Original Article

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The diagnostic value of tumor markers (CA242, CA19-9, CEA) in patients with adenocarcinoma of the stomach

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ABSTRACT

Background: Gastric cancer is a significant health issue worldwide; it ranks fourth among cancers, following those of the lung, breast, and colon. Tumor markers can be utilized as screening and diagnostic tests for neoplastic diseases. **Aim**: This study aims to evaluate value and the efficacy of tumor markers (CA242, CA19-9, CEA) in patients with gastric carcinoma and to investigate the utility of single and combined tumor markers for the diagnosis of gastric carcinoma. **Methods**: The serum level of CA242, CA19-9, and CEA were measured in 40 patients with gastric carcinoma, using the ELISA technique, compared with 20 patients with benign gastric conditions and 20 healthy controls. Chi-square tests and F-test were employed for statistical analysis. **Results**: The mean age of patients with gastric cancer was 54.7 ± 12.8 years, with a male-to-female ratio of approximately 1.2:1. Serological data indicated that 60%, 37.5%, and 50% of these patients had positive results for CA242, CA19-9, and CEA, respectively. A statistically significant difference was observed in the mean serum level of CA19-9 between gastric cancer patients and controls. Additionally, CA242 demonstrated the best sensitivity (CA242 71%), while CA19-9 exhibited the highest specificity. The combination of tumor markers (CA19-9 and CEA), (CA242 and CEA), and (CEA and CA19-9) increased specificity to 97%. **Conclusion**: The novel tumor marker CA242 was the most sensitive for gastric cancer while CA19-9 was the most specific. Furthermore, a significant increase in serum CA19-9 levels was of diagnostic value. The combination of two tumor markers enhanced the specificity of the test.

Keywords: tumor marker, CA242, CA19-9, CEA, adenocarcinoma of stomach.

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INTRODUCTION

In recent years, there has been a marked increase in the incidence of adenocarcinoma of the proximal stomach (around the cardia), alongside a decrease in distal gastric cancer. These regional variations primarily reflect differences in the prevalence of *H. pylori,* which is responsible for more than 60% of gastric cancer cases worldwide.[1–5]

Tumor markers are molecules produced by cancer or by body cells in response to cancer or certain benign (non-cancerous) conditions. Most tumor markers are produced by both normal and cancer cells; however, the levels are significantly higher in cancerous conditions. These molecules can be found in urine, stool, blood, tumor tissue, or other tissues.[6]

Tumor markers have become an attractive method for detecting and diagnosing neoplastic diseases. Each tumor marker has a variable profile of usefulness for screening, diagnosis, prognosis, assessing response to therapy, and monitoring for cancer recurrence.[7]

CA242 is a new marker that has shown sensitivity slightly lower than that of CA19-9 but is more specific. It has been reported that CA242 is only slightly and infrequently elevated in the sera of patients with benign conditions such as chronic pancreatitis, chronic hepatitis, and liver cirrhosis. This characteristic is more apparent in patients with obstructive jaundice, suggesting that the level of this marker is minimally affected by cholestasis. The serological results with CA242 in diagnosing pancreatic cancer were comparable to those obtained with CA19-9, except that CA19-9 was falsely negative in some patients with early-stage pancreatic cancer.[7,8] These findings suggest the value of this marker for screening pancreatic cancer.

CA19-9 is a sensitive marker for pancreatic and hepatobiliary malignancies and is most often associated with gastrointestinal cancer.[9–11]

CEA is routinely used as a serological marker for colorectal cancer, but it can also be elevated in other cancers, including melanoma, lymphoma, thyroid, pancreas, liver, stomach, kidney, cervix, ovary, prostate, and bladder cancer. If the CEA level is elevated initially, it can be used to monitor the response to treatment.[12]

Stomach cancer is curable if detected early; however, patients often present at advanced stages, possibly because symptoms appear late and are often non-specific.[13] In most of the Western world, the 5-year survival rates from 5%–10%, while in other regions, it is about 50%.[13]

MATERIALS AND METHODS

Subjects

The study groups consisted of patients attending Baghdad Medical City Teaching Hospital, particularly the endoscopic department, from December 2011 to July 2012. Ethical permission to conduct the research was obtained from this center and from all participants. Case selection was conducted with the assistance of specialists in the department. Each study group completed a detailed questionnaire (Appendix-1).

Patient Study Group

Forty gastric cancer patients aged 27–75 years were included in this study. These patients were diagnosed clinically and histopathologically by specialists. Patients in this group were in advanced stages of gastric adenocarcinoma.

Patient Control Group

This group included 20 patients clinically diagnosed with benign gastric diseases.

Healthy Control Group

This group consisted of 20 apparently healthy individuals with no clinical evidence of disease, matched for age and sex with the patient group. They were selected from among the relatives attending the outpatient clinic.

Materials

Instruments and Equipment

- Centrifuge (Universal 16 A, Hettich, West Germany)
- Human Enzyme Linked Immunosorbent Assay (ELISA) system (human washer/Germany, human reader/Germany, and incubator Sanofi Pasteur/France)
- Micropipette
- Multichannel pipette
- Disposable tips
- Shaker
- Water bath
- Cylinder
- Absorbent paper for blotting the microtiter plate
- Eppendorf tubes
- Microplate reader with 450 ± 10 nm filter
- Deionized or distilled water
- Container for wash solution

Kits And Reagents

The kits were sandwich enzyme immunoassays for in vitro quantitative measurement of CA242 (4581-DRG Instruments GmbH, Germany), CA19-9 (3925-300 Monobind Inc., USA), and CEA (1825-300 Monobind Inc., USA) in human serum.

