

# Usefulness of chorionic gonadotropin in premalignant gastric lesions

## Utilidad de la gonadotropina coriónica en lesiones premalignas gástricas

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### ABSTRACT

**Introduction:** knowledge of premalignant gastric lesions is crucial because only in this way can it be informed, educated, and a surveillance plan drawn up when they are diagnosed.

**Objective:** to evaluate the diagnostic value of chorionic gonadotropin as a tumor marker in premalignant gastric lesions in patients treated in the Gastroenterology service of the “Dr. Agostinho Neto” General Teaching Hospital. Guantánamo. January 2021 – January 2023.

**Method:** an analytical, longitudinal, prospective study was carried out in patients treated in the gastroenterology service.

**Results:** the elevated lesion predominated in 55,5 %, a greater number of patients with positive chorionic gonadotropin in 75,6 %, with high sensitivity of 92,3 % for dysplasia, specificity and positive predictive value of 100 % and high negative predictive value between 78,4 % and 90,5 %.

**Conclusions:** in the investigation, there was a predominance of the endoscopic finding of an elevated lesion, a greater number of patients with positive chorionic gonadotropin, and it turned out to be a marker with diagnostic value to be taken into account as a tool in premalignant gastric lesions.

### KEYWORDS

Premalignant Gastric Lesions; Chorionic Gonadotropin; Stomach Cancer.

### RESUMEN

**Introducción:** el conocimiento de las lesiones premalignas gástricas resulta crucial pues sólo de este modo se puede informar, educar y trazar un plan de vigilancia cuando se diagnostican.

**Objetivo:** evaluar el valor diagnóstico de la gonadotropina coriónica como marcador tumoral en lesiones premalignas gástricas en pacientes atendidos en el servicio de gastroenterología del Hospital General Docente “Dr. Agostinho Neto”. Guantánamo. Enero 2021- enero 2023

**Método:** se realizó un estudio analítico, longitudinal, prospectivo en pacientes atendidos en el servicio de gastroenterología.

**Resultados:** predominó la lesión elevada en el 55,5 %, mayor cantidad de pacientes con gonadotropina coriónica positiva en el 75,6 %, con sensibilidad alta de 92,3 % para displasia, especificidad y valor predictivo positivo de 100 % y valor predictivo negativo alto entre 78,4 % y 90,5 %

**Conclusiones:** en la investigación hubo predominio del hallazgo endoscópico lesión elevada, mayor cantidad

de pacientes con gonadotropina coriónica positiva y resultó ser marcador con valor diagnóstico a tener en cuenta como una herramienta en lesiones gástricas premalignas.

## PALABRAS CLAVE

Lesiones Gástricas Premalignas, Gonadotropina Coriónica, Cáncer Gástrico.

## INTRODUCTION

Gastric cancer is preventable, develops over the years, and is preceded by a series of so-called premalignant lesions, described in the Correa Cascade, ranging from atrophic gastritis, intestinal metaplasia, and gastric dysplasia, where genetic and environmental factors favor the process.<sup>(1,2,3,4,5,6)</sup>

Tumor markers (TM) are a non-invasive test that is simple, easy, and available to the population. They are the greatest achievement in accelerating the process of early diagnosis of cancer before any sign of cancer appears and even when the lesions that precede it point to its possible establishment.<sup>(7)</sup>

Human chorionic gonadotropin (HCG) is synthesized by the trophoblast and by some cells in the process of salinization. It is released into the bloodstream, a fluid in which it can be determined, especially the  $\beta$ -subunit (HCG- $\beta$ ), of great interest as a marker not only for diagnosis but also for monitoring treatment.<sup>(8,9,10)</sup>

Because it is specific for HCG, the  $\beta$ -subunit becomes the best means to measure the excess of the hormone in the blood. Its complexity, multiple and fascinating functions, and importance in gestation and tumor labeling make HCG a versatile and transcendental hormone in vital processes.<sup>(9,10,11)</sup>

