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## LETTER TO EDITOR

### Proton Pump Inhibitors and Gastric Cancer Correlation; Time to Take It Seriously?

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#### ARTICLE INFO

*Received: 2018-10-02*

*Accepted: 2018-10-23*

*Published: 2019-02-30*

*Volume: 4*

*Issue: 1*

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*Conflicts of interest: None*

*Funding: None*

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#### ABSTRACT

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#### DEAR EDITOR

Proton pump inhibitors (PPI) are the most commonly prescribed medications around the world globally, are highly potent gastric acid suppressors, currently approved by the US Food and Drug Administration for the management of a variety of gastrointestinal disorders including peptic ulcers, gastroesophageal reflux disease (GERD), eradication of *Helicobacter pylori* (in combination with antibiotics) as well as for the prevention of primary or recurrent peptic ulcers in individuals exposed to aspirin or non-steroidal anti-inflammatory drugs (NSAIDs) or with Zollinger-Ellison syndrome (a gastrin-secreting pancreatic tumor) (1). Gastric cancer is the fourth most predominant cancer and it is the second leading cause of cancer-related mortality around the globe. It is also considered as a lethal disease that hugely affects the economic, social, psychological and physical aspects of the patients (2).

Though PPIs have been introduced in 1989, their correlation with gastric cancer has not been studied eminently yet). However, majority of the literature review suggests a substantial risk of gastric cancers to be associated with PPI (1-3). The commonly proposed underlying mechanism is in close association with a study conducted 30 years ago, which reported excessive inhibition of gastric acid secretion in rodents with secondary hypergastrinemia leading to enterochromaffin-like-cell (ECL) hyperplasia (1, 4). Moreover, histopathological changes (such as hyperproliferation of gastric mucosa, replacement of normal mucosal glands with intestinal glands), loss of physiologic defense due to blocked gastric acid secretion, leads to chronic inflammation and bacterial colonization, and hence can ultimately cause gastric cancers (1). However, in contrast to other studies, two meta-analyses found no association between long-term use of PPI and any malignant changes

in the gastric mucosa (1).

Overall, based on insufficient literature, we can conclude that the safety of PPI can be challenged considerably and hence, complications of taking PPI should be taken seriously and more comprehensively designed and well-conducted randomized controlled trials with a long-term follow-up should be conducted. These improvements can significantly decrease the chances of bias while evaluating the long-term effects of PPI on gastric mucosa. In a country like Pakistan, where the health care is underperforming and there is inadequate patient follow up, it is startling to see the excessive use of PPI, both in tertiary care hospitals as well as in clinics. A study reports that patients are taking high doses of PPI for months and years without any clinical recommendation and follow-ups. Hence, in such developing countries it is not only a huge economic burden on the healthcare but is also associated with a life-threatening correlation of gastric cancer (5). Therefore, drugs alternative to PPI, with no complicated side effects, should be strongly encouraged. Physicians should inform their patients about its long-term side-effects and also about avoiding any misuse.

#### ACKNOWLEDGMENTS

NONE

#### AUTHOR CONTRIBUTIONS

All authors equally contributed in this study

#### CONFLICT OF INTERESTS

NONE

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