

Clinical Value of Serum Cancer Antigen 19-9 as a Tumor Screening Marker among Healthy Individuals

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Abstract:

Background: Serum tumor markers are convenient, non-invasive, acceptable to patients and play an important role as an ancillary tumor diagnostic tool. CA 19-9 has become a common tumor marker, specific for digestive system tumors. The study was carried out to determine the value of CA 19-9 as a tumor screening marker among healthy individuals.

Materials and Methods: This study had been carried in Dhaka Medical college Hospital from January 2016 to January 2018. The serum CA 19-9 level was detected using a microsome luminescence method. Individuals with high CA 19-9 levels underwent further examination, including routine fecal testing, thoracic and abdominal computed tomography (CT) scan, gastroscopy, and colonoscopy. These individuals had regular follow-up examinations.

Results: Over a 3-year period, the serum CA19-9 levels of 960 healthy individuals were estimated. The CA 19-9 level of 15 individuals was positive (positive rate: 1.56%), including 7 men (7/699; 1.001%) and 8 women (8/261; 3.06%). There was a significant difference between males and females ($p < 0.01$). The overall tumor detection rate was 0.72% (7/960) including 6/699 men (0.85%) and 1/261 women (0.38%).

Conclusion: Therefore, elevated CA 19-9 level can be used to assist in the diagnosis malignancy.

Key words: Tumor marker, CA 19-9, Malignancy.



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Introduction:

Serum tumor marker measurements are convenient, non-invasive, acceptable to patients, and play an important role as an ancillary tumor diagnostic tool.^{1,2} Aberrant glycosylation occurs on the cell membrane during

tumorigenesis resulting in the production of glucose by-products. Tumor markers can be used as an ancillary cancer screening test and to monitor treatment and evaluate tumor recurrence.³ CA 19-9 is composed of glycosidoproteins and sialylated lacto-N-fucopentose- α ⁴ and is mainly found in fetal intestinal, gastric, and pancreatic epithelial cells. Serum CA 19-9 levels are low in > 95% of healthy individuals ($< 37 \times 10^3$ U/mL). Nearly all patients who have high CA 19-9 levels ($> 1000 \times 10^3$ U/mL) have tumor metastasis.⁵ The sensitivity of this tumor marker varies with the stage of the tumor.⁶ CA 19-9 has become a common tumor marker, specific for digestive system tumors. To evaluate the cost benefits and prognostic ability of CA 19-9, levels were evaluated in healthy individuals recruited over a period of 3 years in our hospital.

Materials and methods:

Participants were recruited in Dhaka Medical college Hospital from January 2016 to January 2018. Written informed consent was obtained from all participants. The

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serum CA 19-9 level was detected using a microsome luminescence method using an i2000 automatic immunoassay unit (Abbott, USA). Four microliters of venous blood were collected, and serum was harvested after centrifugation. Serum CA 19-9 levels were measured based on the automatic immunoassay instructions. General data such as sex, age and disease history were collected using registration forms of physical examination. Individuals with high CA 19-9 levels underwent further examination, including routine fecal testing, thoracic and abdominal computed tomography (CT) scan, gastroscopy, and colonoscopy. These individuals had regular follow-up examinations. Statistical analyses were performed using SPSS 10.0 software (SPSS Inc., Chicago, Ill). The CA 19-9 positive rate and tumor detection rate between males and females were compared using χ^2 test and Fisher's exact test. Data were presented as mean \pm standard deviation (SD).

Results:

There were 960 healthy individuals that participated in the study (699 men and 261 women); their mean age was 54 ± 12 years. Data from individuals who were examined at our hospital within the previous 3 years were recorded. Results on the detection of serum CA 19-9 levels and follow up, 5 of 236 individuals (2.12%) had elevated CA 19-9 levels, including 1 woman whose CA 19-9 level ranged from 69.38 to 2056.32 U/mL (Table I). A 57-year-old man whose CA 19-9 level was 2056.32 U/mL underwent gastroscopy and biopsy confirmed a gastric signet ring cell carcinoma. A 54-year-old man with a CA 19-9 level of 265.42 U/mL underwent gastrointestinal endoscopy and chest CT examination, but no tumor was found. His CA 19-9 level had increased significantly 2 years later. During that period, he underwent repeated CT, magnetic resonance imaging (MRI), and positron emission tomography/CT (PET-CT) examinations that finally confirmed the presence of a cholangiocarcinoma. Surgery was performed but the tumor recurred after 1 year. An 82-year-old man, whose CA 19-9 and CEA levels were 118.59 U/mL and 441.36 $\mu\text{g/L}$, respectively, refused further examination and died after 6 months. Two other individuals with CA 19-9 levels of 69.38 U/mL and 80.30 U/mL did not show increase in CA 19-9 levels or any tumor signs after 2 years.

