

RESEARCH ARTICLE

Editorial Process: Submission:10/10/2024 Acceptance:09/23/2025 Published:10/19/2025

Oxidative Stress Dynamic among *Helicobacter pylori*-Positive Patients with Various Stages of Premalignant Histologic Lesions: A Prospective Study in Cameroon

Laure Brigitte Kouitchou Mabeku^{1,2*}, Faujo Nintewoue Ghislaine Florice¹, Lionel Danny Tali Nguefak¹, Isabelle Ntang Timba³, Ghislaine Ngatcha⁴, Sartre Michele Tagni⁴, Paul Talla⁵, Carole Marlyse Menzy Mounjo-Ndjole⁵

Abstract

Objective: This study sought to evaluate biomarkers of oxidative stress among *H. pylori* infected patients in relation to neoplastic transformation within the gastric mucosa. **Methods:** This study included 191 *H. pylori*-positive patients: 14 healthy individuals, 40 with chronic gastritis, 69 with atrophic gastritis, 22 with intestinal metaplasia, and 46 with dysplasia. *H. pylori* was detected on biopsies samples. Hematein/eosin staining was used for the histologic examination of gastric mucosa. Reduced glutathione (GSH) and malondialdehyde (MAD) content, activity of superoxide dismutase (SOD) and catalase (CAT) were measured in serum. **Results:** The serum levels of GSH were higher among patients with chronic gastritis ($P = 0.0277$), atrophic gastritis ($P = 0.0451$), and dysplasia ($P = 0.0069$) compared to the controls. The highest concentration of GSH was recorded in dysplasia ($P = 0.0157$). The content of lipid peroxidation products (MAD) significantly increased in patients with gastric pre-malignancies compared to the controls ($P < 0.0001$). SOD activity was higher among patients with gastric mucosa injury compared to the controls, with the highest concentration in metaplasia ($P = 0.0182$). Catalase activity was similar to that of superoxide dismutase ($P > 0.05$). **Conclusion:** Our findings showed significant higher and progressive serum levels of lipid peroxidation and antioxidant protective factors with progression in precancerous lesions related to *H. pylori* infection. This suggests a higher free radical formation and oxidative stress, which increases from chronic gastritis to malignancy.

Keywords: Oxidative stress-*Helicobacter pylori* infection-Gastric premalignant and malignant lesions

Asian Pac J Cancer Prev, 26 (10), 3609-3618

Introduction

Chronic *Helicobacter pylori* infection represents a significant health burden affecting approximately half of the world's population [1]. This pathogen is mainly implicated in the pathophysiology of diverse gastrointestinal conditions including gastritis, peptic ulcer disease, gastric adenocarcinoma, and mucosa-associated lymphoma [2].

Gastric cancer is the second leading cause of cancer-related mortality worldwide, with an estimate mortality of about 1 in 12 of all oncological deaths [3]. The Correa et al. model hypothesizes that normal gastric mucosa can develop gastritis, a continuous process which progresses to atrophic gastritis, intestinal metaplasia, dysplasia, and leading finally to gastric adenocarcinoma [4]. There are many factors that contribute to the initiation of gastritis and the progression to cancer such as host gene

polymorphisms, dietary factors, and *H. pylori* infection among others.

H. pylori exerts exponential chemotaxis on immune cells, particularly on neutrophils [5]. In response to this stimulation, neutrophils become active and release into the inflammatory tissue of the gastrointestinal tract large and excessive amounts of oxidizing agents such as hydrogen peroxide (H_2O_2), hydroxyl radical ($-OH$), and superoxide anions (O_2^-), as well as peroxyxynitrite ($OONO^-$) and nitric oxide (NO) respectively known as reactive oxygen species (ROS) and reactive nitrogen species (RNS) [6]. Despite the well-established association between chronic *H. pylori* infection and gastric adenocarcinoma, there is a contradictory observation referring as the "African enigma" illustrating that in sub-Saharan Africa where *H. pylori* infection prevalence is high, gastric cancer incidence is lower [7].

Physiologically, free radicals are produced from

¹Microbiology and Pharmacology Laboratory, Department of Biochemistry, Faculty of Science, University of Dschang, Dschang, Cameroon. ²Medical Microbiology Laboratory, Department of Microbiology, Faculty of Science, University of Yaoundé I, Yaoundé, Cameroon. ³Regional Hospital Bafoussam, Bafoussam, Cameroon. ⁴Centre Médicale la Cathédrale, Yaoundé, Cameroon. ⁵General Hospital Yaoundé, Yaoundé, Cameroon. *For Correspondence: laurebkouitchou@yahoo.fr

oxygen molecules in normal cell's metabolic pathways, notably in redox-dependent transcriptions, ion channels, and enzymes activation [8]. However, they accumulate when produced in high quantities. The imbalance between the production and accumulation of ROS in cells and tissues and the ability of the biological system to detoxify these reactive products is termed oxidative stress [9].

The first line of defense against oxidative agents consists of antioxidant enzymes such as superoxide dismutase (SOD), catalase (CAT), glutathione peroxidase, peroxiredoxins, and paraoxonase. Their role is to prevent the formation of free radicals and to neutralize those already formed. The second line consists of free radical scavengers, which neutralize free radicals by donating electrons, including glutathione (GSH), uric acid, cysteine, bilirubin, carotenoids, and vitamins A, E, and C [10, 11].

