Oxidative Stress Damage and H. Pylori Gastric Cancer: A Narrative Review

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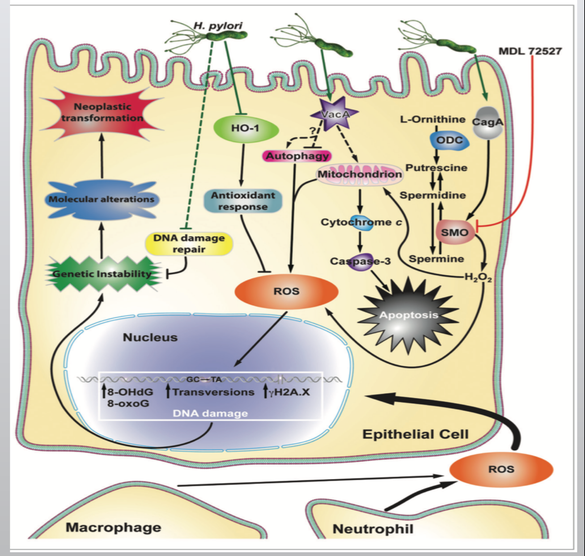
INTRODUCTION

- Gastric Cancer is the number one most common cause of cancer-related death in the USA for men, and number three for female.
- The risk that a man will develop stomach cancer in his lifetime is about 1 in 95. For women the chance is about 1 in 154.

The role of Reactive Oxygen Species (ROS) in Cancerogenesis



OBJECTIVES

- What role or potential role does Oxidative Stress play in the development of gastric cancer?
- What evidence of involvement does oxygen containing radicals – ROS (Reactive Oxygen Species) and H. pylori associated inflammation, contribute to the increased risk of developing gastric cancer?

METHODS

Literature search was conducted using PubMed database using keywords:

"oxidative stress"

"H.Pylori",

"gastric cancer",

with the use of the Boolean operator "AND"

RESULTS

H.Pylori triggered Oxidative stress is main factor to development of gastric cancer

Author	Year	Findings
Hardbower et al.	2013	• Uncovering of a mechanism by which polyamine oxidation by spermine oxidase causes H 2O 2 release, DNA damage and apoptosis. • Studies indicate novel targets for therapeutic
Correa P	2006	• H. Pylori does not induce carcinogenesis by itself. The present scientific consensus is that the bacterial oncogenic role is mediated by the chronic active inflammation it elicits in the gastric mucosa. Although the ultimate basic mechanism of carcinogenesis is unknown, strongly suggestive evidence points to oxidative stress as having a pivotal role in the process.

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Author	Year	Findings
Xu H. et al.	2004	• H. Pylori-infected tissues, showed increased expression of SMO(PAOh1) in both human and mouse gastritis. • These results identify a pathway for oxidative stress-induced epithelial cell apoptosis and DNA damage due to SMO(PAOh1) activation by H. pylori that may contribute to the pathogenesis of the infection and development of gastric cancer.
Chaturvedi et al.	2004	• These studies demonstrate a new mechanism for pathogen-induced oxidative stress in macrophages in which activation of PAO1 leads to H(2)O(2) release and apoptosis by a mitochondrial-dependent cell death pathway, contributing to deficiencies in host defense in diseases such as H. pylori infection.

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Author	Year	Findings
Chaturvedi et al.	2011	• Determined if pathogenic effects of CagA are attributable to SMO. • CagA(+) strains or ectopic expression of CagA, but not cagA(-) strains, led to increased levels of SMO, apoptosis, and DNA damage in gastric epithelial cells, and knockdown or inhibition of SMO blocked apoptosis and DNA damage. • By inducing SMO, H pylori CagA generates cells with oxidative DNA damage, and a subpopulation of these cells are resistant to apoptosis and thus at high risk for malignant transformation.
Suhn et al.	2019	• Helicobacter pylori increases production of reactive oxygen species (ROS), activating inflammatory and carcinogenesis-related signaling pathways in gastric epithelial cells. • Therefore, reducing ROS, by up regulating antioxidant enzyme, such as superoxide dismutase (SOD), may be a novel strategy to prevent H. pylori-associated gastric diseases.

H.Pylori triggered Oxidative stress is main factor to development of gastric cancer

Author	Year	Findings
Rupesh et al.	2011	• These studies demonstrate a new mechanism for pathogen-induced oxidative stress in macrophages in which activation of PAO1 • leads to H2O2 release and apoptosis by a mitochondrial-dependent cell death pathway, contributing to deficiencies in host defense in diseases such as H. pylori infection.

