

Serum Cholesterol Level in Iraqi Depressed Patients: Results and Review

تركيز الكوليستيرول في مصول العراقيين المصابين بالكآبة: نتائج واستعراض

Hussein K. Abdul Hussein (PhD)

Amir Fadhel (M.B.Ch.B.)

Amir Omran (M.B.Ch.B.) (CAMB)

Abstract:

Background: Cholesterol is widely distributed in all tissues, but it is especially abundant in the nervous system, where it is important for many aspects of cellular structure and function. Depression is present in high range in patients admitted to hospital after a myocardial infarction and is an independent risk factor for increased mortality. Cholesterol is one of the risk factor of ischaemic heart diseases (IHD). Any association between depression and cholesterol level is complex and may be confounded by the increase use of antidepressants and other medications among persons with depression.

In this work, an attempt was carried out to link depression, serum cholesterol, and the effect of treatment by measuring serum cholesterol in the tricyclic antidepressants (TCAs) treated depressed patients and compare with control and untreated depressed patients to evaluate the effect of treatment

on serum cholesterol. The second aim of this study is to review the majority of researches that studied serum cholesterol in different categories of depressed patients in different countries.

Patients and Methods: This study included (38) depressed patients who are on TCAs as one of the drugs prescribed for the treatment. The second group consists of seventy two untreated depressed patients. Fifty apparently healthy subjects (no depression and IHD) were selected as a control group. Their sex and age were comparable to those of patients.

Total serum cholesterol was measured by using enzymatic method for the three groups under study. **Results:** There is a significant decrease ($p < 0.05$) in mean serum cholesterol in untreated depressed patients as compared with control or treated depressed patients. While no significant changes noticed from the comparison between treated depressed patients and control group. The results showed that there is a significant difference between males and females in control and untreated depressed patients groups while there is no significant difference in serum cholesterol in between male and female in Treated Depressed Patients.

Conclusion: From the results of this research and the review, it can be concluded that:

Depression is not yet a consistent risk factor for IHD. Low cholesterol in suicide patients (usually severely depressed) can be predicted by a severe decline in appetite and cease of food ingestion. Therefore, cholesterol levels in their serum should be decreased.

Treatment with TCAs results in improvement in depression symptoms, including appetite, but has bad side effects on heart. Hence, the diagnosed depressed patients, who already under treatment, have a higher risk of IHD than control. In those groups of depressed patients, serum cholesterol will be normal or higher than the baseline, but they have a higher risk of IHD.

Keywords: Cholesterol, tricyclic antidepressants, ischaemic heart diseases, depression.

الخلاصة:

المقدمة: ينتشر الكوليستيرول في كل الأنسجة ولكنه يتركز في الجهاز العصبي حيث له أهمية في تركيب ووظائف الخلايا. تنتشر الكآبة عند المرضى الراقدين نتيجة الجلطة القلبية وتعتبر عامل خطر في ازدياد الوفيات لديهم. إن ارتفاع الكوليستيرول في الدم هو من العوامل المسببة لأمراض القلب الاحتشائية. إن أي علاقة بين مستوى الكوليستيرول و الكآبة هي علاقة معقدة وتزيد تعقيدا تناول الأدوية من قبل مرضى الكآبة.

في هذا البحث تمت محاولة لإيجاد رابط بين الكآبة والكوليستيرول ودراسة تأثير تناول مضادات الكآبة ثلاثية الحلقات على تركيز الكوليستيرول في مصول المرضى العراقيين المصابين بالكآبة ومقارنتها مع الأصحاء والمرضى غير الذين لا يتناولون العلاج. الغرض الآخر من البحث هو استعراض كمية كبيرة من البحوث التي تناولت العلاقة بين الكوليستيرول و الكآبة في بلدان وظروف مختلفة.

طريقة العمل: اشترك في هذه الدراسة 38 شخصا مصابا بالكآبة ويتناول أدوية ثلاثية الحلقات كأحد الأدوية للعلاج. المجموعة الأخرى تكونت من اثنين وسبعين مريضاً لا يأخذون العلاج. واخذ خمسون شخصا سليماً من مرض لغرض المقارنة. تم تقدير الكوليستيرول الكلي في مصل الدم باستعمال الطريقة الأنزيمية للمجاميع الثلاثة.