Reagents of CA242 Kit

1. Antibody solution (6 ml)
2. Enzyme conjugate (conjugate; 6ml); anti-CA242 antibodies conjugated to horseradish peroxidase
3. Sample diluents (11 ml)
4. Reference standards (0.5 ml each vial), calibrated to 0, 5, 25, 50, 100, and 200 U/ml)
5. Low and high control (0.5 ml each vial)
6. TMB solution (11 ml); buffer solution containing peroxide and tetramethylbenzidine
7. Washing buffer concentrate (10 ml; 100x); working solution prepared by adding 5 ml washing buffer concentrate into 990 ml distilled water

8. Stopping reagent

*All kit contents were stored at 2–8°C.

Reagents of CA19-9 Kit

1. Human serum reference (1 ml/vial): six vials and calibrators at concentrations of 0 (A), 10 (B), 50 (C), 100 (D), 250 (E), and 500(F) U/ml
2. CA19-9 biotin reagent: 13 ml/vial of anti-human CA19-9 conjugate in a protein matrix
3. CA19-9 enzyme reagent: 13 ml/vial conjucate in a protein-stabilized matrix
4. Streptavidin-coated plate: 96 wells
5. Wash solution: 20 ml/vial
6. Substrate A: 7 ml/vial, containing tetramethylbenzidine (TMB) in acetate buffer
7. Substrate B: 7 ml/vial, containing hydrogen peroxide (H_2O_2) in acetate buffer
8. Stop solution: 8 ml/vial (HCl)

*All reagents were stored at 2–8°C.

Reagents of CEA Kit

1. Carcinoembryonic antigen (CEA; 1 ml/vial): six vials and calibrators at concentrations of 0 (A), 10 (B), 10 (C), 25 (D), and 250 (E) ng/ml
2. Anti-CEA enzyme reagent: 13 ml/vial containing enzyme-labeled antibody, biotinylated monoclonal mouse IgG in buffer
3. Streptavidin-coated microplate: 96 wells
4. Wash solution: 20 ml/vial
5. Substrate A: 7 ml/vial containing tetramethylbenzidine (TMB) in acetate buffer
6. Substrate B: 7 ml/vial containing hydrogen peroxide (H_2O_2) in buffer
7. Stop solution: 8ml/vial (HCL)

*All reagents were stored at 2–8°C.

Methods

Blood Sample Collection and Preparation

A venous blood sample was drawn from each individual in the study groups. The blood was allowed to clot at room temperature then centrifuged. Serum was collected into two Eppendorf tubes and stored at -20°C until needed for investigation.

Identification of Tumor Markers by ELISA

CA242

Principle: The CA242 cancer assay was a solid-phase enzyme-linked immunosorbent system employing plastic wells coated with streptavidin. The sample, standards, biotinylated antibodies, and controls were allowed to incubate in the wells. During incubation, specific cancer antigen (CA242) was bound to CA242 antibodies on the wells. Unbound CA242 antigen was removed by washing, following which conjucate was added to each well. After incubation, unbound enzyme conjucate was washed off, and the amount of bound peroxidase was correlated with the concentration of the CA242 antigen present in the sample. Upon addition of the chromogen substrate, the intensity of color developed was proportional to the concentration of CA242 antigen in the sample and could be quantified using a photometric well reader at a wavelength of 450 nm.

Test Procedure:

1. The desired number of coated wells was secured in the holder.
2. 25 µl of sample diluent was added into the well as a blank, and 25 µl of standards, samples, or controls were added into the appropriate wells. 50 µl of biotinylated solution was added to each well except the blank well.
3. 50 µl of enzyme conjugate was dispensed into each well except the blank well.
4. This was incubated for 60 minutes at room temperature.
5. This was washed five times with the washing buffer (300 ml/well/each rinse).
6. 100 ml of TMB solution was dispensed into each well.
7. The well was incubated for 30 minutes at room temperature.
8. The reaction was stopped by adding 50 µl of stop solution to each well.
9. The absorbance in each well was measured at 450 nm.

CA19-9

Principle: The essential reagents required for an immunoenzymometric assay include high affinity and specificity antibodies (enzyme and immobilized). Immobilization occurs during the assay at the surface of a microplate well.

After mixing reaction results in the native antigen and antibody, an antibody-antigen complex is formed. After a suitable incubation period, the antibody-antigen bound fraction is separated from unbound antigen by decantation or aspiration. Another labeled antibody with an enzyme is added, forming an enzyme-labeled antibody-antigen-antibody complex on the surface of the wells. Excess is washed off, and a substrate is added to produce color measured with a spectrophotometer. The enzyme activity on the well is directly proportional to the

native free antigen concentration. By utilizing several standards, a standard curve can be generated from which the antigen concentration of unknown samples can be ascertained.

Procedure:

1. 25 µl of the appropriate serum references (calibrators), controls, and samples were pipetted into assigned wells.
2. 100 µl of biotinylated labeled antibody was added to the well.
3. This was incubated at room temperature for 60 minutes.
4. The well was washed with 300 µl of wash buffer three times.
5. 100 µl of CA19-9 enzyme reagent labeled antibody was added to the well..
6. The well was incubated at room temperature for 60 minutes.
7. The well was washed with 300 µl of wash buffer three times.
8. 100 µl of working substrate solution was added.
9. The well was incubated at room temperature for 15 minutes.
10. 50 µl of stop solution was added.
11. The absorbance in each well was read at 450 nm (with a wavelength of 620–630 nm).

CEA

Principle: Immunoenzymometric assay requires high-affinity and specificity antibodies (enzyme and immobilized). In this procedure, the immobilization occurs on the surface of a microplate well through the interaction of streptavidin with the added biotinylated monoclonal anti-CEA antibody.

Upon mixing the monoclonal biotinylated antibody with serum containing the native antigen, a soluble sandwich complex is formed (without competition). The antibody-antigen bound fraction is separated from unbound antigen by decantation or aspiration. The enzyme activity is proportional to the native antigen concentration. By utilizing several reference standards of known antigen concentration, a standard curve can be generated from which the antigen concentration of unknown samples can be ascertained.

