 months.
- Patient unwilling to participate in the study.
- Patients who did not complete at least two follow-up visits throughout the research period.

Data collection form was used to collect all the relevant information which includes Medical records including clinicians' admission notes, discharge summaries of previous hospitalizations (available with the patients or in the out-patient file), For both inpatients and outpatients, sources of past medical and medication history included reference notes from other clinicians and discussions with the patient or their caretakers at the time of their inclusion. Clinicians' notes, discussion with the clinicians/ postgraduate (PG) students were the important sources of information for current medical conditions. To gather the information regarding medication, use during hospital stay, treatment charts and nurses' notes were reviewed throughout the patient's stay in hospital. Standard medication information resources were used to gather the data needed to assess the risk of drug-induced osteoporosis.

After filling out an informed consent form from their respective departments, the patients were recruited in the research. The patient data collecting form contains all demographic and

clinical information from each patient's medical records. The patient's basic information, such as age, gender, employment, phone number, weight, and height, were obtained.

The patient's demographic information, lab results, current and previous medical and prescription histories were all recorded. All medicines, their frequency, dose, dosage form, and the dates they were initiated and discontinued were included. Allergies, co-morbidities were also included part of the medical and medication history data obtained.

Clinical information and other data include underlying disease, name and duration of other drugs used, total length of stay of hospital, history to drug allergy, bone mineral density, x-ray findings. Data related to the prescription of the above mentioned drugs, their dose and duration will be collected with reference to the study. This data will be evaluated and processed to calculate the incidence of osteoporosis. Patient risk assessment was measured by using Osteoporosis Risk assessment instrument (ORAI), Simple calculated osteoporosis risk assessment estimation (SCORE) and Osteoporosis self-assessment tool (OST)

Group I: Drugs (Corticosteroids, Anti-depressants, Anti-epileptics, Loop Diuretics, and PPIs).
Group Ia: Respective drugs alone.
Group Ib: Drugs along with prophylactic.
Group II: Not exposed to drugs (Corticosteroids, Antidepressants, Antiepileptics, Loop Diuretics, and Anticoagulants)

H. Statistical Analysis

To identify a significant relationship between numerous factors involved in the study, the average values of all parameters was computed and analyzed. Individual medications' osteoporosis incidence was determined. The overall risk of drug-induced osteoporosis was determined. The relative and absolute risk reductions, as well as the number needed to treat, was calculated.

I. Ethical Clearance

Ethical clearance was obtained from the Institutional Ethical Commiitee Vide ref. no. 012/SIMS/Research/2021

OBSERVATION AND RESULTS

The research comprised a total of 950 patients.

TABLE I
GROUP-WISE DISTRIBUTION OF SAMPLES

Groups	Number of Patients (n=950)
Ia	341 (35.89%)
Ib	280 (29.47%)
II	329 (34.63%)

In our study 341 (35.89%) study subjects are in Group Ia followed by 280 (29.47%) subjects are in Group Ib and 329 (34.63%) subjects are in Group II.

TABLE III
AGE-WISE DISTRIBUTION OF SAMPLES

Age Group	Number of Patients (n=950)			Total
	Ia	Ib	II	
30-44	32	18	37	87
45-60	128	121	125	374
61-75	159	127	140	426
>75	22	14	27	63
Gender				
Male	190	142	166	498

Female	151	138	163	452
Total	341	280	329	950 (100%)

In Group Ia, majority belonged to the age group of 61 to 75 yrs with 159 cases followed by 128 cases in 45-60 years group.

In Group Ib, majority belonged to the age group of 61 to 75 yrs with 127 cases followed by 121 cases in 45-60 years group.

In Group II, majority belonged to the age group of 61 to 75 yrs with 140 cases followed by 125 cases in 45-60 years group.

The overall mean age was 60.17 ± 10.92 years.

From the Osteoporosis risk assessment instrument (ORAI), 17.78% of sample population were found to be having high risk for osteoporosis where as 22.21% were found to have moderate and 60% of sample population were having low risk for osteoporosis.

From the simple calculated osteoporosis risk assessment (SCORE), 17.15% of sample population were found to be having high risk for osteoporosis where as 22.31% were found to have moderate and 60.52% of sample population were having low risk for osteoporosis.

TABLE IIIII
DIAGNOSIS OF OSTEOPOROSIS BY BMD

Groups	Osteoporosis	Osteopenic	Normal BMD
Ia	58	70	196
Ib	50	63	183
II	55	79	196
Total	163	212	575

After the complete follow up of study, the impact of drugs on bone was to found to be osteoporotic or osteopenic. While in Group Ia, 58 patients were having osteoporosis and 70 were osteopenic. In group Ib, 50 patients were having osteoporosis and 63 were osteopenic. In group II, 55 patients were having osteoporosis and 79 were osteopenic.

