Study Some of the Risk Factors on Total Antioxidant Capacity in Iraqi Patients with Sporadic Colorectal Cancer

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Abstract

Colorectal cancer is one of the most frequent malignant diseases in the developed countries. It was reported that total antioxidant status is being play a very important roles in development of carcinogenesis. The aim of this study to assess of some risk factors such as age, gender, obesity, and smoking status on total antioxidant status in patients with sporadic colorectal cancer in Iraq. This investigate was completed by using colorimetric method to measure of total antioxidant capacity (T-AOC) and assess the risk factors depending on the levels of T-AOC. All patients included in the present study were getting adjuvant chemotherapy regimen and subdivided into two groups according to Duke’s classification of malignant into early stages A+B and advance stages C+D, cancer site (colon or rectum), and according to the number of dose of chemotherapy regimen (half dose or total dose). The present study showed negatively correlation (r = -0.567) (p<0.05) between T-AOC and ages of patients with sporadic CRC (p< 0.001). The levels of T-AOC decreased in both ever and never smoking compared to control group (p< 0.05). The results showed highly significant difference (p< 0.001) of T-AOC levels between A+B and C+D groups depending on age. The levels of T-AOC was decreased markedly in patients with ages less than 50 years compared to ages more or equal 50 years in both combination stages A+B and C+D (the higher difference was observed in same age and different state). In conclusion the risk factors that studied in this work may be have the main role to decrease levels of T-AOC and in result will increase the probability of injury with colon and rectal cancer in Iraqi population.

Keywords: Total antioxidant capacity, Smoking status, Sporadic Colorectal cancer, Adjuvant chemotherapy, Obesity status.

Ethical Issues: depends on the following.
- Approval of scientific committee of the Biochemistry Department in Babylon Medical College (University of Babylon, Iraq).
- The objectives and methodology will be explained to all participants in the current study to gain their verbal acceptance.

Introduction

Sporadic CRC described the cancers that occurs in the absence of a family history and the inherited syndromes. Despite the name, sporadic cases of colorectal cancer certainly require a significant genetic contribution[1]. Sporadic carcinomas devoid of any familial or inherited predisposition, accounts for approximately 70-90% of CRC [2]. Sporadic cancer is common in persons older than 50 years of age, probably as a result of dietary and environmental factors as well as normal aging. Fewer than 10% of patients have an inherited predisposition to colorectal cancer[3]. There are several factors considered to be causally associated with the development of CRC. For instance, the risk of CRC is clearly increased by a Western diet. Genes responsible for the most common forms of inherited and non-inherited (sporadic) colorectal cancer have also been identified [4]. Some of lifestyle factors and dietary components are suggested to be associated with risk of CRC. Different environmental factors are probable cause damage to DNA through direct binding of metabolites (adduct formation) or oxidative stress[5]. Some of the epidemiological studies have shown that
systematically high intake of dietary fat, meat and protein is positively related to increase risk of CRC[7]. Some of the prospective studies showed that overweight and obesity increase risk of colon cancer[8]. Antioxidants play an important role in preventing the formation of and scavenging of free radicals and other potentially toxic oxidizing species. There are three categories of antioxidant species: enzyme systems (GSH reductase, catalase, peroxidase, etc.), small molecules (ascorbate, uric acid, GSH, vitamin E, etc.).

Different antioxidants are vary in their reducing power [9,10]. Western culture is the main cause of increasing in the incidence of sporadic CRC in development countries [11]. The developed countries accounts for over 63% of all cases of colorectal cancer [12]. Iraqi population started to transformed to developing countries by shifting towards the western- lifestyle that has high probability to increasing of the colorectal cancer occurrence[13]. The aim of this study to assess of some risk factors such as age, gender, obesity, and smoking status on total antioxidant status in patients with sporadic colorectal cancer in Iraq.

Materials and Methods

This study was completed at the laboratories of Biochemistry Department, College of Medicine, and University of Babylon. The collection of samples was carrying out during the period from 1st of March 2014 till 30th of June 2015. The patients group who subjected in this study was 52 patients in the age group ranging from 39-75 years; the mean ± (SD) was (59.3 ± 10.68 years). This group involved of males (58%), with their age ranging from 39-75 years old, the mean ± SD was (61.8 ± 11.4 years), and females (42%) with age ranging from 39-73 years, and mean ± SD was (63.1 ± 11.3 years). The ages of patients group <50 years old were 22(42%) and at ≥50 years old were 30 (58%). All of those patients were monitored and treated with chemotherapy with clinical symptoms of colorectal cancer. The diagnosis of colorectal cancer was performed by sigmoidoscopy, colonoscopy or CT scan and clinical diagnosis was confirmed in all patients by histological examination. Fifty two apparently healthy individuals were taken as a control group with the age ranging from 37-75 years, the mean ± SD was (57.8 ± 11.1 years).