Overproduction of ROS can indirectly induce changes in cellular macromolecules through signaling pathway cascades that eventually target DNA damage [12]. In addition, hydrogen peroxide (H₂O₂), can diffuse throughout mitochondrial and other cell membranes to produce cell injury, including lipid peroxidation [13, 14].

Some investigators have shown that the enhanced production of ROS in peripheral blood significantly decreased after the eradication of *H. pylori*, while the eradication of *H. pylori* caused a significant decrease in catalase level in asymptomatic patients [15]. Conversely, others have found that 4-hydroxynonenal-protein, a marker of lipid oxidative damage remain elevated in spite of *H. pylori* eradication [16].

Reactive oxygen species (ROS) can induce oxidative damage in biological molecules and yield various primary and secondary reaction products or markers. These markers included, malondialdehyde (MAD) and 4-hydroxynonenal as indicators of lipid oxidative damage [17, 18]; 8-oxoguanine and thymine diol as marker of DNA oxidative damage [19, 20]; hydroxybutyryl, carbonyl protein, hydrovaline, and nitrotyrosine as oxidative products of protein and amino acid [21, 22].

The study aimed to determine the host's response to generating oxidative stress in *H. pylori* infection and the relation with the dynamism of neoplastic transformation within the gastric mucosa. Thus, antioxidant protective enzymes such as superoxide dismutase (SOD), catalase (CAT), free radical scavengers including glutathione (GSH), and one product of lipid peroxidation, malondialdehyde were chosen as biomarkers for the oxidative stress evaluation in blood sample of dyspeptic patients from Cameroon. Knowledge on the degree of oxidative stress related to *H. pylori* infection in dyspeptic patients and their roles in the progression from *H. pylori* infection to premalignant state and gastric cancer in the Cameroon context of low gastric cancer incidence and high *H. pylori* prevalence may bring new insights into the African enigma.

Materials and Methods

Selection of participants

The patients were selected among those seen at the gastroenterology unit at three reference hospitals in

Cameroon; the General Hospital of Yaoundé, the Centre Medicale la Cathedrale of Yaoundé and the Regional Hospital of Bafoussam. The study recruited all dyspeptic patients aged from 15 years and above who underwent an upper gastrointestinal endoscopy, obtaining gastric biopsies for investigation of their dyspepsia and who accepted to partake in the study. A structural questionnaire was used to collect socio-demographic data (age, sex), life style (alcohol consumption, tobacco use, level income) and medication history (antibiotics consumption, proton pump inhibitors or bismuth salts consumption, non-steroidal anti-inflammatory drugs (NSAIDs) consumption) from participants. All patients were interviewed face-to-face and all of them answered the questionnaire. Patients with history of NSAIDs consumption, those who took antibiotics for 6 to 8 weeks, and those who took proton pump inhibitors or bismuth salts six weeks before the present consultation were not included in the study. Information related to medical history of patients (Chronic disease, history of gastric surgery, active gastrointestinal bleeding...) were collected from their medical reports (patient file), and patients with chronic disease of various organs/systems, those with history of gastric surgery, and those with active gastrointestinal bleeding were not included. We also excluded patients with misidentification or those who had errors during analysis.

H. pylori detection was performed among all the recruited subjects using both histological examination and rapid urease test and only *H. pylori*-positive patients were included in the study.

Controls were *H. pylori*-positive dyspeptic patients without histological detected injury in the gastric mucosa (gastric normal mucosa). All participants with histological detected gastric mucosa injury were classified as patients with chronic gastritis, atrophic body gastritis, intestinal metaplasia, dysplasia and gastric cancer.

H. pylori Detection

H. pylori detection was performed from the biopsies specimen using both histological examination and rapid urease test (RUT). A patient was considered as *H. pylori* positive if both the two tests were positive. Only *H. pylori*-positive patients were included in the study.

H. pylori detection using rapid urease test (RUT)

Helicobacter pylori AMA Rapid Urease Test 1 kit (AMAT RUT 1, Association of Medicine and Analytics, Saint Petersburg, Russia) was used to detect the present of the bacterium in biopsies.

H. pylori detection using histological examination

The gastric biopsies from the 10% formaldehyde solution were transferred into an accessioned cassette for dehydration, clearing and impregnation with paraffin and cut into tiny microscopic sections samples (4 µm thick). These paraffin sections were stained with Giemsa for histological evaluation of *H. pylori* presence.

Histological examination

Paraffin sections from biopsies sample prepared as indicated above were stained with Hematein and Eosin

for the histologic examination of the gastric mucosa features. The histological features encountered among participants were classified as normal mucosa (mucosal without injury), chronic gastritis, atrophic body gastritis, intestinal metaplasia, dysplasia and gastric cancer.

Study of oxidative stress

Determination of serum catalase activity (CAT)

Initially, the total protein content in the serum was determined according to the method described by Gornall using the bovine serum albumin as the standard [23]. The absorbance was read at 540 nm.

