P53 protein and Ki-67 expression in chronic gastritis patients with positive Helicobacter pylori infection

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1. Introduction

Helicobacter pylori (HP) infection is one of the most common chronic infections worldwide. Half of the global population is infected by HP [6]. Chronic inflammation with H. pylori infection leads to mucosal atrophy and intestinal metaplasia, conditions that are believed to be precursors of gastric cancer [6,12]. The development of gastric cancer has been shown to be a multi-step process, ranging from chronic gastritis to atrophy, intestinal metaplasia, dysplasia and finally gastric cancer [9]. Both gastric atrophy and intestinal metaplasia are considered...
to be premalignant stomach cancer lesions [10]. Chronic colonization establishes sustained insult to the gastric mucosa, and hyper-proliferation of gastric epithelium in response to injury. This in turn increases the risk of DNA damage (mutations), epigenetic and morphological changes (intestinal metaplasia, dysplasia), loss of responsiveness to apoptotic signals and, presumably, emergence of a clone of malignant cells that develop into gastric cancer [7]. Expression of p53 protein is an early event in tumorigenesis as observed in minute intramucosal gastric adenocarcinoma [9,1]. P53 is an important prognostic factor in early gastric carcinoma [4].

Increased epithelial cell proliferation has also been observed in H. pylori-associated gastritis, atrophic gastritis, and gastric cancer [5]. Imbalance in epithelial cell proliferation and apoptosis may be involved during the early stages of malignant transformation [8]. The expression of the human Ki-67 protein is strictly associated with cell proliferation. Because the Ki-67 protein is present during all active phases of the cell cycle, but is absent from resting cells, it makes an excellent marker for cell proliferation [13,6].

The aim of study was to investigate the mucosal expression of mutant p53 protein in association with proliferative (Ki-67) markers in patients with atrophic gastritis secondary to H. pylori infection.

2. Material and methods

At the Gastrointestinal clinic in the National Hepatology and Tropical Medicine Research Institute, the twenty dyspeptic patients were subjected to full history taking including gastrointestinal symptoms and both general and local abdominal examination and upper oesophago-gastroduodenoscopy (GOD) and multiple antral biopsies (after stopping any Proton Pump Inhibitor and antibiotics for at least 4 weeks) as well as full routine labs.

Gastric antral biopsies were pathologically assessed in 20 dyspeptic patients with helicobacter infection. Epithelial proliferative activity (Ki-67) and p53-expression were examined quantitatively with cell counting after immunohistochemical staining.

3. Statistical methods

Categorical variables were expressed by number and percent. Absence or presence of expression of P53 and/or Ki67 was assessed with or without histopathological changes in the studied patients using Chi-square test or Fischer’s exact test when appropriate. Kendal–tau c values were calculated to assess such ordinal association. In all tests, P value was considered significant if less than 0.05.

4. Results

Patients mean age was 53 ± 5.1 with male to female ratio 1.75:1. Biopsies from 20 patients with H. pylori infection were included in the study. Inflammatory gastritis, intestinal activity, intestinal metaplasia, atrophy and dysplasia were diagnosed in 20%, 14%, 8%, 10% and 6%, respectively. There was no significant association between the expression of Ki67 and P53 in the studied cases. There was no significant association between Ki67 and P53 with intestinal atrophy, intestinal metaplasia, intestinal activity and intestinal inflammation. There was significant association between Ki67 and P53 with intestinal dysplasia, \( P = 0.015, 0.025 \), respectively. Ki67 and P53 were not age or sex dependent (Figs. 1–9).
Figure 4  There is no significant association between Ki67 and P53 with intestinal activity.

Figure 5  There is no significant association between Ki67 and P53 with intestinal metaplasia. Though expression of Ki67 is approaching significance with intestinal metaplasia ($P = 0.074$).

Figure 6  There is significant association between Ki67 and P53 with intestinal dysplasia. $P = 0.015, 0.025$, respectively.

Figure 7  There is no significant association between Ki67 and P53 with intestinal atrophy.
5. Discussion

In our study the patients’ mean age was 53 ± 5.1 with male to female ratio 1.75:1. Mbulaiteye et al. [7] reported in his study a range of age 55–81 years and male to female ratio 5:6.

Inflammatory gastritis, intestinal activity, intestinal metaplasia, atrophy and dysplasia were diagnosed in 20%, 14%, 8%, 10% and 6%, respectively. Mbulaiteye et al. [7] claimed that infection rates peak at 80–100% during adolescence, and may persist throughout life, particularly in less developed countries. By contrast, in developed countries infection is acquired later in childhood or adolescence, is cleared in about 10% of cases, and peaks at 50–70% during young adulthood.

There was no significant association between P53 and Ki67 in presence of atrophy ($P = 0.01$) or metaplasia. This is in accordance with Niimi et al. [9] and Waluga et al. [11] who hypothesized that over expression of p53, and Ki-67 is not specific neither for mucosal atrophy nor metaplasia. On the contrary, Kim et al. [6] reported that Ki-67 was significantly correlated with intestinal inflammation, intestinal metaplasia and atrophy.

There was significant association between Ki67 and P53 in presence of intestinal dysplasia this coincides with the findings of Choi et al. [3] who found that the high expressions of Ki-67 and p53 in gastritis may be one of the main mechanisms in the development of gastric carcinoma. Brajsa et al. [2] hypothesized that long persisting infection is related with higher colonization grades of bacteria, p53 and Ki-67 expression.

6. Conclusion

The high expressions of the proliferative marker Ki-67 and apoptotic marker p53 protein in gastritis may be one of the main mechanisms in the development of gastric carcinoma.

References