DETERMINATION OF CANCER MARKER CARCINOEMBRYONIC ANTIGEN (CEA) AND LEVELS OF REPRODUCTIVE HORMONE, TESTOSTERONE IN SERUM OF SMOKER MAN THAT CORRELATE TO SEMEN PARAMETERS IN BAGHDAD CITY CAVIL’S

Introduction
The leading causes of preventable illness and early death worldwide, smoking is a worldwide epidemic. Annually, smoking-related illnesses claim the lives of about 4 million people, as reported by the World Health Organization (1). There are several ways to smoke tobacco, including cigarettes, cigars, electronic cigarettes, and water pipes (2). No matter how a person smokes, nicotine releases over seven thousand toxic chemicals, the majority of which are known to have carcinogenic properties (3). Emphysema, ischemic heart disease, erectile dysfunction, and an increased

Abstract: Objective: Subfertility, erectile dysfunction, recurrent abortions, and other health problems are associated with smoking, which is a rapidly expanding global epidemic. Furthermore, the impact on the male endocrine system, particularly testosterone levels, is an ongoing topic of debate due to the contradictory findings that have been recorded. Using a non-smoking control group (n=50) and a group of male smokers (n=90), the researchers examined the effects of smoking on serum free testosterone (T) and carcinoembryonic antigen (CEA). In regards to serum free testosterone (T), which was 15% higher in smoker cases (p < 0.01), and on carcinoembryonic antigen (CEA), and the P values is < 0.001 and less than 0.001, respectively, our study found a positive and statistically significant difference between the smoker and non-smoker groups. Furthermore, a negative link between smoking duration and semen parameters was shown to be statistically significant (p < 0.01). Conclusion: Further evidence that smoking has beneficial effects on blood testosterone and CEA concentrations was added to the current investigation.

Key words: Testosterone hormones, CEA, semen, subfertility, smoking.

1 Technical Nursing Department, Medical Technical Institute, Middle Technical University, Baghdad, Iraq

1. Dr. Loqman Juma Tawfiq

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incidence of cancer are among the many health concerns linked to smoking (4), (5).

Numerous reviews devote considerable time and energy to elucidating the most fundamental roles that testosterone plays in the human body. In humans, testosterone is essential for the maturation of the testes and prostate, among other male reproductive tissues, and for the promotion of extra sexual characteristics, such as adipose tissue expansion, bone and muscle mass raised, and formation of hair. There is a correlation between it and a rise in violent and criminal acts.(6). passion, the desire to win over romantic interests, and other actions associated with courtship (7). Also, testosterone plays a role in health and wellness for both sexes; it affects, cognition, social and sexual behavior and general mood, energy production and metabolism, the and prevention of osteoporosis (8), (9). Just recently A lower risk of prediabetes was associated with higher serum testosterone levels in adults in the United States, according to research by Jason Wang et al. in 2022 (10).

The Carcinoembryonic antigen (CEA) is a term used to designate a family of glycoproteins called glycosyl phosphatidyl inositol (GPI) that promote cell adhesion. Normal synthesis of CEA in fetal gastrointestinal tissue ceases just before delivery. Due to this, good and healthy persons typically they have extremely low CEA levels in blood (nearly 2-4 ng/mL) (11). Nevertheless, it can be used as a good markers of tumor in clinical investigation due to the elevated serum levels observed in some cancer types. Excessive smoking might also lead to increased serum levels (12).

CEAs are specifically sialofucosylated glycoproteins that bind to the surface of cells (13). They are classified as belonging to the CD66 cluster of differentiation according to immunological analysis. Proteins such as CD66a, CD66b, CD66c, CD66d, CD66e, and CD66f are represented (14).

Materials and methods:
Ninety samples collected from Baghdad city cavil’s and 60 samples as control group, from the period 1st September 2021 to 1st February 2023.