النتائج: أظهرت النتائج انخفاضاً معنوياً ($p < 0.05$) في تركيز الكوليستيرول في مصول المرضى الذين لا يأخذون العلاج مقارنة بالمرضى الذين يتناولون العلاج أو مع مجموعة السيطرة. بينما لم يلاحظ فرق معنوي بين المرضى الذين يتناولون العلاج مقارنة بمجموعة السيطرة. أظهرت النتائج فروقات معنوية الرجال والنساء في مجموعتي السيطرة والمجموعة غير الخاضعة للعلاج. بينما لا يوجد فرق معنوي بين الرجال والنساء المعالجين بالأدوية.

الاستنتاج: من خلال نتائج هذا البحث واستعراض نتائج البحوث الأخرى يمكن استنتاج إن كون مرض الكآبة عاملاً أساسياً للإصابة بأمراض القلب الاحتشائية لا زال غير مؤكداً بشكل قاطع. إن انخفاض الكوليستيرول عند المرضى الذين لديهم ميول انتحارية نتيجة شدة مرض الكآبة يعود إلى أنماط التغيرات في الشهية والتوقف عن تناول الطعام لدى هؤلاء المرضى لذلك يكون الكوليستيرول في دمهم أوطأ من الناس الأصحاء. إن العلاج بمضادات الكآبة ثلاثية الحلقات يؤدي إلى تحسن أعراض الكآبة ومن ضمنها تحسن الشهية مع أن هذه الأدوية لها تأثير سلبي على القلب. لذلك فإن المرضى الذين يخضعون للعلاج يكون لديهم مستوى كوليستيرول طبيعي أو أعلى بقليل من الطبيعي ولكنهم أكثر عرضة للإصابة بأمراض القلب من الناس الأصحاء.

الكلمات الرئيسية: الكوليستيرول، الكآبة، أدوية مضادة للكآبة ثلاثية الحلقات، أمراض القلب الاحتشائية.

Introduction:

The depressed patients tend to view the world as a difficult place, filled with obstacles and burdens, set themselves as victimized and lack hope⁽¹⁾. Hence, up to 15% of patients with severe major depressive disorder commit suicide and death by suicide occurs at the rate of about 1% per year. The findings of many scientists support a hypothesized relation between lowered serum cholesterol and depressive symptoms^(2, 3) and suicide^(3, 4, 5, 6). Overall, the evidence for an association between low cholesterol and depression is not as strong as the link with suicidal ideation. Sullivan *et al* (1994)⁽⁷⁾ studied the cholesterol level in patients with major depressive episode and found that the suicidal ideation or attempt was five times more likely in the lowest cholesterol group (≤ 4.1 mmol/L) than in the highest group (≥ 6.2 mmol/L).

It is generally accepted that major depression tends to run in a chronic or recurrent course⁽⁸⁾. The course or recurrent depression is variable. Some patients have few isolated episodes separated by stable intervals (years) of normal functioning. Others have clusters of episodes and still others have increasingly frequent episodes with shortening of the interepisodes intervals⁽⁹⁾.

In a study carried out in New Mexico, 3.8% of adults had recurrent symptoms of depression and have certain health conditions (e.g., high blood pressure, high blood cholesterol, arthritis, and asthma) than persons without depression⁽¹⁰⁾. Therefore, the estimation of cholesterol at different interval through the course of episodes is an important issue.

Cholesterol is widely distributed in all tissues, but it is especially abundant in the nervous system, where it is important for many aspects of cellular structure and function⁽¹¹⁾. Cholesterol concentration is influenced by dietary and genetic factors and by health.^(12, 13, 14) Cholesterol affects both the permeability and fluidity of cell membrane and the exchange processes, and it is a precursor for steroid hormones⁽¹⁵⁾.