Procedure:

1. 25µl of the appropriate serum references (calibrators), controls, and samples were pipetted into assigned wells.
2. 100 µl of the anti-CEA labeled enzyme reagent was added.
3. This was incubated at room temperature for 60 minutes.
4. This was washed with 300 µl of wash buffer three times.
5. 100 µl of CEA enzyme reagent labeled antibody was added.
6. 100 µl of working substrate solution was added.
7. The well was incubated for 15 minutes at room temperature.
8. 50 µl of stop solution was added.
9. The absorbance in each well was read at 450 nm (with a wavelength of 620–630 nm).

Reference range: Values above 5 ng/ml were considered positive for non-smokers and above 10 ng/ml for smokers.

Calculation of Results: The results were calculated automatically using a 4-Point curve fit, and the concentration of the sample was obtained.

Statistical Analysis

Data were translated into codes using a specially designed coding sheet and then entered into a computerized database structure. Statistical analysis was performed using Statistical Package for Social Science (SPSS).

The statistical significance, direction, and correlation between quantitative variables were measured using the Chi-square test, and the correlation between mean variables was assessed using Fisher's test (F-test). A p-value of less than 0.05 was considered statistically significant.

The performance characteristics (validity) of the test included specificity, sensitivity, negative predictive value, and positive predictive value.

RESULTS

The age of gastric cancer patients in this study (n = 40) ranged from 28 to 75 years, with a mean age of 54.7 ± 12.8 years. The majority were aged between 41 and 60 years (Table 1). The age of the control group (benign gastric disease; n = 20) ranged from 28 to 77 years, with a mean age of 49.6 ± 13.5 years. The majority were aged between 41 and 60 years. The age of the healthy control group (n = 20) ranged from 32 to 62 years, with a mean age of 48.6 ± 8.6 years (Table 1).

Among gastric cancer patients, there were 22 males and 18 females, resulting in a male-to-female ratio of 1.2:1. The patient control and healthy control groups had sex ratios (M:F) of 1:1.2 and 1.2:1, respectively (Table 1).

Seroimmunological Data

Serum Levels of the Tumor Markers in the Study Group

According to the cutoff values, Table 2 shows that 60%, 37.5%, and 50% of gastric cancer patients had seropositive results for CA242, CA19-9, and CEA respectively. On the other hand, in comparison with the patient control group, there was no significant positive correlation between seropositive results for CA242 (p-value = 0.4), CA19-9 (p-value = 0.17), and CEA (p-value = 0.2). However, there was a statistically significant correlation between serum levels of CA19-9 among gastric cancer patients compared to healthy controls (p-value = 0.009; Figures 1, 2, and 3).

Mean Values of Serum Level Concentration of Tumor Markers (CA242, CA19-9, and CEA) in Study Groups

There was a wide range of serum level concentrations of the studied tumor markers (CA242, CA19-9, CEA), which greatly influenced the value of the arithmetic mean. The data were therefore transformed to natural logarithm (ln) to measure the natural logarithmic mean values, as shown in the Figures 4.

In Table 3, the mean serum level showed a difference in levels of CA242 between gastric cancer patients and the control groups, with no significant association (p-value = 0.06).

As shown in Table 5, there was no statistically significant difference in mean serum levels of CEA between gastric cancer patients and the control groups (p-value = 0.7).

Validity Parameters for Studied Tumor Markers in Gastric Cancer

In this study, the tumor marker CA242 exhibited the highest sensitivity (71.4%), while CA19-9 demonstrated the highest specificity (93%), as shown in Table 6.

Validity Parameters for Combination of Tumor Markers in Gastric Cancer

The combination of the new tumor marker (CA242) with other studied markers (CA19-9, CEA) revealed a decrease in sensitivity of about 10%–15% and an increase in specificity up to 97%. Meanwhile, the combination of CA19-9 and CEA showed a decrease in sensitivity with an increase in specificity, as shown in Tables 6, 7.

Table 1: Age and gender (frequency distribution) of the study samples.

	Studied groups		
	Gastric cancer N* (%)**	Patient control N* (%)**	Healthy control N* (%)**
Age groups (years)			
21–40	7 (17.5)	6 (30)	5 (25)
41–60	22 (55)	12 (60)	14 (70)
61+	11 (27.5)	2 (10)	1 (5)
Total	40 (100)	20 (100)	20 (100)
Range	28–75 years	28–77 years	32–62 years
Mean	54.7 ± 12.8	49.6 ± 13.5	48.6 ± 8.6
Gender			
Male	22(55)	9(45)	11(55)
Female	18(45)	11(55)	9(45)
M/F	1.2:1	1:1.2	1.2:1
Total	40 (100)	20 (100)	20 (100)

* = number, ** = percentage

Table 2: Frequency distribution of the study sample according to tumor markers (CA242, CA19-9, and CEA).

Tumor markers	Result according to cutoff value*	Gastric cancer group NO. (%)	Patient control group NO. (%)	Healthy control group NO. (%)
CA242	Positive	24 (60)	8 (40)	6 (30)
	Negative	16 (40)	12 (60)	14 (70)
	p-value		0.4**	0.1**
CA19-9	Positive	15 (37.5)	3 (15)	0(0)
	Negative	25 (62.5)	17 (85)	20(100)
	p-value		0.17**	0.009***
CEA	Positive	20 (50)	5 (25)	7 (35)
	Negative	20 (50)	15 (75)	13 (65)
	p-value		0.21**	0.4**
Total number		40	20	20

*Cutoff value for CA242 = 25 U/ml, CA19-9 = 40 U/ml, CEA = 5 ng/ml for non-smokers and 10 ng/ml for smoker.