Apart from pregnancy, normal tissues such as lung, liver, kidney, stomach, pituitary (in menopausal women), testis and heart extracts are minor producers of HCG. However, abysmal increases of the hormone in blood or urine only occur in the context of pregnancy or malignant cell neoplasia. For this reason, the measurement of hormones has been very useful in the diagnosis of pregnancy and its pathologies (ectopic pregnancies, threatened miscarriages, fetal abortions, etc.), screening for trisomies and infertility in both sexes, among others; in addition, its clinical use as a tumor marker, which is undoubtedly one of its most important clinical utilities.<sup>(12)</sup>

At present, there are no blood markers that can adequately identify the stages that a patient goes through until gastric cancer is reached, which makes it imperative to develop research in this area that seeks the identification of markers and their subsequent application in prevention campaigns of this terrible disease, in order to make an early diagnosis and increase the survival probabilities of these patients. That is why the present study aims to evaluate the diagnostic value of chorionic gonadotropin as a tumor marker in premalignant gastric lesions.

## METHODS

An analytical, longitudinal, prospective study was carried out on patients who attended the gastroenterology service of the General Teaching Hospital "Of Dr. Agostinho Neto." Guantánamo. January 2021- January 2023.

The universe consisted of all patients with suspected gastric premalignant lesions (atrophic gastritis, metaplasia, or dysplasia), from which a sample of 45 patients was selected by simple random sampling who met the inclusion criteria (patients over 18 years old, with endoscopic suspicion and histological confirmation of gastric premalignant lesion and presence of *Helicobacter pylori*).

An initial endoscopic study was performed in the Gastroenterology service, with the use of an Olympus CV-140 video endoscope, and the histopathological study was performed in the Anatomic Pathology service by the specialist in charge of the digestive tract program. The biopsy samples were studied with hematoxylin-eosin (diagnostic sensitivity 94 %), and the visual analog scale of the updated Sydney System was used to grade the histological variables of gastritis and the presence of premalignant lesions. Blood sampling was performed at the hospital's SUMA clinical laboratory using the Mindray BC-3200 automated hematology complex and Hitachi automated biochemical analyzer, respectively. For the determination of chorionic gonadotropin, the UMELISA HCG produced by the Immunoassay Center was used, which uses ultramicro ELISA strips (10  $\mu$ L per well) coated with monoclonal and polyclonal beta HCG antibodies as a solid phase. The information required for the investigation was extracted from the upper gastrointestinal endoscopy registry of the Gastroenterology department and the biopsy report logbooks of the Anatomic Pathology department. For LGP with more than one diagnosis by anatomic pathology, the most severe one was chosen. The UMELISA HCG result was collected from the results record book of the Clinical Laboratory department and entered into a voiding form designed for this purpose.

The variables were summarized in absolute numbers and proportions, expressed as percentages. To evaluate the

diagnostic value of chorionic gonadotropin as a tumor marker in gastric premalignant lesions, the sensitivity, specificity, and positive and negative predictive values were estimated because in the study performed, the gonadotropin variable was assumed to be qualitative, which is why, even when it is known that other methods exist, such as the ROC curve, it was not possible to use it because it is aimed at discriminating by establishing cut-off points when the variable is quantitative. The point estimates and confidence intervals were calculated from the following contingency table. The histological diagnosis, which defines premalignant gastric lesions, was taken as the reference test (rule of thumb). Estimates were made using the program Epidemiological Analysis of Tabulated Data EPIDAT 4.0.

Diagnosis (Chorionic Gonadotropin)	Premalignant gastric lesions		Total
	Positive	Negative	
Positive	a (True positives)	b (False positives)	a+b (Positive)
Negative	c (False negative)	d (True negatives)	c+d (Negative)
Total	a+c (Sick)	b+d (Not sick)	n

Sensitivity = True positives/Not sick

Specificity = True Negative/Not Sick

PPV = True Positive/Positive

NPV = True negative/Negative

The following were considered:

**True positives:** those patients tested positive for gastric premalignant lesions by chorionic gonadotropin, and that has been confirmed in the histological study.

