

## Research Article

# Diagnostic Value of Carcinoembryonic Antigen as an Indicator for Irritable Bowel Syndrome

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### Abstract

**Background:** Irritable Bowel Syndrome (IBS) is an important common disease of the gastrointestinal tract, which is caused by the effect of various factors. The carcinoembryonic antigen (CEA), which mainly used for detection of colorectal cancer, was chosen to evaluate its ability to diagnosis of IBS. **Methodology:** A cross-sectional study was designed to determine the level of CEA in the blood of 95 patients with IBS and 80 healthy individuals. The serum level of CEA was measured by ELISA technique. **Results:** Of 95 patients with IBS, 8 (8.4%) of non-smoker males had a significant high levels of carcinoembryonic antigen ( $5-10 \text{ ng mL}^{-1}$ ). Meanwhile, another an old age male showed higher than  $10 \text{ ng mL}^{-1}$  of carcinoembryonic antigen with a significant difference value ( $p < 0.01$ ) from the normal level. All of involved females showed a normal level of CEA. **Conclusion:** The IBS is responsible for increasing the CEA level within a limited range ( $< 10 \text{ ng mL}^{-1}$ ). The level higher than  $10 \text{ ng mL}^{-1}$  of carcinoembryonic antigen in patient with IBS may be considered a primary indicator for the development of colorectal cancer. Further specific tests are recommended for such type of case.

**Key words:** CEA, IBS, colorectal cancer, ELISA, cancer

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**Competing Interest:** The authors have declared that no competing interest exists.

**Data Availability:** All relevant data are within the paper and its supporting information files.

## INTRODUCTION

Irritable Bowel Syndrome (IBS) is one of the functional gastrointestinal disorder that arise in the small bowel or colon<sup>1</sup>. The specific cause of IBS is unclear until now, but there are many factors, responsible to trigger the disease, including the disruption either of the connection between the brain and gut or overgrowth of intestinal bacteria<sup>2,3</sup>. The IBS is most common in females and it mainly occurs at the ages between 15 and 65 years<sup>4</sup>. It's a worldwide distributed disease<sup>5</sup> that found in 5–11% of the population of most countries<sup>6</sup>. Also, it is documented as global distribution with a pooled prevalence of 11.2% from all regions of the world as mentioned in a systematic review prepared by Lovell and Ford<sup>7</sup>. The primary estimate in Europe and North America revealed that the prevalence of IBS represented 10-15%, while, its 0.82% in Beijing, 5.7% in Southern China, 6.6% in Hong Kong, 8.6% in Singapore, 14% in Pakistan and 22.1% in Taiwan<sup>4</sup>.

Carcinoembryonic antigen (CEA) is an important cell surface glycoprotein which is composed of 60% carbohydrate with a molecular mass of 180-200 kDa<sup>8</sup>. The family of CEA includes two divisions, one related to cell adhesion molecules and second to pregnancy-specific glycoproteins<sup>9</sup>. In normal condition, different types of human organs, including the gastrointestinal tract, liver, pancreas, lung, kidney, urinary bladder, prostate, breast, ovary and thyroid contain various levels of CEA, while, the blood of healthy persons is usually contained lower level of CEA<sup>10</sup>. The higher level of CEA is practically recorded in patients with different type of malignant diseases, especially with colorectal cancer. Thus, CEA is often used as a useful marker to follow patients with colon cancer as well as detected of the early stage of this type of cancer<sup>11</sup>. One of the first description of the correlation between CEA and colorectal cancer disease is reported by Thomson *et al.*<sup>11</sup> who found that most of patients with colorectal cancer disease had elevated level of CEA compared with other types of cancer diseases<sup>12</sup>. Later, CEA is considered a good indicator for diagnosis of colorectal cancer and some of other malignant diseases such as lung cancer, esophagus cancer and breast cancer<sup>13-19</sup>. Furthermore, many of benign diseases can also elevate the CEA level, such as with the kidney function disorder, high glucose level, carotid atherosclerosis and chronic pulmonary disease<sup>20-23</sup>. The IBS as, one of benign disease that may have the effect on the level of CEA and then the measurement of CEA will play a valuable role in the diagnosis of IBS.