Lowering or low cholesterol concentrations influence mood or behavior by neurochemical consequences⁽¹⁶⁾. The proposed mechanism for this effect on mood has been a change in neuronal membrane fluidity and subsequent alteration in serotonin binding, reuptake, or

metabolism,⁽¹⁷⁾ but there is no agreement that this is a valid explanation^(18, 19, 20). Many researchers^(21, 22) found that parasuicide patients had significantly lower cholesterol levels than the control group of non-suicidal patients. While other group⁽²³⁾ showed higher levels of cholesterol in the parasuicide patients. Furthermore, it is found that cholesterol levels were associated inversely with situational feelings of depression, but positively with more persistent depressive feelings. One explanation for this may be that lowering cholesterol concentration causes changes in the cholesterol content of the synaptosomal membrane and a decrease in the number of serotonin receptors. Because a low serotonin concentration has been associated with suicidal depression and impulsive behaviour^(24, 25). This explanation may be more acceptable.

In a review of studies, Katon and Sullivan (1990)⁽²⁶⁾ concluded that 6% of patients in primary care settings and 11% of medically in-patients have major depression, accompanied with a 3% incidence in general population. Depression is present in over 45% of patients admitted to hospital after a myocardial infarction⁽²⁷⁾ and is an independent risk factor for increased mortality^(28, 29, 30) and increased morbidity^(31, 32) after myocardial infarction. Although this is not certain, depression may lead to myocardial infarction^(33, 34, 35). Research

in this area has been limited to studies of small numbers of highly selected hospital patients, often without any control group ⁽³⁶⁾. Furthermore, the overall relation between depression, ischaemic heart disease (IHD), and cholesterol concentration is unclear. Elevated serum cholesterol levels have consistently been identified as a major conventional risk factor for cardiovascular disease ^(37, 38, 39). While depression is associated with low cholesterol concentration, then a lower prevalence of depression in patients who subsequently develop IHD would be expected. However, this is not the usual case.

Further work will be needed to clarify the relation between cholesterol level and depressive disorder. In this work, an attempt was carried out to link depression, serum cholesterol, and the effect of treatment by measuring serum cholesterol in the tricyclic antidepressants (TCAs) treated depressed patients and compared with control and untreated depressed patients to evaluate the effect of treatment on serum cholesterol. The second aim of this study is to review the majority of researches that studied serum cholesterol in different categories of depressed patient in different countries. Addition of the findings of this study to the whole international works in this field may help in the achieving of a complete picture about the correlation between depression and cholesterol and subsequent effect of depression on IHD.

Patients and Methods:

A-Patients:

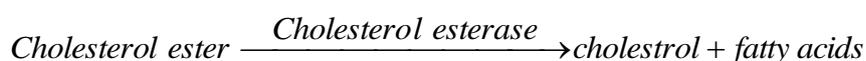
This study occurred in Al-Husaini General Hospital at Karbala city and included (38) depressed patients (22 men and 16 women). The patients aged (38.4 ± 26.5 years) (mean \pm standard deviation). These patients are on TCAs as one of the drugs prescribed for the treatment. The second group consists of seventy two untreated depressed patients (32 men and 42 women) and they were previously tested for blood cholesterol level in previous work in our laboratory. The age of the untreated group was (36.2 ± 14.4 years) (mean \pm standard deviation). The patients were diagnosed by the psychiatrists using a semi-structured psychiatric interview schedule for the diagnosis of depressive disorder based on the ICD-10. Patients were evaluated by full medical history to exclude any existing systemic disease that may affect the cholesterol level particularly diabetes, liver disease, renal disease, and chronic drug intake; otherwise the patient was excluded from the study. Consent was obtained from the patient or his close relatives.

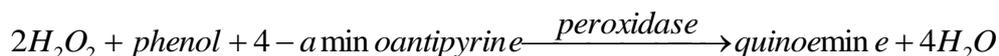
B-Controls:

Fifty apparently healthy subjects were selected as a control group. Their sex and age were comparable to those of patients. None of these subjects was obese, alcoholic, or having a history of heart diseases, other metabolic disorders, and none of the females was on contraceptive pills.

C-Cholesterol Estimation:

Total serum cholesterol was measured by using cholesterol kit (PAP 100 bioMerieux) according to Richmond (1973) ⁽⁴⁰⁾. The principle of this method was to lysis the cholesterol ester to the cholesterol and fatty acids, and then oxidized it to get the quinoemine:





The absorbance was measured spectrophotometrically at 500 nm after five minutes at 37°C. The intensity of the color produced was directly proportional to the total cholesterol concentration in the sample⁽⁴⁰⁾.