**True negative:** those patients with negative chorionic gonadotropin for gastric premalignant lesions and no premalignant lesions are reported in the histological study.

**False positives:** those patients positive for gastric premalignant lesions by chorionic gonadotropin that have not been confirmed in the histological study.

**False negatives:** those patients who are not positive for gastric premalignant lesions by chorionic gonadotropin and in the histological study these lesions are reported.

A significance level  $\alpha = 0,05$  was prefixed to all hypothesis tests.

This research was adjusted to the Declaration of Helsinki of the World Medical Association, complying with the principles of the international code of medical ethics and the Cuban model, guaranteeing the confidentiality of the information obtained. The information collected was entered in a Microsoft Excel database.

## RESULTS

**Table 1.** Endoscopic findings and premalignant gastric lesions. "Dr. Agostinho Neto". January 2021 to January 2023

Endoscopic findings	Endoscopic findings						Total	
	Atrophic gastritis		Intestinal metaplasia		Dysplasia			
	N	%	N	%	N	%	N	%
Gastric ulcer	9	20	2	4,5	6	13,3	17	37,8
Elevated lesion	7	15,5	1	2,2	17	37,8	25	55,5
Vegetative lesion	0	0	0	0	3	6,7	3	6,7
Total	16	35,5	3	6,7	26	57,8	45	100

Table # 2 shows the advantage of the endoscopic finding of elevated lesions in 25 (55,5 %) patients, followed by gastric ulcers in 17 (37,8 %) patients and 3 (6,7 %) patients with vegetating lesions. When we compare the endoscopic findings and the LGP, we found that the elevated lesion continues to be the one with the highest incidence in dysplasia with 17 (37,8 %) patients, followed by a gastric ulcer with 6 (13,3 %) and then the vegetating lesion with 3 (6,7 %) patients; gastric ulcer stands out in atrophic gastritis with 9 (20 %) patients and in intestinal metaplasia with 2 (4,5%) patients, similar behavior of the elevated lesion for atrophic gastritis and intestinal metaplasia with 7 (15,5 %) and 1 (2,2 %) respectively.

**Table 2.** Diagnostic correlation between chorionic gonadotropin and premalignant gastric lesions. “Dr. Agostinho Neto”. January 2021 to January 2023

Premalignant gastric lesions	Chorionic gonadotropin			
	Positive		Negative	
	N	%	N	%
Atrophic gastritis	8	17,8	8	17,8
Intestinal metaplasia	2	4,5	1	2,2
Dysplasia	24	53,3	2	4,4
Total	34	75,6	11	24,4

When running the diagnostic correlation between chorionic gonadotropin and gastric premalignant lesions, where we can distinguish the preponderance of positive chorionic gonadotropin over negative in 34 (75,6 %) patients and 11 (24,4 %) patients respectively, in correspondence with LGP, we found that positive chorionic gonadotropin maintains the order in frequency given by 24 (53,3 %) patients with dysplasia, 8 (17,8%) patients with atrophic gastritis and 2 (4,5 %) with intestinal metaplasia. In the case of negative chorionic gonadotropin, another order is established where atrophic gastritis is in first place with 8 (17,8 %) patients, in second place dysplasia with 2 (4,4%), and third place intestinal metaplasia with 1 (2,2 %) patient.

When investigating the diagnostic correlation between chorionic gonadotropin and endoscopic findings, the same information was maintained in relation to chorionic gonadotropin. However, when compared with endoscopic findings, positive chorionic gonadotropin is higher in the elevated lesion with 18 (40 %) patients, followed by a gastric ulcer with 13 (28,9 %) patients and vegetating lesion with 3 (6,7 %) patients. On the other hand, negative chorionic gonadotropin shows elevated lesions also in first-order with 7 (15,5 %) patients and second-order gastric ulcer with 4 (8,9 %) patients.