Non-Significant Association** Significant Association***

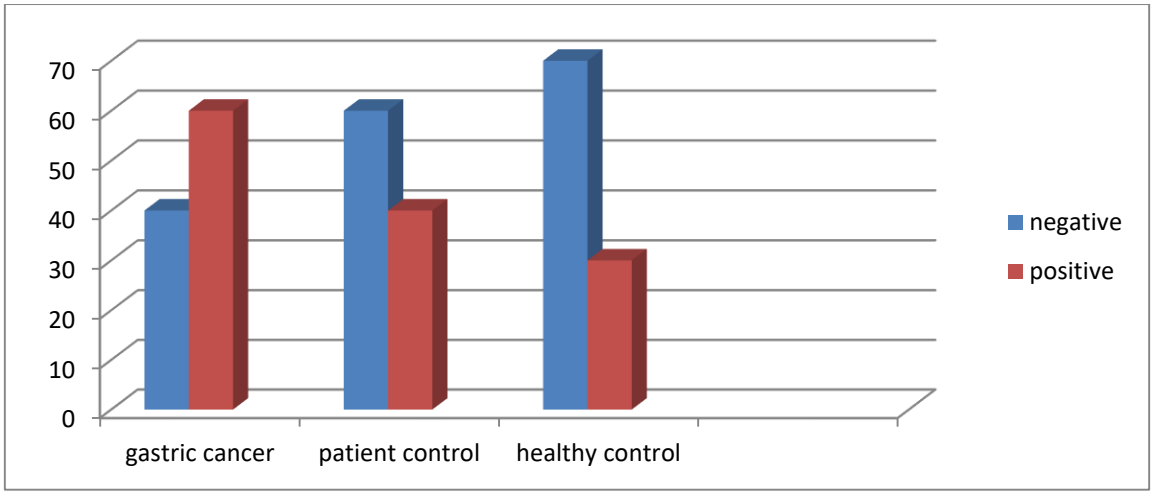

Figure 1: Frequency distribution of seropositive and seronegative CA242 results in the study groups.

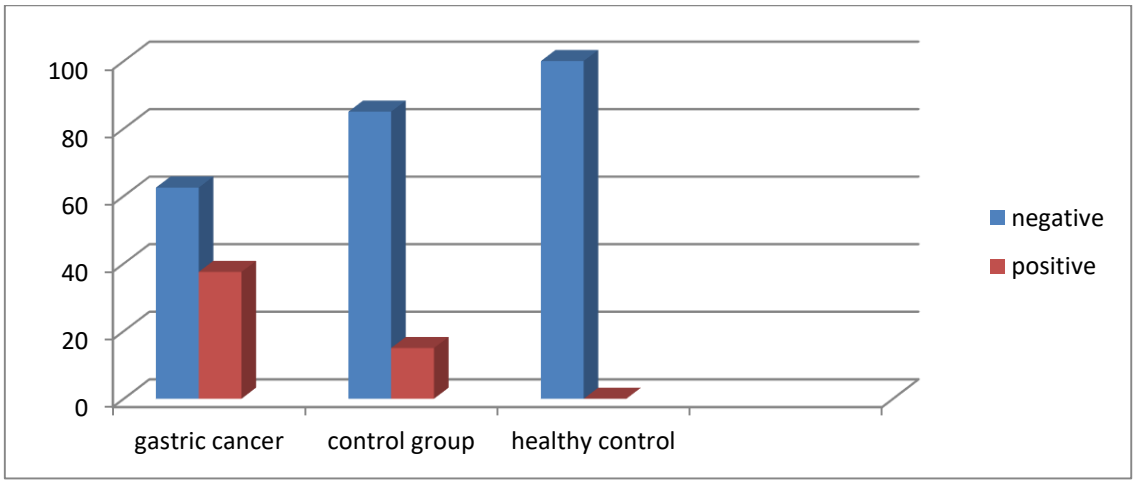

Figure 2: Frequency distribution of seropositive and seronegative CA19-9 results in the study groups.

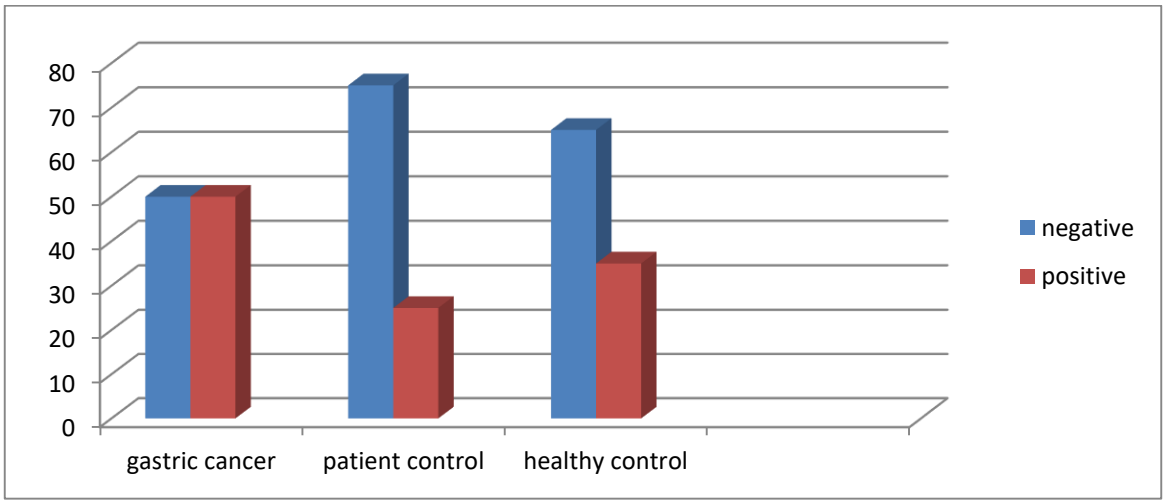

Figure 3: Frequency distribution of seropositive and seronegative CEA results in the study groups.