The concentration of CEA was measured in patients with Irritable Bowel Syndrome (IBS) in order to determine the possible relationship between them.

## MATERIALS AND METHODS

**Patients:** A cross-section study designed to measure the level of CEA in the blood of 80 healthy individuals (51 males and 29 females) at the age range (35-55 years) and 95 patients (66 males and 29 females) with Irritable Bowel Syndrome (IBS) at the age range (35-60 years). The diagnosis of IBS disease based on clinical features determined by the physicians committee of AL-Hussein general teaching hospital of Karbala province in 2015. Some of diagnosed patients were smokers, while others were not. The patients with other than IBS diseases was eliminated from the sample collection.

**Reagents:** The CEA ELISA kit was purchased from Human Gesellschaft für Biochemica and Diagnostica mbH (Germany).

**Assay:** The serum without lipemic or hemolysis of all patients were collected. Sandwich ELISA with biotin for streptavidin was used for detection of CEA level in the serum. The absorbance of the final product was measured at 450 nm within 30 min by a BioTek ELx800 ELISA reader (U.S.A). The normal value of CEA for non-smoking individuals is <5 ng mL<sup>-1</sup>, while it is 10 ng mL<sup>-1</sup> for smokers.

**Statistical analysis:** The values were analyzed statistically with paired "t" test between results and the normal value of patients. The minimum level of p-value was <0.01 as significant level.

## RESULTS

The serum CEA was tested in 95 patients with IBS. From Table 1, the blood of 8 (8.4%) of non-smoker males had high levels of CEA that ranged between 5 and 10 ng mL<sup>-1</sup> with a

Table 1: Carcinoembryonic antigen level in patients with irritable bowel syndrome

Patient's gender	CEA level (ng mL <sup>-1</sup> )			Total
	>5	5-10	10-15	
Male, N (%)	57±2 (60)	8±0.7 (8.4)*	1±0.3 (1.0)*	66
Female, N (%)	29±(30.5)	0	0	29
Total	86 (90.5)	8 (8.4)	1 (1.0)	95

Mean±SD, \*Significant differences between test value and normal level at p<0.01, N: Number

significant difference from the normal level, while other male patients had normal values of CEA (60%) with no significant differences from the control group. Meanwhile, all females with IBS showed a normal value of CEA. Furthermore, an old male (48 years) possessed more than 10 ng mL<sup>-1</sup> (14.73 ng mL<sup>-1</sup>) of the CEA with significant difference value ( $p < 0.01$ ) from the normal level. Thus, the male with such higher level of CEA was suspected to have the colorectal cancer disease and other tests were recommended.

## DISCUSSION

The CEA is an important biomarker for detecting of colorectal cancer and some of other malignant diseases<sup>13-19</sup>. The sensitivity of CEA represents 40% of colon and 47% of rectal cancer after testing in 153 and 107 patients suffering from colon and rectal cancer, respectively<sup>24</sup>. Additionally, the CEA level found to be elevated when it preoperative measured in patients with colorectal cancer disease<sup>25</sup>. However, the concentration of CEA is depending on the pathologic stage of cancer disease and its localizations<sup>26</sup>. In patients with colorectal cancer disease located in the right colon, CEA showed the prognostic value than in the left colon<sup>27</sup> and it was also higher in patients with stage IV colorectal cancer disease<sup>25</sup>.