Samples collection:
The samples collected from smokers and nonsmokers they are lived in Baghdad city:
1. Blood serum was taken from arm blood vessel by disposable 5mm syringe.
2. By using Lab. Centrifuge we separate the serum to be used finally for laboratory assay.
3. Testosterones were directly measured in the serum using radioimmunoassay kits (Catalog number: 07BC-1115, Bangalore Genei Private Limited) with reference values(15)
4. 4-Using a non-competitive "sandwich principle" approach, we determined the CEA levels in a commercial enzyme immunoassay kit (16) and was assessed using the full-automatic eCobas e601 platform (Roche Diagnostics, Rotkreuz, Switzerland) with the Elecsys® CEA immunoassay.
5. Body mass index were obtained by division of weight versus length with square meter.
6. Seminal fluid examination is performed according to (17)

Statistical analysis
"STATISTICA" (version 8.0) was used to conduct statistical analysis for the data. Mean (SD), median (with 5th and 95th percentiles), and table and text descriptive statistics are used. For this investigation, we utilized the Kruskal-Wallis ANOVA test to determine whether there were statistically significant variations in parameters between the smoking groups non-smokers and smokers. Statistical significance was determined by a p value less than 0.05.
Results

1. The current study include 90 regular smoking men where the number of cigarettes per day does not decrease less than 20 cigarette. Information was collected for all volunteers as shown in table (1): 90 smoking men, age range, (Mean ± SE) (30.30 ± 1.69 years) and 50 controls (Mean ± SE) (30.11± 2.34 years). Table (1) express a similarity in mean BMI (Kg/M2 ) between the two categories smokers (25.5± 1.65) and nonsmokers (26.80± 1.05). Finally, the results of this study indicated that there is a similarity between Smokers and non-smokers in Waist Circumference (37.23 ± 0.65), (33.69± 0.47), respectively.

Table (1): general illustration of the samples included in our study

<table>
<thead>
<tr>
<th>Parameters</th>
<th>Groups</th>
<th>Number</th>
<th>Mean ± SE</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age / year</td>
<td>Smokers</td>
<td>90</td>
<td>30.30 ± 1.69</td>
</tr>
<tr>
<td></td>
<td>Non-Smokers</td>
<td>50</td>
<td>30.11± 2.34</td>
</tr>
<tr>
<td>BMI/ kg/m2</td>
<td>Smokers</td>
<td>90</td>
<td>25.5± 1.65</td>
</tr>
<tr>
<td></td>
<td>Non-Smokers</td>
<td>50</td>
<td>26.80± 1.05</td>
</tr>
<tr>
<td>WC / cm</td>
<td>Smokers</td>
<td>90</td>
<td>37.23 ± 0.65</td>
</tr>
<tr>
<td></td>
<td>Non-Smokers</td>
<td>50</td>
<td>33.69± 0.47</td>
</tr>
</tbody>
</table>

2. Role of smoking and testosterone hormone: we finding that smoking increase the level of this hormone (nmol/L) with a significance (p < 0.01) in comparison with nonsmoker persons.

Figure (1): correlation between smoking and nonsmoking cases.

3. Regarding the levels of CEA (normal value 0- 2.5 ng/mL), our study resulted that in smokers person and more clearly in heavy cases, the values are higher statically (p < 0.001) in comparison to nonsmoker models. Table (2).

Table (2): levels of CEA (ng/mL) in smokers and nonsmokers persones.

<table>
<thead>
<tr>
<th>Models</th>
<th>CEA (ng/mL)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nonsmokers</td>
<td>1.25 ± 2.1</td>
<td></td>
</tr>
<tr>
<td>Moderate smokers</td>
<td>2.37 ± 2.3</td>
<td>p &lt; 0.001</td>
</tr>
<tr>
<td>Heavy smokers</td>
<td>4.98 ± 2.5</td>
<td>p &lt; 0.001</td>
</tr>
</tbody>
</table>
4. This new study also involve the effect of smoking habit on the essential semen parameters (volume, leucocyte, concentration (million/ml), motility percent, leucocyte % and morphology percent. The results shows that there are a decrease in all of mentioned parameters in smoker group in comparison with nonsmoker groups (p < 0.001), with the exception of volume. Table (4).

Table (4): parameters of semen in smoker and non-smoker sample subjects (mean (SD)).