This group included of males (61%) their age ranging from 39 -73 years, mean ± SD was (60.4 ± 10.2 years), and females (39%) their age ranging from 37-75 years, mean ± SD was (64.5 ± 11.6 years). The age and sex of this group were matched to age and sex of patient group, where statistical analysis showed non-significant differences in the age and sex between patient and control groups (p> 0.05). Each person who contributed in the control group underwent full history and physical examination including: address, age, gender, smoking, education, dwelling, past history of diseases and medications. T-AOC was measuring depending on Ferric Reducing Antioxidant Power analysis (FRAP). Results were expressed as U/ml [10].

Results

In the present study, sporadic colorectal cancer patients were classified into two groups depending on cancer stages, cancer site, and adjuvant chemotherapy status, as shown in Figure-1

![Figure 1: Classification of patient groups depending on age and gender](image-url)
The results were classified depending on risk factors:

**Age**

Patients with sporadic colorectal cancer were classified according to the age into two groups, as shown in Figure 2.

![Figure 2: Age distribution of patient group](image)

Patients were involved in this study had an age of 59.3 ± 11.3 years.

The minimum and maximum age were 38 and 75 years respectively, in which about 58% of the patients lie in the age ≥50 years of old and 42% lie in the age <50 years of old. Although colorectal cancer may occur at any age, but most occurs mainly in the age ≥50 years of old.

**Gender**

Amongst 52 patients with sporadic colorectal cancer who contributed in the current study, there were 27 males and 25 females, and this represents 52% and 48% of patients respectively, as shown in Figure (3).

![Figure 3: Gender distribution of patient group](image)

There was a very slightly percentage increasing in the number of males compared to females and this is consistent with some studies that consider that males have same incidence rate of colorectal cancer compared to females.

**Obesity Status**

In the present study, 54% of the patient group have a normal weight, 46% overweight while no patients were obese, as shown in Table (1).

![Table 1: Distribution of sporadic colorectal cancer patients according to obesity status](image)

<table>
<thead>
<tr>
<th>BMI*</th>
<th>N</th>
<th>%</th>
<th>Mean</th>
<th>SD**</th>
</tr>
</thead>
<tbody>
<tr>
<td>Normal weight</td>
<td>28</td>
<td>54%</td>
<td>22.4</td>
<td>2.2</td>
</tr>
<tr>
<td>Over weight</td>
<td>24</td>
<td>46%</td>
<td>26.7</td>
<td>1.4</td>
</tr>
<tr>
<td>Total</td>
<td>52</td>
<td>100%</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

*BMI: body mass index
**SD: standard deviation.
Smoking Status

According to the history of smoking among sporadic colorectal cancer patients, the ever smokers were 30 (58%), and non-smokers (never) were 22 (42%) as shown in Figure (4). The percentage of males those were ever smokers 94% against 4% females.

Figure 4: Distribution of patients depending on smoking status

To demonstrate the effect of age as a risk factor on T-AOC concentration, the correlation between serums T-AOC of sporadic colorectal cancer patients was tested with each of these groups, as shown in Table (2).

Table 2: Effect of the age on serum T-AOC concentration

<table>
<thead>
<tr>
<th>Cancer stage</th>
<th>T-AOC (U/ml)</th>
<th>≥50</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>mean± SD</td>
<td></td>
</tr>
<tr>
<td>&lt;50</td>
<td></td>
<td></td>
</tr>
<tr>
<td>A+B</td>
<td>13.4± 2.2</td>
<td>9.6± 1.8</td>
</tr>
<tr>
<td>C+D</td>
<td>7.5± 2.8 **</td>
<td>6.6± 2.1 **</td>
</tr>
<tr>
<td>Colon</td>
<td>8.8± 2</td>
<td>8.6± 2.1</td>
</tr>
<tr>
<td>Rectum</td>
<td>7.9± 2</td>
<td>8.5± 1.9</td>
</tr>
<tr>
<td>Chemotherapy</td>
<td>Half dosage</td>
<td>7.6± 1.5</td>
</tr>
<tr>
<td>status</td>
<td>Total dosage</td>
<td>8.2± 1.2</td>
</tr>
</tbody>
</table>

Table 2 shown highly significant difference (p< 0.001) of TAO-C levels between A+B and C+D groups depending on age.

The levels of T-AOC was decreased markedly in patients with ages less than 50 years compared to ages more or equal 50 years in both combination stages A+B and C+D (the higher difference was observed in same age and different state).

Also the results of present study showed no statistical difference (p > 0.05) between the levels of T-AOC in anther group’s colon and rectum or half dosage and total dosage depending on ages.

To investigate the effect of smoking status on T-AOC levels in sera of sporadic CRC patients as a risk factor, ever and never smoking status of all patients was compared with control group as shown in fig(5).

This study suggests no significant differs in T-AOC levels in sera of ever and ever smoking patients with sporadic CRC patients (P >0.05). The levels of T-AOC decreased in both ever and never smoking compared to control group (p< 0.05).
To demonstrate the effect of obesity status on sporadic CRC as a risk factor, over weight and normal weight of all patients group was compared with control group as shown in Fig. 6.