The enzymatic activity of catalase was assessed by the decrease of the hydrogen peroxide concentration in the spectrophotometer absorbance at 240 nm [24]. A hydrogen peroxide substrate solution 50 mM was prepared with 0.1 mM phosphate buffer, pH 7.4 (750 μ l). Then 50 μ l of serum was mixed with 200 μ l of substrate solution and incubated at 25°C for 1 minute. The potassium dichromate in glacial acetic acid was added at the end and the absorbance was read at 240 nm in a spectrophotometer. The catalase activity was expressed in mM of hydrogen peroxide/min/ mg of total protein.

Determination of Serum Glutathione (GSH)

Glutathione (GSH) concentration in the samples was determined using the Ellman's reagent [25]. 80 μ l of distilled water and 20 μ l of 50% trichloroacetic acid were added into 100 μ l of serum for protein precipitation. After that, the sample was centrifuged 30 rpm for 15 min at 4°C. Then, 200 μ l aliquots of the supernatant were mixed with 200 μ l of 0.1M phosphate buffer, pH 6.5 and with 5 μ l of DTNB (5,5-dithiobis-2-nitro-benzoic acid). The mixture was homogenised for 40s and incubated for 60 minutes. The absorbance was read at 412 nm. The concentration of GSH was expressed in mol/g of protein.

Determination of serum level of malondialdehyde (MDA)

Malondialdehyde (MDA) concentration was determined by means of lipid peroxidation [26]. A mixture

solution was prepared with 250 μ l of serum, 125 μ l of 20% trichloroacetic acid and 250 μ l of 0.67% thiobarbituric acid in test tubes. The tubes were then covered using glass beads, heated to 90°C in a water bath for 10 minutes and the contain was centrifuged at 3000 rpm in room temperature for 15 minutes. The supernatant was collected and the absorbance read at 530 nm against the blank. Total serum concentration of MAD was expressed in mol/g of protein.

Determination of Serum Superoxide Dismutase (SOD) Activity

The activity of superoxide dismutase was determined based on its ability to inhibit the conversion of adrenaline to adrenochrome [27]. A volume of 1666 μ l of carbonate buffer (0.05 M, pH 10.2) was added to 134 μ l of serum sample in the test tube. The reaction was triggered by adding 200 μ l of adrenaline (0.3 mM) in each test tube and the absorbance read at 480 nm. The results were expressed as number of units of SOD per milligram of protein (U/ mg de protein).

Statistical analysis

Statistical data processing was carried out using the SPSS software (version 22.0). Agostino & Pearson omnibus normality test was used to see if the values of the studied parameters come from Gaussian distribution. The levels of GHS, CAT, SOD, and MAD were expressed in range, mean + standard deviation, median and interquartile range (IQR). Student's two-tailed t-test was used for pairwise comparison of groups. The level of significance was set at a P value ≤ 0.05 .

Results

Characteristics of the sample population

We examined 191 *H. pylori*-positive patients aged 15 to 88 years old (Mean 48.11 ± 17.42 years), among which 14 were with normal mucosa (Control group), 40 were patients with chronic gastritis, 69 were patients with atrophic body gastritis, 22 were patients with intestinal

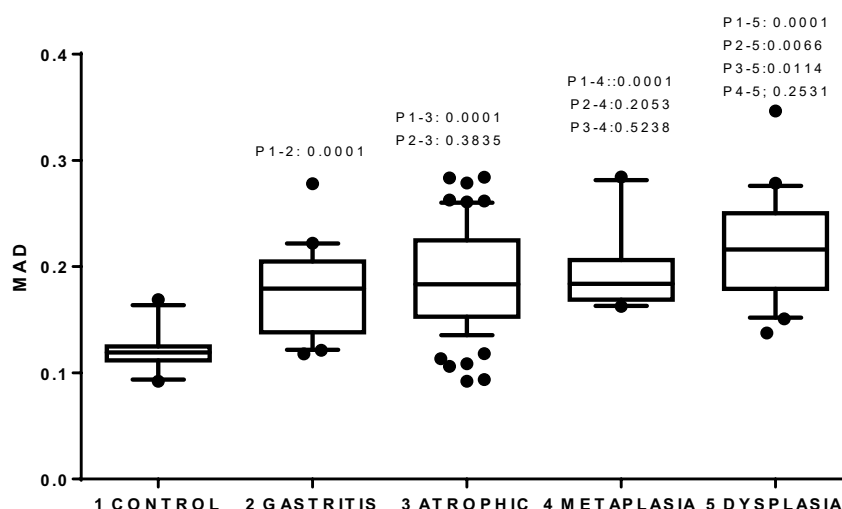


Figure 1. Content of Malondialdehyde (MAD) in the Blood Serum of Patients According to Precancerous Lesions. P-value for pairwise comparison within groups 1: Control, 2: Chronic gastritis, 3: Atrophic gastritis, 4: Intestinal metaplasia, 5: Dysplasia, *: significant.