TABLE IVV
INCIDENCE OF DRUG INDUCED OSTEOPOROSIS

Group	Number of Patients (n=950)	Positive for Osteoporosis (n=163)	Incidence
Ia	341	58	0.266
Ib	280	50	0.145
II	329	55	0.12

From the above table, the overall incidence of Osteoporosis is Group Ia, Ib and II were found to be 0.266, 0.145 and 0.12 respectively.

TABLE V
ASSESSMENT OF RISK OF OSTEOPOROSIS ASSOCIATED WITH OVERALL DRUG EXPOSURE

Incidence of Osteoporosis	Relative Risk
Group I (Ia and Ib) = 0.21	1.935 (95% CI=1.2036 to 3.1113) P = 0.0064
Patient exposed to Corticosteroids	
Group Ia =0.31	2.8558 (95% CI=1.5939 to 4.9189) P = 0.0003
Group II=0.12	
Patient exposed to Furosemide	
Group Ia =0.28	2.52 (95% CI=1.2881 to 4.9548) P = 0.0070
Group II=0.12	
Patient exposed to Carbamazepine	
Group Ia =0.25	2.3 (95% CI=1.1597 to 4.7240) P = 0.0176
Group II=0.12	

The risk of drug-induced osteoporosis was found to be 1.935 times that of non-exposure. This suggests that individuals who have been exposed to medication classes such as Glucocorticoids, Anti-epileptics, Anti-depressants, Diuretics, and PPI have a higher risk of osteoporosis than those who have not been exposed to them.

The relative risk of osteoporosis in individuals exposed to corticosteroids was found to be 2.9 when compared to the non-exposed group (Group II). This suggests that patients who were exposed to corticosteroids had a greater risk of osteoporosis than those who were not.

The relative risk of osteoporosis in Furosemide-exposed patients was found to be 2.5 when compared to the non-exposed group (Group II). This suggests that individuals who were exposed to Furosemide had a greater risk of osteoporosis than those who were not.

The relative risk of osteoporosis in individuals exposed to Carbamazepine was found to be 2.3 when compared to the non-exposed group (Group II). This suggests that individuals who were exposed to Carbamazepine had a greater risk of osteoporosis than those who were not.

DISCUSSION

The current study include 950 patients were prescribed Glucocorticoids, Antidepressants, Antiepileptics, Loop Diuretics, and PPIs for a minimum of 3 months after treatment initiation were classified as Group Ia, whereas those who received the same class of medications plus calcium as preventative therapy were classified as Group Ib.

Our study's assessment of the sample population based on ORAI and SCORE correlates with Basafa and Armand et al, who concluded that the majority of the study population's drug exposures were determined to be high risk.[15] In this study, the incidence of drug-induced osteoporosis was essentially identical to that discovered by Darrell et al, who reported that study participants who had been exposed to drugs (no prophylactic treatment) had a higher incidence.[16]

When compared to individuals who were not exposed to medication classes such Glucocorticoids, Anti-epileptics, Anti-depressants, Diuretics, and PPI (Group Ia), patients who were exposed to them had a higher risk of osteoporosis (Group Ib). The relative risk was calculated to corroborate which found to be 1.9 (95% CI=1.2036 to 3.1113) with a P value of <0.001.

According to statistical analysis, patients who received preventative medication (calcium) together with medicines including corticosteroids, anti-epileptics, anti-depressants, diuretics, and PPI had a much lower incidence of drug-induced osteoporosis.

This study's relative risk of drug-induced osteoporosis compared to non-exposure was primarily comparable to Shen et al's study with a relative risk of 2.1.[17] Our research's relative risk of osteoporosis in individuals exposed to corticosteroids compared to the non-exposed group (Group II) is similar to Romas et al's study, which found a relative risk of 2.7.[18] The relative risk of osteoporosis in patients exposed to diuretics when compared to the non-exposed group (Group II) in our study is comparable to Wayne et al's study, which found that patients exposed to Furosemide had a greater risk of osteoporosis than those who were not.[19] This study's relative risk of osteoporosis in patients exposed to anti-epileptics when compared to the non-exposed group (Group II) is similar to Vestergard et al's study, which found a relative risk of 2.2.[20]

Prophylactic therapy can help patients avoid developing osteoporosis; among patients who had been exposed for more than a year, adding prophylactic therapy (Group Ib) dramatically decreased the incidence of osteoporosis when compared to individuals who did not get prophylactic therapy (Group Ia). Drug-induced osteoporosis is most typically related with glucocorticoids (GCs), followed by furosemide and carbamazepine.

CONCLUSION

When compared to individuals who were not exposed to medication classes such Glucocorticoids, Anti-epileptics, Anti-depressants, Diuretics, and PPI (Group Ia), patients who were exposed to them had a higher risk of osteoporosis (Group Ib). Calculating the relative risk, which was determined to be 1.9, corroborated this. Patients who received preventative medication (calcium) together with medicines such as corticosteroids, anti-epileptics, anti-depressants, diuretics, and PPI had a substantial decrease in the risk of drug-induced osteoporosis.