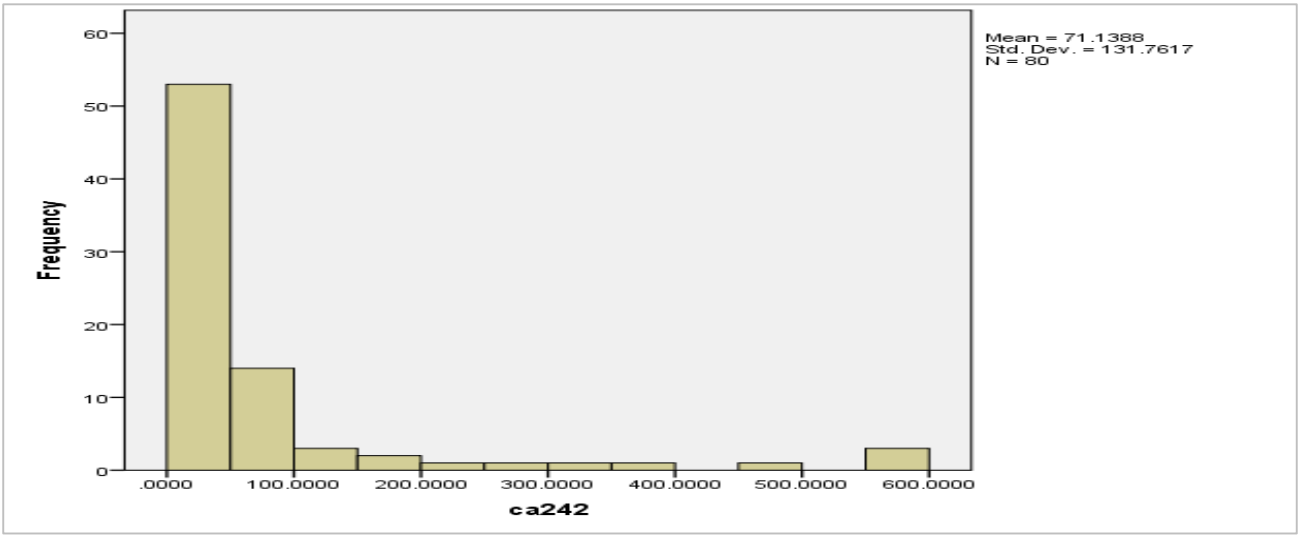

Figure 4:Frequency distribution of serum concentration of CA242 in the studied sample.

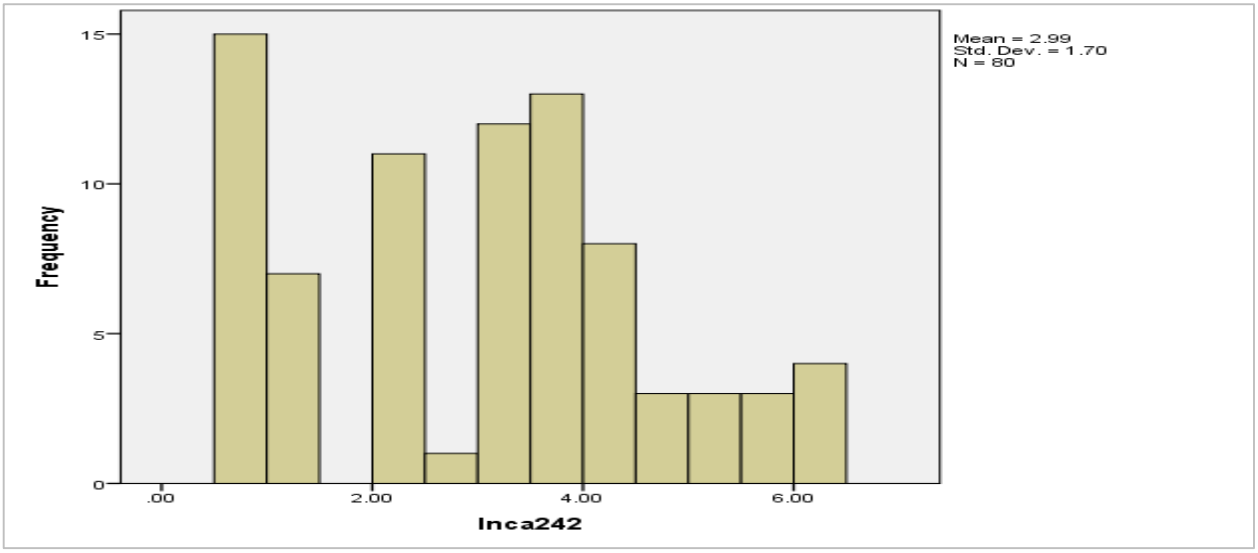

Figure 5:Frequency distribution of natural logarithmic (ln) values of CA242 in the studied sample

Table 3: Difference in mean values of tumor marker CA242 between study groups.

CA242	Gastric cancer group	Patients control group	Healthy control group
Range(U/ml)	2–591.6	1.7–201.4	1–81.3
Geometric Mean ± SD	3.4 ± 1.8	2.8 ± 1.5	2.3 ± 1.4
F-test	2.8		
D.f	2		
p-value	0.06		