Table 1. Repartition of the Study Population in Different Histological Features Group according to Sociodemographic and Lifestyle Characteristics

Variable	Number	Control n=14	Chronic gastritis n=40	Atrophic gastritis n=69	Intestinal metaplasia n=22	Dysplasia n=46	P-value
Age (years), Mean $\pm$ SD	48.11 $\pm$ 17.42	45.43 $\pm$ 14.11	49.55 $\pm$ 20.26	47.19 $\pm$ 17.23	50.91 $\pm$ 17.28	49.09 $\pm$ 17.46	0.93
$\leq$ 50 years n(%)	102(53.40)	6 (5.88)	22 (21.57)	38 (37.25)	10 (9.80)	26 (25.49)	
$>$ 50 years n(%)	89 (46.60)	8 (8.99)	18 (20.22)	31 (34.83)	12 (13.48)	20 (22.47)	
p-value			0.68	0.7	1	0.67	
Gender n(%)							
Male	96(50.26)	10 (71.43)	20 (50.00)	32 (43.38)	8 (36.36)	26 (56.52)	
Female	95(49.74)	4 (28.57)	20 (50.00)	37 (56.62)	14 (63.64)	20 (43.48)	
p-value			0.16	0.09	0.04*	0.32	
Alcohol consumption n(%)							
Yes	106 (55.50)	10 (71.43)	22 (55.00)	36 (52.17)	16 (72.73)	28 (60.87)	
No	85 (44.50)	4 (28.57)	18 (45.00)	33 (47.84)	6 (27.27)	18 (39.13)	
p-value			0.28	0.19	0.93	0.12	
Smoking n(%)							
Yes	15 (7.85)	2 (14.29)	2 (5.00)	7 (10.14)	2 (9.09)	2 (4.35)	
No	176(92.15)	12 (85.71)	38 (95.00)	62 (89.86)	20 (90.91)	44 (95.65)	
p-value			0.25	0.65	0.63	0.19	
Income level n(%)							
Low	91 (47.64)	8 (57.14)	16 (40.00)	31 (44.92)	12 (54.55)	22 (47.83)	
High	100 (53.36)	6 (42.86)	24 (60.00)	38 (55.08)	10 (45.45)	24 (52.13)	
p-value			0.27	0.4	0.7	0.54	

N, n: Number, p-value comparing the frequency of individual from each premalignant state to those from the control group, *, significant

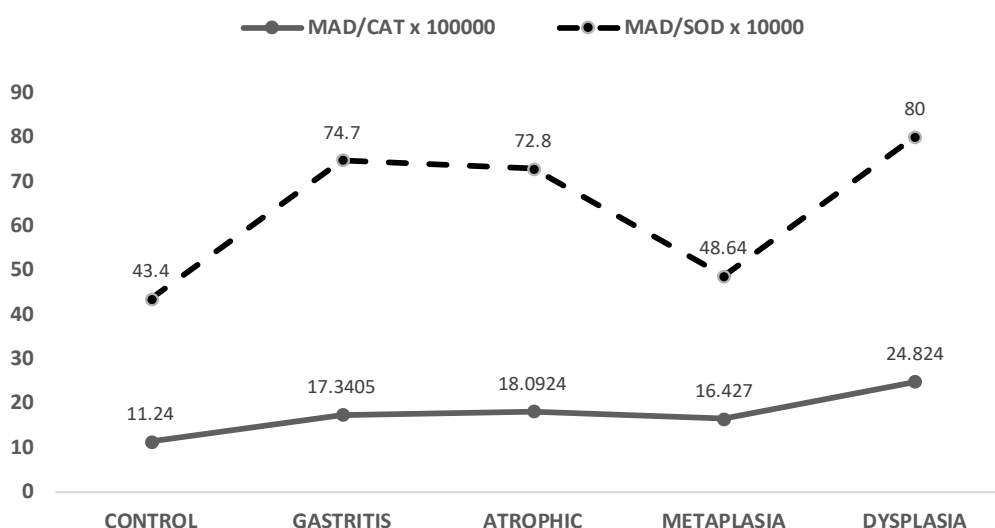


Figure 2. Dynamic MAD/SOD and MAD/CAT Ratios in the Studied Precancerous Groups

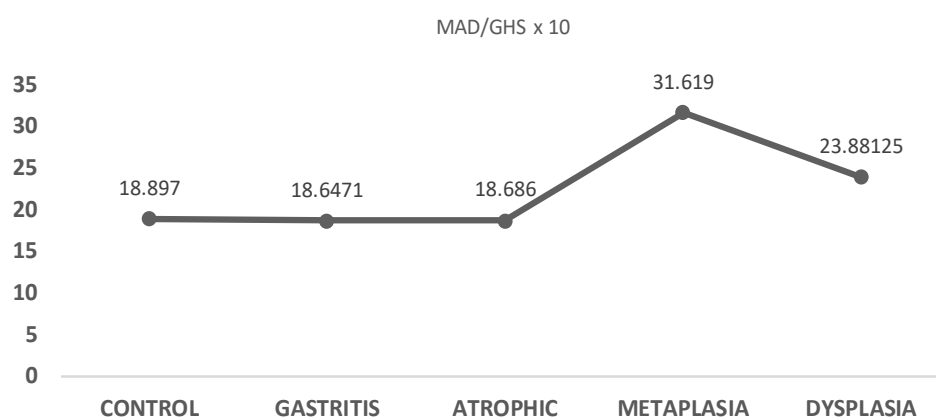


Figure 3. Dynamic MAD/GHS Ratio in the Studied Precancerous Groups

metaplasia, 46 were patients with dysplasia.

Approximately 54 percent (53.40) of our sample population were aged less than fifty years old, 50.26% were male, 55.50% used to consume alcohol frequently, 53.36% were with high level income, few of them were smokers (7.85%) (Table 1).