Although, CEA is one of the valuable biomarker for colorectal cancer and some of other malignant diseases. Other non pathological factors can also affect in concentrations of serum CEA and may cause elevation of its level, especially smoking factor<sup>28-30</sup>. Some of the patients in this study were smokers, but the level of CEA in their blood was within the normal range ( $< 10$  ng mL<sup>-1</sup>). However, the elevation effect of smoking on the level of CEA can depend on other factors like type of tobacco products, age and gender<sup>22,29-30</sup>. For example, smoking cigarettes can raise CEA value more than other type of smoking as with hookah<sup>29-30</sup>. Additionally, the serum of smoker males is usually have high level of CEA in comparison with smoker females<sup>31</sup>. On the other hand, Ursavas *et al.*<sup>14</sup> found that there is no relationship between CEA level and age, gender and smoking habit in patients with non-small cell lung cancer (NSCLC)<sup>14</sup>.

Irritable Bowel Syndrome (IBS) is a very common type of intestinal disorder with symptoms of crampy pain, gassiness, bloating, changes in bowel habits that leading to constipation and diarrhea<sup>32</sup>. These symptoms usually arise from many factors, including psychosocial factors, prior gastroenteritis,

abnormal motility, gas retention and heightened sensation<sup>1</sup>. However, IBS does not cause permanent harm to the gastrointestinal tract and does not lead to intestinal bleeding of the bowel or to a life-threatening disease, such as cancer<sup>31</sup>. Based on Rome III criteria that depended on the basis of the patient's stool characteristics, IBS divided into three types: IBS-D (IBS with diarrhea), IBS-C (IBS with constipation) and IBS-M (IBS with mixed bowel habits or cyclic pattern)<sup>4</sup>.

Among patients of IBS, the serum of eight non-smoker males had high level of CEA (5-10 ng mL<sup>-1</sup>) with a significant differences from normal range (5 ng mL<sup>-1</sup>). The most suggested causing of this elevation of the CEA level in which it is less than 10 ng mL<sup>-1</sup> could be related to the presence of one of benign conditions<sup>33</sup>. The IBS is one of these benign diseases which proposed that the high value of CEA may be resulted<sup>34</sup>. Moreover, the colitis disease which was not diagnosed in patients found to be increased the level of CEA<sup>35</sup>.

In the case of an old male who had a higher than 10 ng mL<sup>-1</sup> of CEA, this higher level could be eliminated the responsibility of IBS as a causative agent. Thus, the best explanation for the higher level of CEA in this case is resulting from the presence of colorectal cancer. This suggestion relies on the level mentioned by Anonymous<sup>36</sup>. Thus, more tests for other tumor markers are recommended for such type of case.

According to the survey that depended on life insurance applicants, elevation of the CEA level between 5 and 9.9 ng mL<sup>-1</sup> increased the mortality rate of all human ages and it will become higher in individuals with 10 ng mL<sup>-1</sup><sup>10</sup>. Generally, Duffy mentioned that the concentrations of CEA in patients with colorectal is affected by various factors, including tumor stage, liver status, tumor site within the colon, presence or absence of bowel obstruction, smoking and ploidy status of tumor<sup>33</sup>. However, CEA is not valuable indicator for diagnosis of the early stage of colorectal cancer disease, but it's useful for detecting the advanced stages<sup>26</sup> and the recurrent situation<sup>33</sup>.

Although, there is a similarity between IBS and colon cancer in symptoms which include abnormal defecation and abdominal pain<sup>11</sup>, IBS does not cause or lead to any type of cancer or inflammatory bowel disease in the intestines<sup>1,4</sup>. Thus, the application of CEA as biomarker for differentiation between IBS and colorectal cancer can be useful only when we depend on the concentration of CEA, clinical features and other tests. However, there are many factors can be effected on the sensitivity of CEA to differentiate between colorectal cancer disease and other benign diseases as well as IBS.

## CONCLUSION

The IBS may be responsible for increasing the CEA level within a limited range ( $<10 \text{ ng mL}^{-1}$ ). In case of increasing level of CEA more than  $10 \text{ ng mL}^{-1}$ , it can be considered as an indicator for colorectal cancer disease. However, other tests are recommended to confirm the accuracy of CEA to detect IBS or any of malignant diseases in the gastrointestinal tract when its concentration is high.

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