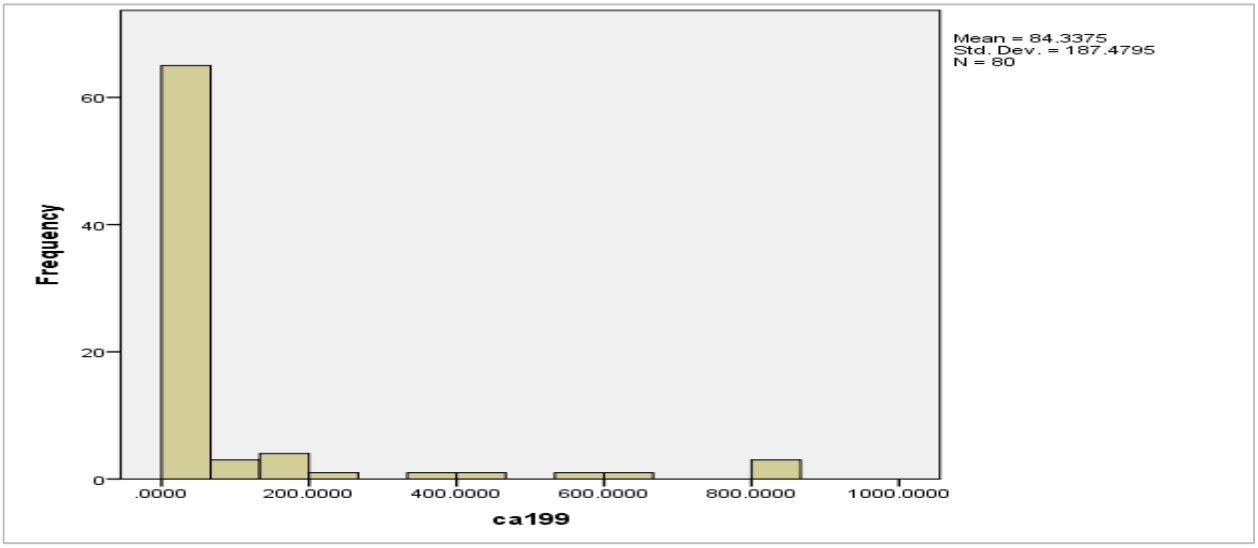

Figure 6: Frequency distribution of serum concentration of CA19-9 in the studied sample.

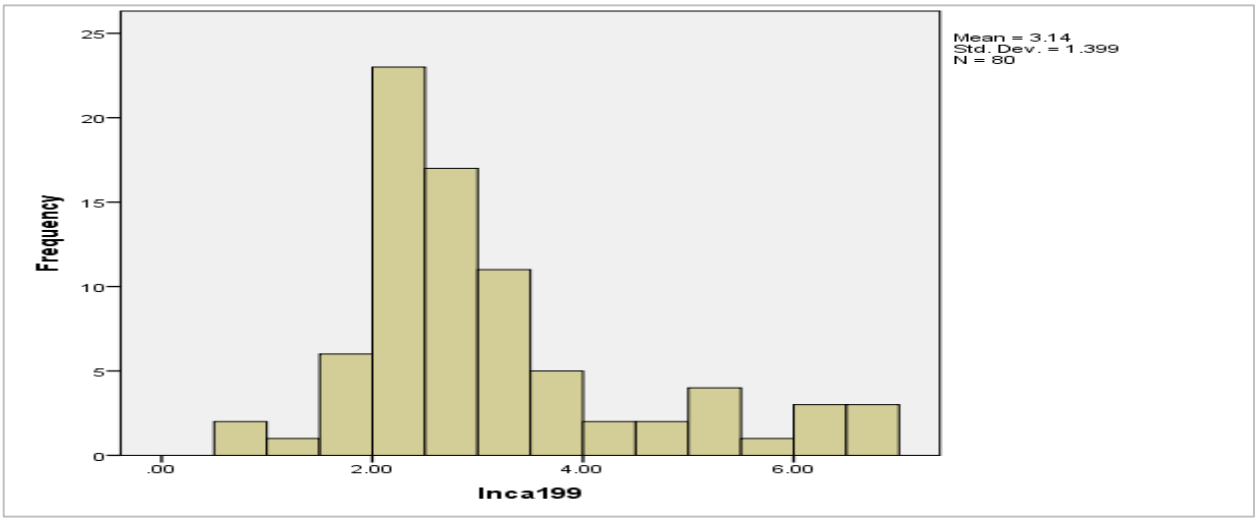

Figure 7: Frequency distribution of natural logarithmic (ln) values of CA19-9 in the studied sample.

Table 4: Difference in mean values of tumor marker CA19-9 between study groups.

CA19-9	Gastric cancer group	Patients control group	Healthy control group
Range (U/ml)	1.6–860.7	1.02–46.8	1.9–30.8
Geometric Mean ± SD	3.7 ± 1.7	2.7 ± 0.95	2.5 ± 0.5
F-test	6.7		
D.f	2		
p-value	0.02		

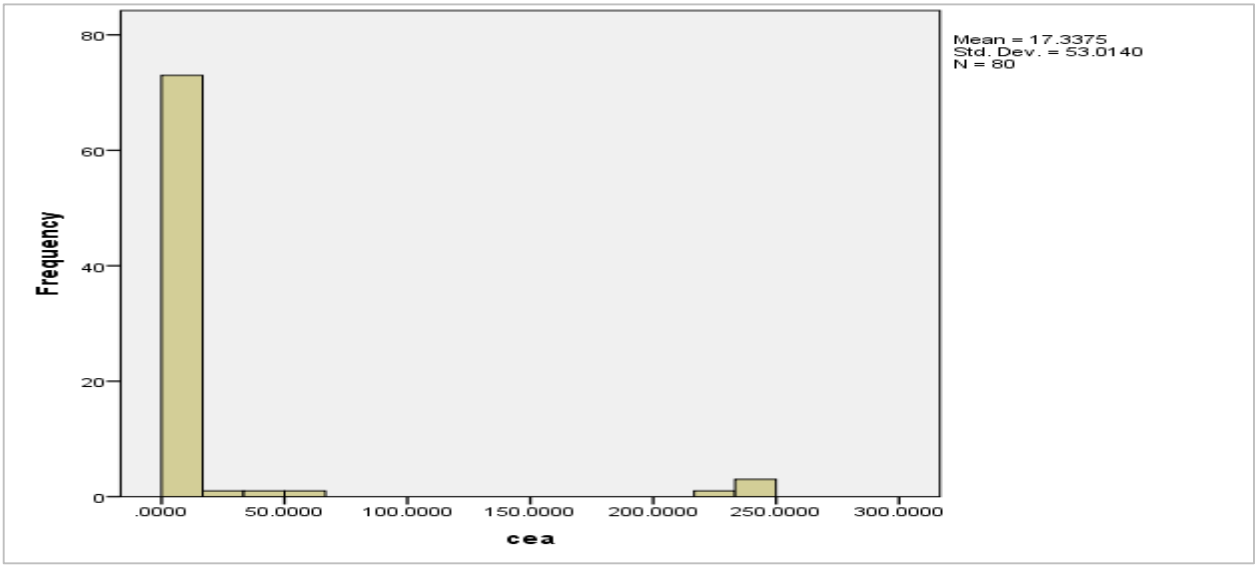

Figure 8: Frequency distribution of serum concentration of CEA in the studied sample.