Distribution of oxidative stress indicators according to the characteristics of the population

The highest MDA contents were noticed among participants with low income and smokers with a significant difference ($P = 0.03$) and a marginal one ($P = 0.05$) respectively (Table 2).

Median (25th percentile-75th percentile) value of oxidative indicators according to the precancerous lesions

The higher level of GSH were among patients with gastric mucosa injury in comparison with patients from the control group with a significant p-value regarding chronic gastritis ($P = 0.03$), atrophic gastritis ($P = 0.04$), and dysplasia ($P = 0.01$). We also noticed a significant

lower GSH level among patients with chronic gastritis compared to those with metaplasia ($P = 0.04$), and those with dysplasia ($P = 0.01$) (Table 3). Compared to patients in the control group, SOD activity was significantly higher only among patients with intestinal metaplasia ($P = 0.049$), (Table 3). Catalase activity increase within patients with gastric injury compared to those in the control group although the difference were not significant ($P > 0.05$). Activities of catalase and SOD showed a similar dynamism pattern with the progression in gastric malignancy (Table 3).

The content of lipid peroxidation products in the serum was significantly increased in patients with gastric premalignant state in comparison with the control group ($P < 0.0001$). Among patients with gastric pre-malignancies, patients with dysplasia had a significant higher level of MDA in the serum in comparison with patient in chronic gastritis ($P = 0.01$) or atrophic gastritis group ($P = 0.01$) (Figure 1).

The lowest ratio of MDA/SOD and MDA/CAT was noticed in patients with metaplasia compared to patients

Table 2. Distribution of Serum GHS Concentration, MAD Concentration, CAT Activity, and SOD Activity According to the Characteristic of the Study Population

Variables	SOD	CAT	GHS	MAD
Age ≤ 50 years				
Yes	22.34 (12.25- 33.65)	1019 (763.7- 1215)	0.07220(0.05572-0.1091)	0.1788 (0.1537- 0.2343)
No	26.57 (15.03- 41.00)	1011 (825.9- 1260)	0.08071 (0.06095- 0.1220)	0.1819(0.1512- 0.2173)
t-value (p-value)	1.775 (0.0782)	0.2787 (0.7809)	0.1995(0.8422)	0.8303 (0.4079)
Gender				
Male	24.76 (15.97- 37.34)	985.5 (796.3- 1190)	0.08499 (0.06482- 0.1139)	0.1852 (0.1510- 0.2271)
Female	24.52 (9.879- 37.95)	1055 (804.2- 1291)	0.06842 (0.05041- 0.1211)	0.1720 (0.1520- 0.2144)
t-value (p-value)	0.5914(0.5553)	0.9829 (0.3275)	0.8104 (0.4192)	0.1908(0.8490)
Alcohol consumption				
Yes	25.24 (15.49- 37.58)	1052 (770.5- 1351)	0.07719 (0.05511- 0.1132)	0.1786 (0.1490- 0.2126)
No	23.31 (9.758- 37.58)	1001 (827.8- 1171)	0.07786 (0.06154- 0.1225)	0.1799 (0.1538- 0.2318)
t-value (p-value)	0.8075 (0.4209)	1.338 (0.1833)	0.4205 (0.6748)	1.098 (0.2741)
Smoking				
Yes	24.64 (15.49-35.78)	1178 (935.4- 1278)	0.06514 (0.04032- 0.1015)	0.1551 (0.1434- 0.1713)
No	21.41 (13.02- 38.63)	1011 (796.3- 1236)	0.07752 (0.05736- 0.1146)	0.1833 (0.1536- 0.2221)
t-value (p-value)	0.4203 (0.6749)	0.09563 (0.9240)	0.6055 (0.5459)	1.973 (0.0506)
Income level				
Low	24.76 (14.86- 40.85)	1056 (853.1- 1277)	0.08499 (0.06258- 0.1153)	0.1904 (0.1567- 0.2293)
High	24.52 (12.90- 35.89)	993.5 (764.7- 1206)	0.07099 (0.05418- 0.1099)	0.1689 (0.1472- 0.2020)
t-value (p-value)	0.7136(0.4767)	1.238 (0.2072)	0.8789 (0.3811)	2.205 (0.029*)

Data presented as median (25th percentile- 75th percentile), SOD, Superoxide dismutase; GHS, Glutathione reductase; CAT, Catalase; MAD, Malondialdehyde; *, significant.

Table 3. Comparison of Serum GHS Concentration, CAT Activity, and SOD Activity between Studied Precancerous Groups