The present study showed negatively correlation \((r=-0.567)\) \((p<0.05)\) between T-AOC and ages of patients with sporadic CRC\((p< 0.001)\), as shown in Fig. 7. The correlation between T-AOC and age in control group was \((r=-0.702)\) and this means the fall of T-AOC was mainly affected by age. This correlation still very strong and the age was the main causing of fall in T-AOC concentration but the cancer status may be remain the second cause.

**Discussion**

Although colorectal cancer may occurs at any age, but most occurs mainly in the age \(\geq 50\) years of old. Cappell et al were reported that the risk of developing CRC increase with age, and over 90% of sporadic CRC occur in subjects over the age of 50 [14]. Karsten et al. suggested that the incidence of CRC in young
patients has been rising [15]. Siegel et al. (2014) were reported that during the past decade (2001 to 2010), overall incidence rates decreased by an average of 3.4% per year. However, trend differ substantially by age and the rates decline by 3.9% per year among adults aged 50 years and older, for a total the incidence of CRC decrease by 30%. In contrast, rates amplified by 1.1% per year among men and women aged younger than 50 years [16].

The incidence of colorectal cancer in Iraqi population that recorded in the present study was 42% at ages of less than 50 year, and this agreement with the previous study. The present study also agreement with other study in Iraq that reached to there are a higher number of young patients in Iraq and developing countries infected with colorectal cancer compared to the Western communities.

The difference in age distribution could be related to age longevity in the Western countries as compared to the developing countries in the Middle East [17]. In the general population, age-specific CRC incidence and mortality are lower in women than in men, which imply that women reach comparable levels of CRC incidence and mortality at higher ages than men. However, within countries, the same age of initiation is generally suggested for women and men, in spite of important differences between genders in the epidemiology of CRC [18].

Agrawa et al. suggested that colorectal cancer affects all races and genders equally, with a slightly higher incidence and mortality rate among African-American males. Also they reported that the women at age 60 years and older have an equal risk of being diagnosed with breast cancer or colorectal cancer [19].

The World Health Organization (WHO) estimates that 1.5 billion people are overweight and 500 million are obese in worldwide [20]. Polednak et al., were preformed a meta-analysis on 153,760 American subjects. They reported that the relative risk (RR) for developing CRC was 1.4 for obese men and 1.1 for obese women. This suggests that the association is weaker for women when compared to men. The mechanism leading to a gender difference remains unclear, but it does suggest that there are likely a number of factors that influence whether an obese individual will develop CRC [21]. On the other hand, a direct link between obesity and CRC remains controversial. Obesity, particularly abdominal obesity, was associated with increased risk of CRC and was found to affect oxidative status in obese people [22].

Coussens and Werb suggested that chronic inflammation secondary to obesity has an established association with cancer [23]. A number of studies have shown that being overweight is associated with increased risk of CRC. As well, increasing obesity can lead to insulin resistance (decreasing of insulin sensitivity), which has been reported to triple the risk of CRC mortality [24].

The smoking causes a two-fold increase risk of developing colorectal cancer. Many epidemiological studies in Western populations have identified smoking as an independent risk factor for colorectal cancer and evidence also demonstrates an earlier incidence of colorectal cancer in men and women who smoke cigarettes [25]. Wu et al. 2005 reported on correlation between cigarette smoking and adenomatous polyps, and these larger polyps found in the colon and rectum were associated with long-term smoking.

They also found that elevated number of adenomatous polyps in former smokers even after 10 years of smoking cessation [26]. The toxic compounds present in tobacco causes depletion of antioxidants and accumulation of pro oxidants (ROS), this imbalance between antioxidants and pro oxidants leads to increasing oxidative stress, and this may stimulates the developing of CRC [27].

Since the control group had no smoking subjects , a comparison was made of the mean levels of T-AOC between never smoker patients and control group , resulting in a significant difference (P < 0.05), this eliminates the possibility that decreased level of T-AOC is not due to smoking alone but also due to colon or rectum cancer itself . The significantly lowest of T-AOC levels was observed in ever smokers in this study, may be due to the inflammatory state associated normally with smoking may influence the optimal antioxidant concentrations for physiological protection. Thus, in ever smokers, whose evidence exists of a heightened inflammatory status, lower
concentrations of plasma antioxidants may be an adaptation to this state [28]. It was reported that the obesity causes of metabolic syndrome or low-grade chronic inflammation, which may be responsible for constant increase in production of free radicals.

It is assumed that over time such conditions (oxidative stress) create environment favorable to the CRC development [29]. The present study showed decreasing in T-AOC in both over and normal weight patients compare to control group. This indicates that decreasing in antioxidants not due to body mass alone but as result to cancer itself. The difference in measurement methods leads to different results, for example, measurement of T-AOC with FRAP method which cannot determine antioxidants with sulfhydryl groups (or thiol group R-SH) (especially proteins) and showed decrease in T-AOC with age [30]. In other studies an increase in T-AOC with age was found as a secondary observation in patients suffering from cancer disease [31]. The future study included the measured two parameters are good predictors, sensitive and specific and accurate in prediction of other disease [32-35].

Conflicts of Interest
The authors have no conflicts of interest and agree to publishing of this paper.

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References


