**DOI:** https://doi.org/10.54393/pjhs.v4i09.1039

PAKISTAN JOURNAL OF HEALTH SCIENCES

https://thejas.com.pk/index.php/pjhs

Volume 4, Issue 9 (September 2023)

**Original Article**

# Quasi Experimental Study to Ascertain Link of PPI to Bone Profile in Healthy Individuals

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## ARTICLE INFO

***Key Words:***
Vitamin D, Calcium, PPI

***How to Cite:***
Memon, Y., Shaikh, I. A. ., & Karim, I. (2023). Quasi Experimental Study to Ascertain Link of PPI to Bone Profile in Healthy Individuals: Link of PPI to Bone Profile. Pakistan Journal of Health Sciences, 4(09). https://doi.org/10.54393/pjhs.v4i09.1039

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Received Date: 7th September, 2023
Acceptance Date: 27th September, 2023
Published Date: 30th September, 2023

## ABSTRACT

Proton pump inhibitor (PPI) is only acid blocking agent used for treating the disease known as gastroesophageal reflux (non-erosive), erosive esophagitis disease, dyspepsia disease and the peptic ulcer disease because of its efficacy and potency. However, overuse of it is examined an immediate result of absence of determination of need for steady treatment in many outdoor subjects **Objective:** To evaluate impact of proton pump inhibitor (PPI) on bone biochemistry in young individuals of Hyderabad. **Methods**: The study contained 227 young individuals of age 20-45 years, it was conducted in Liaquat University Hospital, Hyderabad City and Medicine OPD's of Jamshoro. The research study is undertaken using Quasi experimental study. The study duration is 6 months starting from 15th March 2020 to 15th September 2020 and sampling technique is non – probability convenience. SPSS 21 software is used to analyze the data. The post stratification chi – square test is performed at the interval of 95% confidence, besides it the P-value is observed ≤ 0.05. **Results:** There is no effect on serum calcium and vitamin D levels with use of proton pump inhibitor PPI. P-value was observed 0.7 for the serum calcium and the p-value for Serum Vitamin D was 0.1. **Conclusions:** Hence, the study showed that proton pump inhibitor PPI use for less than 6 months have no effect on bone biochemistry.

## INTRODUCTION

Proton pump inhibitor PPI works by blocking the hydrogen-potassium ATPase inhibitor H/K ATPase inhibitor located on gastric parietal cells. It blocks the last step of acid production that is why it is more potent and effective than other acid suppressants like H2 blockers, 99% of gastric acid secretion is reduced by using it [1]. The possible mechanism between the use of proton pump inhibitor PPI, serum vitamin D and calcium level probably be linked to action of long-term suppression of acid on calcium metabolism. Persistent hypergastrinemia persuade by use proton pump inhibitor PPI therapy may cause intense hyperplasia of parathyroid gland, that results in increased number loss of calcium from the bone. Second, intense acid suppression in stomach may bring down the availability of calcium for intestinal absorption. Proton pump inhibitor PPI, rational uses are yet increasing. Recent research relieved the divergent data, those subjects in study who are on proton pump inhibitor (PPI) therapy may be at an enlarged number of possibilities for fracture caused by osteoporosis compared with each patient at average possibility of fracture [2-6], however the researcher draw that there is no sequel on change in density of bone with close use of proton pump inhibitor PPI [7-13]. The previous researches revealed that there are number of studies done like case-control, observational and cohort studies, that showed the increasing number of fractures with prolong use of proton-pump inhibitor PPI, but there are further studies which do not show any effect

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on bone mineralization [13-20]. The extend for the use of this drug is not investigated exactly, in several observed studies > 5 years of usage can rise chances of fractures caused through osteoporosis by 1.62 or use of > 7 years can elevate the possibility of fracture of hip due to osteoporosis by 4.55fold. Utilization of Proton pump inhibitor for 6 to 12 months has been reported to be involved with an expanded possibility of fractures of spine and hip because of osteoporosis [21]. Another survey showed at most inconsistency was levels of vitamin D in which, 50 in number out of 58 subjects around (86.2%) had diagnosed hypovitaminosis D with 25-OH levels of vitamin D under 20ng/ml, 60.3% had poor levels in between the 10 and 20ng/ml. 25.9% were having deficiency of vitamin D with the levels below 10ng/ml [22].