Variables	Total value	Control n=14	Chronic gastritis n=40	Atrophic gastritis n= 69	Intestinal metaplasia n= 22	Dysplasia n=46
SOD	24.76(14.11-38.31)	21.20(19.09-38.84)	23.16(10.61-33.57) P1-2:0.39	25.24(10.00-37.58) P1-3:0.65 P2-3: 0.61	40.42(23.06-55.00) P1-4:0.04* P2-4:0.004* P3-4 :0.006*	24.76(16.29-37.10) P1-5: 0.87 P2-5:0.43 P3-5:0.73 P4-5: 0.02*
CAT	1023(823.12-1264)	983.9(859.6-1315)	1032.74(722.50-1280.73) P1-2:0.65	1029.85(870.85-1198.47) P1-3:0.61 P2-3:0.82	1110.3(941.83-1277.89) P1-4:0.95 P2-4:0.78 P3-4:0.77 P4-5:0.86	985.5(737.37-1241.88) P1-5: 0.73 P2-5:0.83 P3-5:0.94 P4-5:0.86
GHS	0.081180(0.05911-0.1180)	0.06074(0.05070-0.07462)	0.0823(0.06444-0.1192) P1-2: 0.03*	0.07786(0.06212-0.1215) P1-3:0.045* P2-3: 0.72	0.05575(0.04122-0.07254) P1-4: 0.82 P2-4: 0.045* P3-4: 0.06 P4-5: 0.015*	0.0918(0.05571-0.1148) P1-5: 0.006* P2-5: 0.76 P3-5: 0.51 P4-5: 0.015*

Data presented as median (25th percentile-75th percentile), P-value for pairwise comparison within groups 1: Control, 2: Chronic gastritis, 3: Atrophic gastritis, 4: Intestinal metaplasia, 5: Dysplasia, SOD: Superoxide dismutase, GHS: Glutathione reductase, CAT, Catalase; MAD, Malondialdehyde; *, significant.

in the others pre-malignancies groups, and this ratio was similar to the ratio from the controls (Figure 2). In contrast to MDA/SOD and MDA/CAT, the highest ratio of MDA/GSH was recorded in patients with metaplasia compared to those in the others pre-malignancies groups, and this ratio was 2 to 3 time high than the ratio value in control and atrophic groups (Figure 3).

Discussion

In this study, we evaluated the activity of two antioxidant protective enzymes (SOD and CAT), the levels of a free radical scavenger named glutathione (GSH), and the levels of malondialdehyde (MDA), a product of lipid peroxidation, in gastric precancerous lesions among *H. pylori* infected patients.

Our finding showed that, GSH levels were significantly higher among patients with chronic gastritis ($P = 0.03$), atrophic gastritis ($P = 0.04$), and dysplasia ($P = 0.01$) compared to those in the control group. Such observation indicate that the production of ROS and oxidative stress surges with gastric injury, as illustrated by the elevated level of GSH. Farinati et al. [28] reported an increased turnover of glutathione in patients with *H. pylori* infection. However, our finding regarding GSH levels is not in agreement with the studies of others, reporting a significant lower GSH levels ($P = 0.001$) in patients with gastric mucosa injury than in controls [29, 30], or among *H. pylori* infected patients than in uninfected patients [31]. The authors suggested that this depletion in gastric GSH may be due to the failure of antioxidant defense system.

SOD activity increase with gastric mucosa injury and reach a peak among patients with intestinal metaplasia ($P = 0.05$). A similar profile was noticed regarding catalase activity within patients with gastric mucosa injury compared to those in the control group. Since these enzymes are produced to neutralize or prevent free radicals formation, their higher activity is indicative of the excessive ROS formation and oxidative stress in relation to gastric injury. Similarly, catalase and superoxide dismutase activities were significantly higher among first-degree relatives of gastric cancer patients [30]. Morishita et al., found in their study that the levels of catalase, and superoxide dismutase were higher in *H. pylori* infected patients compared to uninfected ones [31].

The concentration of MDA significantly increase in patients with gastric mucosa injury compared to those of the control group ($P < 0.0001$ for all). Such observation indicate a high production of ROS and oxidative stress in patients with gastric injury. Our finding is in accordance with previous studies showing a significant higher concentration of MDA ($P = 0.04$) among patients with duodenitis associated to *H. pylori* infection compared to those without *H. pylori* infection [29]. Also, a significant higher tissue level of malondialdehyde was reported in patients with *H. pylori* infection than in uninfected patients [28, 31].

H. pylori infection lead to a condition of continuously overproduction of ROS and oxidative stress, which induce changes in cellular macromolecules such as DNA strand breaks thereby contributing to genomic instability and

carcinogenesis [32, 33]. In agreement, oxidative stress and DNA damage mostly occur in *H. pylori* infected cell with DNA repair mechanisms deficiencies [32, 33]. Similarly, studies have shown an increase of a marker of repair for double-strand DNA breaks, after *H. pylori* infection [34]. Also, *H. pylori* infected mice with deficiency in base excision repair mechanism were more prone to develop gastric lesions [35].

In conclusion, our findings showed that oxidative stress status is higher in *H. pylori* positive patients with precancerous lesions and that the degree of oxidative stress increase with the progression of gastric mucosal injury to malignancy.

Author Contribution Statement

KMLB conceived of the study, designed the experiments and supervised the work. NTI, NG, TSM, and TP recruited the participants, performed their physical examination and collected biopsy samples from participants. MM-NCM performed the histological examination. KMLB, FNGF and TNLD carried out the analysis. KMLB drafted the manuscript. All the authors read and approved the final manuscript

Acknowledgements

Ethical consideration

Participation was voluntary and a written informed consent was obtained from all the participants before inclusion. The protocol was approved by the local Ethical Committee of Medical Sciences from health facility (Approval 2330/L/MINSANTE/SG/DRSPO/HRB/D, 07-19/HGY/DG/DPM/NC-TR, and 01-19CMC/ TSM/ LMS/ AutoRech /2019/10/03) and from the National Ethical Committee on Human Health Research in Cameroon (Approval 1476/ CE/CNERSH/SP).