<table>
<thead>
<tr>
<th>Semen parameters</th>
<th>Nonsmokers</th>
<th>smokers</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Volume (Mean ± SD)</td>
<td>3.13 ± 2.25</td>
<td>3.06 ± 2.27</td>
<td>0.534</td>
</tr>
<tr>
<td>Abnormal Morphology</td>
<td>72 % ± 10.9</td>
<td>59.0 ± 12.2</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Motility %</td>
<td>63.2 ± 13.9</td>
<td>54.5 ± 14.8</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Concentration ×10⁶</td>
<td>38.9 ± 10.9</td>
<td>28.4 ± 13.2</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Leukocyte %</td>
<td>45%</td>
<td>33%</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

Discussion

The aim of the our current study was to evaluation the effect of smoking habit on semen components, body weight, and testosterone levels, in addition to its effect on one of the important indicators of malignant diseases such as CEA in men Iraqi/Baghdad city. In contrast to WHO figures for the global population (36.7%), our research shows that 40.5% of men in Baghdad city, with a median age of 25 (20 - 30 years), smoke cigarettes (18). Our primary objective in this study is to determine the impact of smoking on the characteristics of sperm. To find out how cigarette smoking as an indicator changed with dose, the researchers divided smokers into two groups: moderates who smoked 15-20 cigarettes per day and heavy smokers who smoked 30-40 cigarettes per day. Cigarette smoking primarily reduced sperm parameters such as volume, total count, concentration, progressive motility, and leucocyte percentage, as well as sperm concentration. Consistent with the findings of numerous other research with subfertile men, our findings when applied to individuals from the general population (19), (20), or in case-control studies (21), (22) (23). Direct exposure to the harmful components of cigarette smoke (carcinogens, heavy metals, nicotine and its metabolites, and mutagens) is the likely method by which smoking is associated with negative effects on semen parameters, however the exact process is still not completely understood (24, 25). Furthermore, nicotine and other tobacco components have an impact on the operation of the prostate gland and seminal vesicles, two accessory glands that change the amount of semen and the functional characteristics of sperm (26, 27). Cigarette smoke also reduces oxygen levels, which has an effect on spermatogenesis and ultimately on sperm quality (22, 28).

But generally speaking, research on the link between smoking and hormones that regulate reproduction has shown conflicting results, our study found that testosterone will be increased. The biological explanation for this type of relationship may be due to the increase in SHBG, which reduces the decomposition of testosterone and leads to an increase in the level of this hormone, which is important for physical and sexual health. The exact processes that lead to the favorable correlation between smoking and SHBG are still not well understood. Previous research has shown a similar association, so our findings are consistent with that (29) (30). Despite the results we have reached, there are results that contradict our results, as these results show that the effect of smoking leads to a decrease in the level of testosterone in smokers compared to non-smokers (31) (32). There is also a third group of researchers who found that smoking does not affect the level of this hormone (28, 33).

The important point that prompted us to study the relationship between smoking habit and CEA is that this substance is very important for
diagnosing malignant tumors, determining the strength and spread of the disease in the body, and determining the extent to which the patient will benefit from treatment. It is important to know that this substance is naturally present on the endothelial side of the plasma membrane and has an important role in the apoptosis process and limiting the growth of cancer cells (34). Through our study and other studies, we found a positive relationship between smoking habit and high levels of this important diagnostic substance (35). Thus, it is important to notice an increase in the level of CEA with the presence of smoking status in the person from whom the examination is requested, and to focus on that not every increase in the level of this substance indicates that the person has cancerous tumors, and to prevent interference and accuracy of diagnosis, especially for individuals whose smoking levels are high (30 - 40) Cigarettes per day.

Conclusion:

Some of the properties of seminal fluid (morphology, leukocyte count, and motility) are negatively impacted by cigarette smoking, which can lead to male infertility. As a result, we urge smokers to put the cigarette down, and additional research is required to confirm whether or not this has any effect on male fertility. In contrast, when testing CEA levels for the purpose of diagnosing cancer, it is crucial to distinguish between elevated levels due to smoking status and those caused by other factors.

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