## METHODS

The study was conducted in OPDs of Jamshoro and Hyderabad, Liaquat University Hospital, Medicine department. Conducted research study is Quasi experimental study which was undertaken for 6 months, starting from 15th March 2020 to 15th September 2020. The sampling technique used was Non-Probability Convenience. The size of sample was calculated by applying the Cochran's formula, which was 227. SPSS version 21.0 software was used to analyze the data. The inclusion criteria for individuals in study were a). Those having age 20-45 yrs. b). Those having calcium and vitamin D in normal range. c). Those who have not taken PPI earlier. d) Those having acid-peptic disease and dyspepsia. The exclusion criteria include a). Individuals having calcium supplements b). Individuals previously taking PPI c). Individuals having cardiac, renal and bone diseases d). Individuals having complicate peptic ulcer disease, osteoporosis, and having endocrinopathies like hyperparathyroidism and hypo-parathyroidism. The post stratification chi – square test was performed at the interval of 95% confidence, besides it the p-value is observed ≤ 0.05.

## RESULTS

During six months duration of study, total 227 individuals were studied for their consequences of proton pump inhibitor on serum calcium and vitamin D levels before and after its use. Amongst 227 individuals, 72 (31.7%) were males and 155 (68.3%) were females. 107 (47.1%) were urban and 120 (52.8%) were rural as shown in Table 1.

**Table 1:** Characteristics before and after use of PPI

| Variables | | Frequency (%) |
|---|---|---|
| Participants | Male | 72 (31.7) |
| | Female | 155 (68.5) |
| Residential status | Urban | 107 (47.1) |
| | Rural | 120 (52.8) |
| BMI (Mean ± SD) | | 21.6 ± 0.38 |
| Duration of PPI | | 5.5 Months |

Mean and SD after use of proton pump inhibitor was 8.9 ± 0.26 for the serum calcium and for the serum vitamin D was 48.2±4.16. Hence, the p-value for the serum calcium is 0.7 and for the vitamin D is 0.1 as shown in Table 2. There was no outcome on serum calcium and vitamin D levels with use of proton pump inhibitor PPI.

**Table 2:** Characteristics before and after the Study

| Variables | Before PPI (Mean ± SD) | After PPI (Mean ± SD) | p-value |
|---|---|---|---|
| Serum Calcium | 9.0 + 0.25 | 8.9±0.26 | 0.7 |
| Serum Vitamin D | 50 + 3.15 | 48.2 ±4.16 | 0.1 |

## DISSCUSSION

All subjects selected in our study in age were young so, there was no significant possibility of fractures by diminishing levels of serum calcium and serum vitamin D levels following use of Proton pump inhibitor PPI, although the risk rises in elder individuals as seen in study of Targownik *et al.*, and Right *et al.*, [23, 24], who revealed Proton pump inhibitor PPI use in elderly individuals for longer duration and reduce intake of calcium, causes significant fractures other than spine. In our study, Proton pump inhibitor PPI did not have influence on serum calcium and serum vitamin D levels where, p value was 0.7 calculated for calcium before and after use of Proton pump inhibitor PPI while, the p value 0.1 that is calculated for serum vitamin D. Results in our study are supported by a study that exhibit hypochlorohydria caused by Proton pump inhibitor PPI diminishes calcium absorption [25, 26]. Serfaty-Lacrosniere *et al.*, [27] showed that there is no significant variation in absorption and excretion of calcium despite use of Proton pump inhibitor PPI or not in a study conducted over serum calcium and urinary calcium excretion [28]. Another study was conducted between two groups one having Proton pump inhibitor (PPI) and second not having Proton pump inhibitor (PPI) by O'Connell *et al.*, [29, 30].

## CONCLUSIONS

Hence, the study showed that proton pump inhibitor PPI use for less than 6 months have no effect on serum calcium and serum vitamin D levels. It is quite safe to use proton pump inhibitor. This conclusion is with assertion of the Canadian Association of Gastroenterology which base no valid affirmation that alliance is causal and averred that ongoing data does not hold up a certain difference in assuming proton pump inhibitor therapy because of concerns about the massive risk of the hip fractures.

## Authors Contribution

Conceptualization: YM
Methodology: IAS

**DOI:** https://doi.org/10.54393/pjhs.v4i09.1039

Formal analysis: IK
Writing-review and editing: YM, IAS, IK

All authors have read and agreed to the published version of the manuscript.

## Conflicts of Interest

The authors declare no conflict of interest.

## Source of Funding

The authors received no financial support for the research, authorship and/or publication of this article.

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