REFERENCES

[1] B. Abrahamsen, P. Eiken, R. Eastell, "Proton pump inhibitor use and the antifracture efficacy of alendronate," *Arch Intern Med.*, vol. 171(11), pp. 998-1004, 13 Jun. 2011.
[2] JS. Adams, CF. Song, V. Kantorovich, "Rapid recovery of bone mass in hypercalciuric, osteoporotic men treated with hydrochlorothiazide," *Ann Intern Med.*, vol. 130(8), pp. 658-660, 20 Apr. 1999.
[3] SF. Ahmed, M. Elmantaser, "Secondary osteoporosis," *Endocr Dev.*, vol. 16, pp.170-190, 2009.
[4] "American Association of Clinical Endocrinologists medical guidelines for clinical practice for the prevention and treatment of postmenopausal osteoporosis, 2001 edition, with selected updates for 2003," *Endocr Pract.*, vol. 9(6), pp. 544-564, 2003.
[5] "Assessment of fracture risk and its application to screening for postmenopausal osteoporosis. Report of a WHO Study Group," *World Health Organ Tech Rep Ser.*, vol. 843, pp.1-129, 1994
[6] MA. Bass, A. Sharma, VK. Nahar, S. Chelf, B. Zeller, L. Pham, et al. "Bone Mineral Density Among Men and Women Aged 35 to 50 Years," *J Am Osteopath Assoc.*, vol. 119(6), pp. 357-363, 2019
[7] TJ. Beck, "Extending DXA beyond bone mineral density: understanding hip structure analysis," *Curr Osteoporos Rep.*, vol. 5(2), pp. 49-55, Jun. 2007.
[8] JJ. Body, GA. Gaich, WH. Scheele, PM. Kulkarni, PD. Miller, A. Peretz, RK. Dore, R. Correa-Rotter, A. Papaioannou,DC. Cumming, AB. Hodsman, "A randomized double-blind trial to compare the efficacy of teriparatide [recombinant human parathyroid hormone (1-34)] with alendronate in postmenopausal women with osteoporosis," *J Clin Endocrinol Metab.*, vol. 87(10), pp. 4528-4535, Oct. 2002.
[9] *Office of the Surgeon General (US), Bone Health and Osteoporosis: A Report of the Surgeon General. Rockville (MD)*, Office of the Surgeon General (US), PMID: 20945569, 2004.
[10] LF. Bonewald, "The amazing osteocyte," *J Bone Miner Res.*, vol. 26(2), pp. 229-238, Feb. 2011.
[11] N. Reddy, S. Parveen, A. Syed, "Pharmacovigilance of corticosteroids in dermatological diseases," *Int J Adv Med.*, vol. 6, pp. 287-290, 2019.
[12] N. Khachidze and E. Giorgadze, "Drug induced osteoporosis. Translational and Clinical Medicine," *Georgian Medical Journal*, vol. 2(2), pp. 16-19.
[13] NB. Watts, "Adverse bone effects of medications used to treat non-skeletal disorders," *Osteoporos Int.*, vol. 28(10), pp. 2741-2746, Oct. 2017.
[14] VK. Shanmugam, NM. Zaman, S. McNish, FN. Hant, "Review of Current Immunologic Therapies for Hidradenitis Suppurativa," *Int J Rheumatol*, 8018192, 2017.
[15] E. Basafa, M. Armand, "Subject-specific planning of femoroplasty: a combined evolutionary optimization and particle diffusion model approach," *J. Biomech.*, vol. 47, pp. 2237-2243, 2014.
[16] Weber, K. Nicholas, Fidler, L. Jeff, Keaveny, M. Tony, Clarke, L. Bart, Khosla, Sundeep, Fletcher, G. Joel, Lee, C. David, Pardi, S. Darrell, Loftus, V. Edward, Kane, V. Sunanda, Barlow, M. John, Murthy, Naveen, "Validation of a CT-Derived Method for Osteoporosis Screening in IBD Patients Undergoing Contrast-Enhanced CT Enterography," *American Journal of Gastroenterology*, vol. 109(3), pp. 401-408, Mar. 2014.
[17] CL. Shen, JK. Yeh, JJ. Cao, JS. Wang, "Green tea and bone metabolism," *Nutr Res.*, vol. 29(7), pp. 437-456, Jul. 2009. Erratum in: *Nutr Res.*, vol. 29(9), pp. 684, Sep. 2009.
[18] E. Romas, "Corticosteroid-induced osteoporosis and fractures," *Aust Prescr*, vol. 31, pp. 45-49, 2008.
[19] PM. Wayne, DP. Kiel, DE. Krebs, RB. Davis, J. Savetsky-German, M. Connelly, JE. Buring, "The effects of Tai Chi on bone mineral density in postmenopausal women: a systematic review," *Arch Phys Med Rehabil.*, vol. 88(5), pp. 673-680, May 2007.
[20] P. Vestergaard, "Discrepancies in bone mineral density and fracture risk in patients with type 1 and type 2 diabetes--a meta-analysis," *Osteoporos Int.*, vol. 18(4), pp. 427-444, Apr. 2007.