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### Immunohistochemical Human Epidermal Growth Factor Receptor 2 (HER2) Expression Pattern in Gastric Adenocarcinomas in a Nigerian Tertiary Hospital

*Expression Immunohistochimique du Récepteur 2 du Facteur de Croissance Épidermique Humain (HER2) dans les Adénocarcinomes Gastriques dans un Hôpital Tertiaire Nigérian*

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#### ABSTRACT

**BACKGROUND AND OBJECTIVE:** The demonstration of HER2 in gastric adenocarcinoma (GA) tissues by immunohistochemistry assists in deciding whether targeted therapy would optimise the treatment of GA patients who are HER2 positive. However, this has not been extensively studied in our patients hence the need for this study.

**METHODS:** Recipient tissue microarray blocks were constructed from donor archival formalin fixed paraffin embedded gastric tumour tissue from 80 patients seen over a period of 17 years in a retrospective descriptive study. Slides cut from these blocks were stained with anti-human HER2 antibody by immunohistochemistry and scored using the trastuzumab in gastric adenocarcinomas (ToGA) trial criteria. Data on age, gender, site of lesion and histological subtype of the gastric adenocarcinomas were also retrieved and reviewed.

**RESULTS:** Eighty cases (52 males and 28 females; male to female ratio of 1.9:1), 55.65 ± 13.50 years (modal age group 60-69 years), were studied. Most tumours (91.2%) involved the distal parts (pylorus, antrum and body) with a few (8.8%) involving the proximal part (cardia and fundus) of the stomach. HER2 was overexpressed in a total of 6 (7.5%) cases only. Two of seven (28.6%) proximal tumours showed HER2 positivity whereas only 4 of 73 (5.5%) of the distal tumours showed HER2 positivity.

**CONCLUSION:** We had only a slightly lower HER2 overexpression rate than in studies from many other parts of the world. The observed overexpression was significantly higher in proximal than distally located tumours suggesting that distal tumours are less likely to respond to Trastuzumab than proximal tumours. The known association of distal gastric tumours with *Helicobacter pylori* infection probably provides for a possible difference in the molecular aetiopathogenesis of GAs by site of occurrence. The exact mechanisms for proximal gastric carcinogenesis remain to be more clearly elucidated. More studies, including clinical trials with larger sample sizes, are recommended to elucidate this differential expression of HER2 in gastric adenocarcinoma.

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**KEYWORDS:** Gastric adenocarcinoma, HER2 expression, Immunohistochemistry, Targeted therapy.

#### RÉSUMÉ

**CONTEXTE ET OBJECTIF:** La démonstration de la présence de HER2 dans les tissus d'adénocarcinome gastrique (AG) par immunohistochimie aide à décider si une thérapie ciblée optimiserait le traitement des patients atteints d'AG HER2 positif. Cependant, cela n'a pas été largement étudié chez nos patients, d'où la nécessité de cette étude.

**MÉTHODES:** Des blocs de microarray de tissus destinataires ont été construits à partir de tissus tumoraux gastriques inclus en paraffine d'archives provenant de 80 patients vus sur une période de 17 ans, dans le cadre d'une étude descriptive rétrospective. Les lames découpées à partir de ces blocs ont été colorées avec un anticorps anti-HER2 humain par immunohistochimie et évaluées selon les critères de l'essai trastuzumab dans les adénocarcinomes gastriques (ToGA). Les données sur l'âge, le sexe, le site de la lésion et le sous-type histologique des adénocarcinomes gastriques ont également été récupérées et examinées.

**RÉSULTATS:** Quatre-vingts cas (52 hommes et 28 femmes ; rapport hommes-femmes de 1,9:1), 55,65 ± 13,50 ans (groupe d'âge modal 60-69 ans), ont été étudiés. La plupart des tumeurs (91,2 %) ont touché les parties distales (pylore, antrum et corps) avec quelques-unes (8,8 %) touchant la partie proximale (cardia et fundus) de l'estomac. HER2 a été surexprimé dans un total de 6 cas seulement (7,5 %). Deux des sept tumeurs proximales (28,6 %) ont montré une positivité HER2, tandis que seulement 4 des 73 tumeurs distales (5,5 %) ont montré une positivité HER2.

**CONCLUSION:** Nous avons eu un taux de surexpression de HER2 légèrement inférieur à celui observé dans de nombreuses autres régions du monde. La surexpression observée était significativement plus élevée dans les tumeurs proximales que dans les tumeurs distales, suggérant que les tumeurs distales sont moins susceptibles de répondre au trastuzumab que les tumeurs proximales. L'association connue des tumeurs gastriques distales avec l'infection par *Helicobacter pylori* fournit probablement une différence potentielle dans l'étiopathogénèse moléculaire des AG par site d'occurrence. Les mécanismes exacts de la carcinogénèse gastrique proximale restent à élucider plus clairement. Davantage d'études, y compris des essais cliniques avec des tailles d'échantillons plus importantes, sont recommandées pour élucider cette expression différentielle de HER2 dans l'adénocarcinome gastrique.

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**MOTS-CLÉS:** Adénocarcinome gastrique, expression de HER2, Immunohistochimie, Thérapie ciblée.

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**Abbreviations:** EGFR: Epidermal growth factor receptor; FFPE: Formalin fixed paraffin embedded; GA: Gastric adenocarcinoma; GEJ: Gastroesophageal junction; HER2, HER2/neu, ErbB-2 receptor, p185: Human epidermal growth factor receptor 2; TK: Tyrosine kinase; TKI: Tyrosine kinase inhibitor; TMA: Tissue microarray; ToGA: Trastuzumab in gastric adenocarcinomas