

A study of human epidermal growth factor receptor 2 overexpression by immunohistochemistry in patients with gastric adenocarcinoma

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Abstract. Gastric cancer is one of the leading causes of cancer-related deaths across the world and in the Middle East. Human epidermal growth factor receptor 2 (HER2) overexpression has been observed in gastric cancers. Trastuzumab, a recombinant monoclonal antibody targeting HER2 protein, is being used for treatment of metastatic gastric cancer. To study the frequency and association of HER2 overexpression with age, gender, histopathological subtype and grade of differentiation in patients with gastric adenocarcinoma from Basra, Iraq. This cross-sectional single-center study collected demographic (age, gender), histopathological (histological subtype, grade of differentiation) and immunohistochemical (HER2 overexpression status) data from 100 consenting adult patients (male: 56) with histopathologically confirmed gastric adenocarcinoma from samples obtained through endoscopy or surgery. HER2 overexpression (ToGA score 3+) was observed in 6/100 (6%) of patients, with another 6 showing 'equivocal' HER2 expression (2+). Out of 20 patients with moderately differentiated gastric cancer, 4 (20%) showed HER2 overexpression (P=0.008). Other factors considered (age, gender, histological subtype) did not show statistically significant correlation with HER2 overexpression. More females showed HER2 overexpression than males (4 vs. 2), and more patients with intestinal type gastric cancer showed HER2 overexpression than diffuse gastric cancer (5 vs. 1), but the difference was not statistically significant in both variables. HER2 overexpression was 6% in this population; statistically significant correlation was found with histological grade. Statistically non-significant correlations were observed between HER2 overexpression and gender, age, and histological subtype.

Introduction

Gastric cancer is the fourth most common cancer worldwide, and ranks second among the most common causes of cancer-related deaths (1). Even in the Middle-East, gastric cancer is highly prevalent and is an important cause of mortality (2,3). A large proportion of patients with gastric cancer present at later stage, when the malignancy would have become metastatic and inoperable, and hence is associated with 5-year survival rates as low as 5-20%, and a low median overall survival of less than 1 year (4,5). Since surgery is the mainstay of treatment of gastric cancer, conventional chemotherapeutic options are also not beneficial for such patients with inoperable cancers (6,7).

In an effort to identify novel targets for better treatment options of patients with advanced gastric cancer, the role of human epidermal growth factor receptor 2 (HER2) came under scrutiny. The HER2 is a proto-oncogene encoded by *ERBB2* gene located on chromosome 17. The major role of HER2 is to suppress apoptosis and promote cell proliferation in the tissues where it is expressed, most notably breast, gastrointestinal tract, kidney, and heart. The net outcome of this action is to promote tumorigenesis by facilitating uncontrolled cell growth (8). Trastuzumab, which is a humanized monoclonal antibody targeting HER2 receptor has significantly improved the treatment outcomes of HER2-positive breast cancer (8). Subsequently, it was recognized that HER2 status has significance in severe forms of other cancers, notably gastric cancer. This led to the publication of landmark studies such as the Trastuzumab for Gastric Cancer (ToGA) trial in 2010 (9), which subsequently led to the approval of trastuzumab for the treatment of advanced gastric cancer with confirmed HER2 positivity status by means of immunohistochemistry (IHC) and/or fluorescent in-situ hybridization (FISH) technique (10).

There is a shortage in studies describing the frequency and clinico-pathological features with HER2 overexpression in Iraqi patients with gastric cancer. So, the study was designed to detect how frequent the HER2 overexpression in Iraqi patients with gastric cancer and its clinico-pathological correlation.

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