Data availability

The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

Conflict of interests

The authors declare no competing interests.

References

1. Faujo Nintewoue Ghislaine Florice and Kouitcheu Mabeku Laure Brigitte. Helicobacter pylori infection promotes gastric premalignancies and malignancies lesions and demotes hyperplastic polyps: a 5 year multicentric study among Cameroonian. Asian Pac J Cancer Prev. 2023; 24(1): 171-183.
2. Tali Nguefak LD, Faujo Nintewoue GF, Stanley NN, Talla P, Ngatcha G, Tagni SM, et al. Endoscopic mucosal phenotypes and endoscopic sydney system gastritis assessment in relation to helicobacter pylori infection and upper digestive clinical signs: A 2-year study among patients with gastroduodenal disorders in cameroon. JGH Open. 2024;8(5):e13060. <https://doi.org/https://doi.org/10.1002/jgh3.13060>.

3. Bray F, Ferlay J, Soerjomataram I, Siegel RL, Torre LA, Jemal A. Global cancer statistics 2018: Globocan estimates of incidence and mortality worldwide for 36 cancers in 185 countries. *CA cancer j clin*. 2018;68(6):394-424. <https://doi.org/10.3322/caac.21492>.
4. Correa P. Gastric cancer: Overview. *Gastroenterol Clin North Am*. 2013;42(2):211-7. <https://doi.org/10.1016/j.gtc.2013.01.002>.
5. Florice F, Danny T, Ngemeshe S, Paul T, Moungo-Ndjole C, Michele T, et al. Prevalence of helicobacter pylori and histopathological features of gastric biopsies from patients with dyspeptic symptoms in cameroon: A contraindication of african enigma. *Int J Biol*. 2025;17:1. <https://doi.org/10.5539/ijb.v17n1p1>.
6. Faujo Nintewoue GF, Tali Nguefak LD, Ngatcha G, Tagni SM, Talla P, Menzy Moungo-Ndjole CM, Kouitcheu Mabeku LB. *Helicobacter pylori* infection—A risk factor for lipid peroxidation and superoxide dismutase over-activity: A cross-sectional study among patients with dyspepsia in Cameroon. *Journal of gastroenterology and Hepathology*. 2023 Sep;7(9):618-28.
7. Holcombe C. *Helicobacter pylori*: The african enigma. *Gut*. 1992;33(4):429-31. <https://doi.org/10.1136/gut.33.4.429>.
8. Jones DP. Redefining oxidative stress. *Antioxid Redox Signal*. 2006;8(9-10):1865-79. <https://doi.org/10.1089/ars.2006.8.1865>.
9. Birben E, Sahiner UM, Sackesen C, Erzurum S, Kalayci O. Oxidative stress and antioxidant defense. *World Allergy Organ J*. 2012;5(1):9-19. <https://doi.org/10.1097/WOX.0b013e3182439613>.
10. Ighodaro OM, Akinloye OA. First line defence antioxidants-superoxide dismutase (sod), catalase (cat) and glutathione peroxidase (gpx): Their fundamental role in the entire antioxidant defence grid. *Alexandria J Med*. 2018;54(4):287-93. <https://doi.org/10.1016/j.ajme.2017.09.001>.
11. Mironczuk-Chodakowska I, Witkowska AM, Zujko ME. Endogenous non-enzymatic antioxidants in the human body. *Adv Med Sci*. 2018;63(1):68-78. <https://doi.org/10.1016/j.advms.2017.05.005>.
12. Fritz KS, Petersen DR. An overview of the chemistry and biology of reactive aldehydes. *Free Radic Biol Med*. 2013;59:85-91. <https://doi.org/10.1016/j.freeradbiomed.2012.06.025>.
13. Koike K. Hepatitis c virus contributes to hepatocarcinogenesis by modulating metabolic and intracellular signaling pathways. *J Gastroenterol Hepatol*. 2007;22 Suppl 1:S108-11. <https://doi.org/10.1111/j.1440-1746.2006.04669.x>.
14. Matés JM, Sánchez-Jiménez FM. Role of reactive oxygen species in apoptosis: Implications for cancer therapy. *Int J Biochem Cell Biol*. 2000;32(2):157-70. [https://doi.org/10.1016/s1357-2725\(99\)00088-6](https://doi.org/10.1016/s1357-2725(99)00088-6).
15. Felley CP, Pignatelli B, Van Melle GD, Crabtree JE, Stolte M, Diezi J, et al. Oxidative stress in gastric mucosa of asymptomatic humans infected with helicobacter pylori: Effect of bacterial eradication. *Helicobacter*. 2002;7(6):342-8. <https://doi.org/10.1046/j.1523-5378.2002.00107.x>.
16. Ishidate T, Igarashi S, Kamatani N. Pseudodominant transmission of an autosomal recessive disease, adenine phosphoribosyltransferase deficiency. *J Pediatr*. 1991;118(1):90-1. [https://doi.org/10.1016/s0022-3476\(05\)81854-2](https://doi.org/10.1016/s0022-3476(05)81854-2).
17. Klaunig JE, Kamendulis LM, Hoocevar BA. Oxidative stress and oxidative damage in carcinogenesis. *Toxicol Pathol*. 2010;38(1):96-109. <https://doi.org/10.1177/0192623309356453>.