In 2008, there were 492 individuals who had detectable CA 19-9 levels. Four individuals had been examined in 2007; another 5 individuals had higher CA 19-9 levels, including 4 women. CA 19-9 levels varied from 40.30 to 393.04 U/mL. A 66-year-old woman had the highest CA 19-9 level and imaging confirmed after radical resection of lung carcinoma. Among the other 4 individuals, the highest CA 19-9 level was 73.53

U/mL. During a 1-year follow-up, the serum CA 19-9 levels these 4 individuals were low and no tumor was detected.

In 2009, CA 19-9 was detected in 232 individuals, including 2 who had been identified in the previous 2 years. Another 5 individuals had high CA 19-9 levels, including 3 women. CA 19-9 levels ranged from 38.18 to 399.85 U/mL. A 45-year-old woman had the highest CA 19-9 level and imaging confirmed an ovarian malignant teratoma. Recurrence of a cardiac carcinoma after radical resection of the primary tumor was confirmed by gastroscopy in an 81-year-old man with a CA 19-9 level of 368.53 U/mL. Pancreatic cancer was confirmed by CT in a 73-year-old man with a CA 19-9 level of 186.43 U/mL and a cancer antigen 72-4 (CA 72-4) level > 300 U/mL. Surgery was performed but he died after 3 months. The highest CA 19-9 level among the remaining cases was 81.40 U/mL; at 9 months, the level was low and there were no tumor signs in this individual with the highest CA 19-9 level.

Over the study period, the serum CA 19-9 levels of 960 healthy individuals were estimated. The CA 19-9 level of 15 individuals was positive (positive rate: 1.56%), including 7 men (7/699; 1.001%) and 8 women (8/261; 3.06%) (Table I). There was a significant difference between males and females ($p < 0.01$). The overall tumor detection rate was 0.72% (7/960) including 6/699 men (0.85%) and 1/261 women (0.38%) (Table II & III).

Table I: CA 19-9 positivity

Gender	Population(n)	CA 19-9 positive	Positive rate
Male	699	7	1.001%
Female	261	8	3.06%
Total	960	15	1.56%

Table II: Tumor detection rate

Gender	Population (n)	Tumor positive	Tumor detection rate
Male	699	6	0.85%
Female	261	1	0.38%
Total	960	7	0.72%

Table III: Comparison between CA 19-9 and tumor detection positivity

Gender	Ca 19-9 positive	Tumor positive
Male (n=699)	7 (1.001%)	6 (0.85%)
Female (n=261)	8 (3.06%)	1 (0.38%)

Discussion:

In recent years, cancer incidence has increased in our country, with a postoperative survival rate of patients being significantly lower than in developed countries. Effective detection methods are important to identify patients with early tumors and improve the therapeutic results and patient survival. Serum tumor marker measurements are convenient, non-invasive, and readily accepted by patients when used as an ancillary diagnostic tumor detection method.^{2,3} Many types of tumor markers are currently available but there is no single marker that is ideal for screening and diagnosis.

Tumor markers are secreted by tumor cells into tissues or are produced by the host in response to changes in the body. These markers do not exist in healthy people except in embryos. The levels of tumor markers are higher in patients with tumors than in healthy people.^{2,3} Tumor marker levels can be used to diagnose tumors, analyze the time course, guide therapy, monitor recurrence or metastasis, and provide prognosis.

Tumor markers have been used for more than 30 years and have become a routine tumor detection method.^{2,3} CA 19-9 is usually elevated in many adenocarcinomas including malignant tumors of the digestive tract and pancreatic cancer. However, it is not tumor-specific. The ideal tumor marker should have high specificity and sensitivity and the ideal tumor screening method should have high sensitivity but does not need high specificity.⁷ Some studies have reported that significantly increased CA 19-9 levels had better specificity for tumor diagnosis; however, the sensitivity was only 34.5- 44.9%, which is of limited value for tumor screening.^{8,9,10} This study found an overall positive rate of 1.56% in healthy individuals who were screened for CA 19-9 and the rate was higher in men than in women. Other authors have found that uterine endometriosis is a common reason for increased CA 19-9 levels in addition to malignant chest tumors and benign bile duct diseases.¹¹ In this study uterine endometriosis might be a cause for high CA19-9 levels in women. The overall tumor detection rate was only 0.36% in this study, and participants whose CA 19-9 level was 100 U/mL were found to have new or recurrent tumors. Importantly, most of the patients with recurrent or advanced malignant tumors were detected using CA 19-9 screening. Although some patients were subjected to surgery, tumor recurrence was unavoidable. In summary, the CA 19-9 tumor marker has limited prognostic value and should not be part of routine examinations.

Conclusions:

Tumor markers can be used as an ancillary cancer screening test and to monitor treatment and evaluate tumor recurrence. Elevated CA 19-9 may be found in patients with benign as well as malignant disease. The tumor marker CA19-9 is a sensitive marker for pancreatic, gastric and hepatobiliary malignancies.

Conflict of interest: None.

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