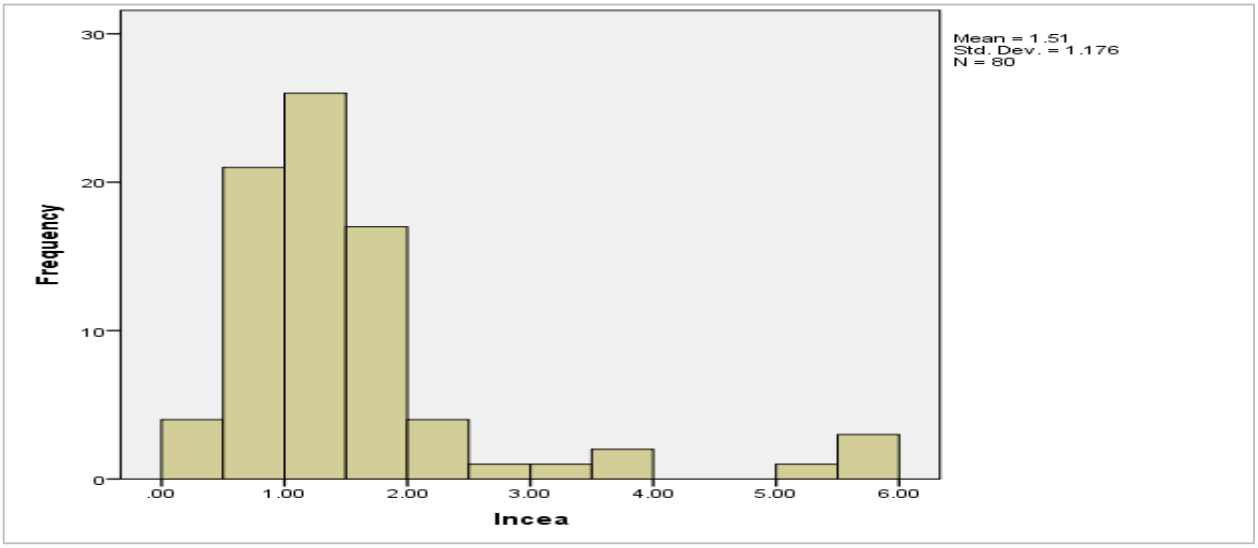

Figure 9: Frequency distribution of natural logarithmic (ln) value of CEA in the studied sample

Table 5: Difference in mean values of tumor marker CEA between study groups.

CEA	Gastric cancer group	Patients control group	Healthy control group
Range (ng/ml)	1.5–173.5	1.1–157	1–38
Geometric Mean ± SD	1.5 ± 1.3	1.6 ± 1.2	1.3 ± 0.8
F-test	0.3		
D.f	2		
p-value	0.7		

Table 6: Validity for studied tumor markers.

Tumor marker	Sensitivity	Specificity	PPV	NPV
CA242	71.4	74.1	74	71
CA19-9	61.5	93	93	61
CEA	66.6	66.6	76.9	58.8

PPV = Positive Predictive Value, NPV = Negative Predictive Value

Table 7: Combined two tumor markers test.

Combination of Tumor markers Test	Sensitivity	Specificity	PPV	NPV
CA242 and CA19-9	59.7	97.5	98	59
CA242 and CEA	54	97	85	52
CA19-9 and CEA	51	100	85	52

PPV = Positive Predictive Value, NPV = Negative Predictive Value

DISCUSSION

The gastrointestinal tract is the site of more cancers than any other organ system in the body. In terms of morbidity and mortality, gastric cancer is the second most common Gastrointestinal tract (GIT) cancer. The use of these tumor markers has become a popular method for detecting and diagnosing neoplastic diseases; however, their value in cancer detection is controversial because no single tumor marker is sufficient to meet strict diagnostic criteria. The present study investigated the clinical usefulness of three tumor markers (CA242, a new tumor marker; CA19-9; and CEA) in the diagnosis of gastric cancer and evaluated the validity of combined or single tumor markers in this context.[7]

Age and Gender Distribution

The present study showed that gastric cancer occurs most frequently during the fourth and fifth decades of life. These results are somewhat consistent with other studies, such as Crew et al., who found that the age of gastric cancer patients was predominantly over 40 years. The current study found that the mean age of gastric cancer patients was 55 years, which is in agreement with results published by several studies in Iraq and other Arab countries.[8,14,15]

However, American and European studies indicate that the mean age of gastric cancer patients is 70 years, while in South Africa, it appears at an earlier age in Whites (mean 53 years) than in Blacks (mean 68 years).[16]

The rise in the incidence of gastric cancer among younger age groups may signal the introduction of new environmental factors, which are considered major contributors to the disease's etiology (including dietary habits, obesity, and radiation exposure). These factors may contribute to the disease appearing at earlier ages.[17]

This study found a male-to-female ratio of approximately 1.2:1, which is consistent with world report statistics indicating a higher incidence in males.[17–19] Steevens et al. suggested that the increased incidence of gastric cancer among males could be attributed to increase in smoking rates, which can also apply to our population.[20]

Serological Studies

In the present work, the percentages of elevated serum CA242, CA19-9, and CEA in preoperative patients with advanced gastric adenocarcinoma were 60%, 37.5%, and 50%, respectively. These findings align with those of

Wobbes et al. and Carpelan-Holmström et al., who reported positivity rates ranging from 34% to 71%. Additionally, the current study found that the percentage of elevated serum levels of CA242, CA19-9, and CEA in patients with benign gastric conditions were 40%, 15%, and 25%, respectively. These results are consistent with those of other researchers who reported similar findings.[21–26]