H.Pylori triggered Oxidative stress is main factor to development of gastric cancer

Author	Year	Findings
Duane et al.	2000	• Gastritis associated with H.pylori infection stimulates the generation of ROS by the inflammatory cells present in the mucosa
Zhang et al.	2015	• Amount of reactive oxygen directly correlated with bacterial load

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Author	Year	Findings
Handa et.al	2011	• H.Pylori increases the production of reactive oxygen species (ROS) and reactive nitrogen species (RNS) in human stomach, and this has been reported to impact upon gastric inflammation and carcinogenesis
Chaturvedi et al.	2012	• Helicobacter pylori strains expressing the virulence factor cytotoxin-associated gene A (CagA) stimulate increased levels of spermine oxidase (SMO) in gastric epithelial cells. SMO catabolizes the polyamine spermine and produces H_2O_2 that results in both apoptosis and DNA damage.

H.Pylori triggered Oxidative stress is main factor to development of gastric cancer

Author	Year	Findings
Hangxiu et al.	2004	• Oxidative stress is linked to carcinogenesis due to its ability to damage DNA. The human gastric pathogen Helicobacter pylori exerts much of its pathogenicity by inducing apoptosis and DNA damage in host gastric epithelial cells. Polyamines are abundant in epithelial cells, and when oxidized by the inducible spermine oxidase SMO(PAOh1) H2O2 is generated. H. pylori up-regulates mRNA expression, promoter activity, and enzyme activity of SMO(PAOh1) in human gastric epithelial cells, resulting in DNA damage and apoptosis.
Zhang et al.	2015	• Vitamin C is an important dietary antioxidant against oxidative stress and might be protective against the development of gastric cancer. • Inflammation induced by H. pylori infection in the stomach not only causes significantly enhanced consumption of vitamin C, but also reduces secretion of the vitamin into the gastric lumen. Most of the evidence relating to vitamin C and H. pylori infection derives from clinical studies and experiments directly examining the effect of vitamin C on H. pylori-associated gastric carcinogenesis and remains limited. • Results from recent studies suggest that vitamin C might also increase the risk of cancer through its pro-oxidant activity and protect against oxidative stress in cancer cells through its antioxidant action.

Prevention of Oxidative Stress

Author	Year	Findings
Zhang et al.	2005	• Vitamin C is an important dietary antioxidant against oxidative stress and might be protective against the development of gastric cancer. • Inflammation induced by H. pylori infection in the stomach not only causes significantly enhanced consumption of vitamin C, but also reduces secretion of the vitamin into the gastric lumen. Results from recent studies suggest that vitamin C might also increase the risk of cancer through its pro-oxidant activity and protect against oxidative stress in cancer cells through its antioxidant action.
Kumar et al.	2019	• It states that consumption of astaxanthin-rich food may prevent the development of *H. pylori*-associated gastric disorders by suppressing mitochondrial oxidative stress.

Prevention of Oxidative Stress

Author	Year	Findings
Zhang et al.	2015	• Amount of reactive oxygen directly correlated with bacterial load. • Resevertol protects against H. Pylori associated gastritis by combating oxidative stress
Yadav et al.	2019	Epidemiologically, it was suggested that curcumin might reduce the risk of inflammatory disorders, such as gastric carcinoma. It can, therefore, be reported from the literature that curcumin Prevents gastrointestinal-induced ulcer and can be recommended as a novel drug for ulcer treatment.

Prevention of Oxidative Stress

Author	Year	Findings
Wang et al	2014	Anti-H. pylori induced gastric inflam- matory effects of plant products, including quercetin, apigenin, carotenoids-rich algae, tea product, garlic extract, apple peel polyphenol, and finger-root extract, have been documented. In conclusion, many medicinal plant products possess anti-H. pylori activity as well as an anti-H. pylori-induced gastric inflammatory effect
Kim et al	2015	Since oxidative stress is related to DNA damage, smoking, and H. pylori infection, scavenging of reactive oxygen species may be beneficial for prevention of gastric carcinogenesis. Lycopene, one of the naturally occurring carotenoids, has unique structural and chemical features that contributes to a potent antioxidant activity. It shows a potential anticancer activity and reduces gastric cancer incidence

CONCLUSIONS

- Unquestioningly H. Pylori Causes 95% Of All Gastric Cancer. [Wei Zhang Et Al ,2014]
- In Our Research, We Found Strong Evidence That H. Pylori Associated Inflammation Increases ROS Which Causes DNA Damage In Gastric Epithelial Cells.
- Errors Arising During DNA Repair Will Result In Development Of Gastric Carcinoma.
- In summary, Oxidative Stress is a significant component to the development of Gastric Cancer.

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