**Table 3.** Diagnostic correlation between chorionic gonadotropin and endoscopic findings. “Dr. Agostinho Neto”. January 2021 to January 2023

Endoscopic findings	Chorionic gonadotropin			
	Positive		Negative	
	N	%	N	%
Gastric ulcer	13	28,9	4	8,9
Elevated lesion	18	40	7	15,5
Vegetative lesion	3	6,7	0	0
Total	34	75,6	11	24,4

Validity indicators to evaluate the usefulness of the tumor marker chorionic gonadotropin in the diagnosis of premalignant gastric lesions.

For the diagnosis of premalignant gastric lesions using the chorionic gonadotropin marker, the sensitivity was high for dysplasias (92,3) and relatively high for intestinal metaplasia (66,7), and for atrophic gastritis only in 50,0 % of patients. In contrast, the specificity is very high (100 %) in all gastric premalignant lesions.

The positive predictive value of the chorionic gonadotropin marker for diagnosis was very high, and the negative predictive value was high for all three gastric premalignant lesions.

**Table 4.** Validity indicators of the result obtained by the chorionic gonadotropin tumor marker in the diagnosis of premalignant gastric lesions. “Dr. Agostinho Neto”. January 2021 to January 2023.

Indicators	Atrophic gastritis	Intestinal metaplasia	Dysplasia
	Point estimate IC (95 %)	Point estimate IC (95 %)	Point estimate IC (95 %)
Sensitivity	50,0 (22,4 - 77,6)	66,7 (0,00 - 100,0)	92,3 (80,1 - 100,0)
Specifity	100,0 (98,3 - 100,0)	100,0 (98,8 - 100,0)	100,0 (97,4 - 100,0)
Positive predictive value	100,0 (93,8 - 100,0)	100,0 (75,0 - 100,0)	100,0 (97,9 - 100,0)
Negative predictive value	78,4 (63,8 - 93,0)	97,7 (92,0 - 100,0)	90,5 (75,5 - 100,0)

## DISCUSSION

In the articles and theses inspected, we did not find similarities. However, we did find differences that allow us to discuss endoscopic findings and premalignant gastric lesions, as in the case of Gómez Zuleta, Chacaltana, and Manrique Lemus, who found peptic ulcer prevalence in 2 (2,2 %), 6 (39,1 %) and 1 (0,5 %) cases, respectively. (12,13,14)

It was not possible to establish comparisons in the following tables because, being a pioneer study in this area, there are no records of having investigated this hormone as a tumor marker in premalignant gastric lesions; however, in practice, it has shown that it has been positive in the largest number of cases in the study.

Sensitivity was high in the case of dysplasias and relatively high for intestinal metaplasia. Therefore, it is useful to rule out the presence of these lesions due to the low rate of false negatives, except in the case of atrophic gastritis, where the marker is useful in the diagnosis only in 50,0 % of the patients.

However, the specificity is very high. Therefore, there will be a very low false positive rate; that is, since the specificity is 100,0 %, the result of the marker is negative in 100,0 % of the patients without premalignant lesions when, in fact, they do not present them.

The positive predictive value is very high, it is expected that for every 100 patients that this marker is positive for premalignant gastric lesions, the percentage of positivity according to the anatomic pathology report will be high.

Since the negative predictive value is high for the three premalignant gastric lesions, for patients with negative results for the presence of premalignant gastric lesions, the percentage of negativity for this condition will actually be high.

The tumor marker chorionic gonadotropin in premalignant gastric lesions in the group of patients studied shows that this marker is relatively useful to take into account as another tool in the diagnosis of these lesions, with high accuracy between the probability of having a premalignant gastric lesion by this diagnostic means and the results of the histological study by pathological anatomy in the diagnosis of dysplasia.

## CONCLUSIONS

In the investigation, there was a predominance of the endoscopic finding of elevated lesions, more patients with positive chorionic gonadotropin, and it turned out to be a marker with diagnostic value to be taken into account as a tool in premalignant gastric lesions.

## RECOMMENDATIONS

That studies with this hormone be carried out in other regions of the country.

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## CONFLICTS OF INTEREST

The authors declare that there are no conflicts of interest.

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