Elevated serum levels of these markers have been associated with gastrointestinal cancers. Previous studies have indicated that the CA242 antigen is related to the antigenic epitopes of CA19-9. The elevation of CA242 levels in serum may be due to low synthesis of the core protein carrying the CA242 epitope in benign conditions and high synthesis of the core protein in cancer. It may also be due to glycosylation of the same protein core in benign and malignant tissues, with preferential expression of CA242 in cancerous tissue.[21,22,27]

Regarding CEA, many studies have reported that liver failure is a frequent cause of increased serum concentration of CEA, as CEA is metabolized by the liver. In the current study, most gastric cancer patients were in advanced stages, and liver failure was expected due to metastasis. Additionally, the elevation of serum CEA and CA242 may be attributed to their drainage by lymph nodes.[7,27]

In this study, elevated serum CA242 levels were found in 40% of patients with benign gastric diseases, compared to 25% for CEA and 15% for CA19-9 when cutoff values were applied. These findings are consistent with previous reports among patients with benign gastric diseases.[7,28] Wobbes et al. concluded that nearly half of patients with benign gastric disease, including inflammatory conditions, exhibited elevated serum tumor marker levels.[26] However, these findings contradict those of Carpelan-Holmström et al., who reported no elevation of any serum tumor markers among patients with benign gastric diseases.[25]

In the present work, among the three studied tumor markers, the mean serum concentration of CA19-9 was significantly higher among gastric cancer patients compared to those with benign gastric disease and healthy controls. Despite the high mean concentration of CA242, it showed no statistical association.

In a study conducted by Attallah et al., it was reported that there were slight increases in the mean concentrations of the studied tumor markers (CA242, CA19-9) in gastric cancer compared to control groups. Additionally, a statistically significant association was found between the mean value of CEA and control groups, with no such significant association for CA242 and CA19-9.[7] Kuusela et al. reported that, in all carcinoma groups, there were patients with relatively large tumors and normal CA242 levels, and vice versa. However, the highest serum values were mostly found in patients with advanced disease. Therefore, there seems to be a correlation between tumor burden and serum levels of CA242.[21] Moreover, Wobbes et al. reported that high preoperative levels of CA242 might reflect the extent of tumor growth.[26]

Additionally, Nilsson et al. suggested that the equilibrium between the rate of synthesis of tumor markers and their hepatic clearance from peripheral circulation may be a contributing factor.[29] As reported by Koo et al., the preoperative serum levels of the three tumor markers (CA242, CA19-9, CEA) were significantly related to the depth of invasion, tumor size, lymph node metastasis, pathological stage, and recurrence.[30] It is crucial to recognize significant changes in serum levels of tumor markers. Therefore, apart from positive marker results, elevated serum values may be important in clinical practice, especially if the marker is used for follow-up.[26]

Validity Parameters

Among the three studied tumor markers (CA242, CA19-9, and CEA), CA242 exhibited the highest sensitivity (71%) and CA19-9 demonstrated the highest specificity (93%). CEA showed sensitivity and specificity of approximately 66%. These results are somewhat consistent with other studies. Yutaka et al. found that the sensitivity of CEA and CA19-9 was about 65.8% in gastric cancer. Kuusela et al. reported that CA19-9 had the highest sensitivity and specificity, while the sensitivity of CA242 was too low to be clinically useful.[21,31]

Carpelan-Holmström et al. found that CA19-9 and CA242 had similar sensitivity of 44% for gastric cancer, while CEA was elevated in 25% of cases. However, one previous study found that none of the studied tumor markers (CA242, CA19-9, and CEA) had sufficient sensitivity (less than 20%) to be considered markers for gastric cancer.[7]

The use of these markers has become a valuable method for detecting and diagnosing neoplastic diseases, and their value in cancer detection has been controversial largely because no single marker is sensitive and specific enough to meet diagnostic criteria.[7]

Furthermore, the cutoff values of tumor markers depend on the mean levels in healthy populations, which may be

affected by environmental factors and certain other illnesses rather than malignant conditions.

There are studies supporting the use of tumor markers in gastric malignancy, while other studies do not favor it. It is possible to improve diagnostic information by combining markers compared to using single markers.[25]

The usual tumor marker combinations routinely used in our country are CA19-9 and CEA. The combination of these two markers in the present study revealed a decrease in sensitivity but achieved 100% specificity. Moreover, the combination of the new tumor marker (CA242) with other studied markers (CA19-9, CEA) revealed a decrease in sensitivity by about 10%–20% and an increase in specificity up to 97%.

The marked decrease in sensitivity when using CA242 with other tumor markers (CEA and CA19-9) might be due to the higher sensitivity of CA242 compared to CA19-9 and CEA in the study group.

Previous investigators have recommended using combinations of tumor markers to increase positivity in gastric cancer.[26] Carpelan-Holmström et al., concluded that the combination of CEA, CA19-9, and CA242 improved diagnostic accuracy in gastrointestinal tract malignancies compared to these markers alone.[25] In contrast, Atlallah et al. found that the combination test of CEA and CA242 increases the sensitivity of CA242 values.[7] Each tumor marker has a wide range of usefulness for screening, determining diagnosis, prognosis, assessing response to therapy, and monitoring for cancer recurrence.

CONCLUSIONS

In the current study, the new tumor marker CA242 showed a non-significant increase in the mean serum level among gastric cancer patients; furthermore, it had the highest sensitivity for gastric cancer, The tumor marker CA19-9 showed a significant increase in the mean serum level and had the highest specificity for gastric cancer. CEA showed no significant increase in mean serum levels among gastric cancer patients. The combination of tumor markers (CA242 and CA19-9) and (CA242 and CEA) increased the specificity of the test to more than 97%.

Recommendations

1. Additional studies are needed to determine the clinical value of CA242 in the diagnosis and follow-up of patients with gastric cancer and to correlate CA242, CA19-9, and CEA concentrations with tumor depth and invasion.
2. Further extensive studies are recommended on the usefulness of tumor marker combinations in gastric cancer. This may help in providing a panel of markers for follow-up and recurrence

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