18. Collodel G, Moretti E, Micheli L, Menchiari A, Moltoni L, Cerretani D. Semen characteristics and malondialdehyde levels in men with different reproductive problems. *Andrology*. 2015;3(2):280-6. <https://doi.org/10.1111/andr.297>.
19. Dąbrowska N, Wiczowski A. Analytics of oxidative stress markers in the early diagnosis of oxygen DNA damage. *Adv Clin Exp Med*. 2017;26(1):155-66. <https://doi.org/10.17219/acem/43272>.
20. Chiorcea-Paquim AM, Oliveira-Brett AM. Nanostructured material-based electrochemical sensing of oxidative DNA damage biomarkers 8-oxoguanine and 8-oxodeoxyguanosine: A comprehensive review. *Mikrochim Acta*. 2021;188(2):58. <https://doi.org/10.1007/s00604-020-04689-7>.
21. Coskun C, Kural A, Döventas Y, Koldas M, Ozturk H, Inal BB, et al. Hemodialysis and protein oxidation products. *Ann N Y Acad Sci*. 2007;1100:404-8. <https://doi.org/10.1196/annals.1395.045>.
22. Dalle-Donne I, Rossi R, Giustarini D, Milzani A, Colombo R. Protein carbonyl groups as biomarkers of oxidative stress. *Clin Chim Acta*. 2003;329(1-2):23-38. [https://doi.org/10.1016/s0009-8981\(03\)00003-2](https://doi.org/10.1016/s0009-8981(03)00003-2).
23. Gornall AG, Bardawill CJ, David MM. Determination of serum proteins by means of the biuret reaction. *J Biol Chem*. 1949;177(2):751-66.
24. Sinha AK. Colorimetric assay of catalase. *Anal Biochem*. 1972;47(2):389-94. [https://doi.org/10.1016/0003-2697\(72\)90132-7](https://doi.org/10.1016/0003-2697(72)90132-7).
25. Sedlak J, Lindsay RH. Estimation of total, protein-bound, and nonprotein sulfhydryl groups in tissue with ellman's reagent. *Anal Biochem*. 1968;25(1):192-205. [https://doi.org/10.1016/0003-2697\(68\)90092-4](https://doi.org/10.1016/0003-2697(68)90092-4).
26. Wilbur K, Bernhein F, Shapiro O. Determination of lipid peroxidation. *Archives of Biochemistry and Biophysics*. 1949;24:3959-3964.
27. Misra H, Fridovich I. Determination of the level of superoxide dismutase in whole blood. Yale University Press New Haven. 1972;166:101-109.
28. Farinati F, Cardin R, Libera GD, Rugge M, Herszényi L, Di Mario F, et al. Determinants for the development of chronic atrophic gastritis and intestinal metaplasia in the stomach. *Eur J Cancer Prev*. 1995;4(2):181-6. <https://doi.org/10.1097/00008469-199504000-00009>.
29. Amal S, Abhijit C, Sujit CJ, Das GPK, Banerjee ND, Guha M. Oxidase stress in gastric mucosa in *H. pylori* infection. *Indian journal of gastroenterology*. 2000;19:21-23.
30. Braga-Neto MB, Costa DVS, Queiroz DMM, Maciel FS, de Oliveira MS, Viana-Junior AB, et al. Increased oxidative stress in gastric cancer patients and their first-degree relatives: A prospective study from northeastern brazil. *Oxid Med Cell Longev*. 2021;2021:6657434. <https://doi.org/10.1155/2021/6657434>.
31. Morishita K, Takeuchi H, Morimoto N, Shimamura T, Kadota Y, Tsuda M, et al. Superoxide dismutase activity of helicobacter pylori per se from 158 clinical isolates and the characteristics. *Microbiol Immunol*. 2012;56(4):262-72. <https://doi.org/10.1111/j.1348-0421.2012.00433.x>.
32. Koepfel M, Garcia-Alcalde F, Glowinski F, Schlaermann P, Meyer TF. *Helicobacter pylori* infection causes characteristic DNA damage patterns in human cells. *Cell Rep*. 2015;11(11):1703-13. <https://doi.org/10.1016/j.celrep.2015.05.030>.
33. Machado AM, Figueiredo C, Touati E, Máximo V, Sousa S, Michel V, et al. *Helicobacter pylori* infection induces genetic instability of nuclear and mitochondrial DNA in gastric cells. *Clin Cancer Res*. 2009;15(9):2995-3002. <https://doi.org/10.1158/1078-0432.Ccr-08-2686>.
34. Kidane D, Murphy DL, Sweasy JB. Accumulation of abasic sites induces genomic instability in normal human

- gastric epithelial cells during helicobacter pylori infection. *Oncogenesis*. 2014;3(11):e128. <https://doi.org/10.1038/oncsis.2014.42>.
35. Meira LB, Bugni JM, Green SL, Lee CW, Pang B, Borenshtein D, et al. DNA damage induced by chronic inflammation contributes to colon carcinogenesis in mice. *J Clin Invest*. 2008;118(7):2516-25. <https://doi.org/10.1172/jci35073>.



This work is licensed under a Creative Commons Attribution-Non Commercial 4.0 International License.