D-Statistical Analysis: Unpaired Student's t-test was used to compare serum cholesterol in the groups under study. When (p-value < 0.05), the difference is considered to be significant. Cholesterol concentrations, according to Morgan *et al* (1993)⁽²⁾ were categorized as low (<4.14 mmol/l), normal (4.14-5.16 mmol/l), borderline (5.17-6.20 mmol/l), or high (>6.21 mmol/l)⁽²⁾.

Results:

The mean serum cholesterol in control and the treated depressed patients are shown in Figure (1) as well as serum cholesterol in untreated depressed patients. There is a significant decrease (p<0.05) in serum cholesterol in untreated depressed patients as compared with control or treated depressed patients. While no significant changes noticed from the comparison between treated depressed patients and control group (Table (1).

Table (2) showed the significant difference in comparing between male and female groups. The results showed that there is a significant difference between male and female in control and untreated depressed patients groups while there is no significant difference in between male and female in Treated Depressed Patients.

Discussion:

The decrease in serum total cholesterol in untreated depressed patients is in agreement with many but not all studies concerning serum cholesterol and depression⁽⁴¹⁾. It was found that the serum total cholesterol concentration in patients with major depression was significantly lower than control⁽⁴²⁾. The serum cholesterol in treated depressed patients was increased toward normal values in clinically recovered patients from depression⁽⁴²⁾. Although Maes *et al*(1994)⁽⁴³⁾ noticed that there is no significant difference in total or free cholesterol concentration between depressed patients and control.

It is not outlandish to suggest that men who are ill may be depressed and that this has influenced their appetite and hence cholesterol concentrations⁽⁴⁴⁾. Other studies have shown that the association between low serum cholesterol and depressive symptoms can be explained by confounders such as poor health⁽¹⁶⁾.

In the present work, there is a significant decrease (p<0.05) in serum cholesterol in untreated depressed patients as compared with control or treated depressed patients. While there was a significant decrease in serum cholesterol in untreated depressed patients as compared with control group (p<0.05)⁽⁴⁵⁾. Furthermore, the correlation coefficient values were low and showed a presence of a slight correlation between cholesterol versus cortisol or total sialic acid⁽⁴⁵⁾. Thus, the results noticed in this work may be due, at least in part, to the effect of treatment by different TCAs and the treated depressed patients may be at high risk of IHD even they have normal or borderline cholesterol level. In addition to the other fact that TCAs especially amitriptyline have myocardial toxicity^(46, 47). There is a potential hazard of antidepressant therapy effects on autonomic functions^(48, 49, 50, 51), appetite, heart rate^(52, 53, 54, 55, 56). They have also antimuscarinic effects⁽⁵⁷⁾, psychomotor, and cardiovascular effects⁽⁵⁸⁾.

⁵⁹⁾. They affect potassium channel ⁽⁶⁰⁾ and act as a potent use-dependent blocker of Na⁺ channels that may, in part, explain its analgesic actions ⁽⁶¹⁾. The common effects of TCAs on the heart muscle conclude that there is only one common receptor site in the channel molecule for the TCAs molecules ⁽⁶²⁾.

Any association between depression and cholesterol level is complex and may be confound by the overlap between generalized anxiety and depression and by the increase use of antidepressants and other medications among persons with depression ⁽⁶³⁾. In one research, high serum cortisol level in depressed patients was thought to be one of the reasons about the increase in the cholesterol level, in their group under study, and possibly, through its effect on sympathetic neurotransmitter availability, affects behavior ⁽⁶⁴⁾. On the other hand, the changes in dietary cholesterol can alter the fluidity of cellular membranes, affecting the activity of ion channels and neurotransmitter receptors ⁽⁶⁵⁾. A decreased receptor activity might lead to decreased uptake by brain cells of serotonin, a neurotransmitter associated with various aggressive behaviors ^(66, 67). Compared with a diet high in fat and cholesterol, a low-fat, low-cholesterol diet (But one containing a similar number of calories) has been reported to lower serotonergic activity ⁽⁶⁸⁾ and lead to more aggressive behavior ⁽⁶⁹⁾ in monkeys. The concept of "vascular depression" in younger subjects was introduced by Iosifescu *et al*(2005) ⁽⁷⁰⁾.

The cardiovascular risk score in depressed patients was significantly associated with treatment nonresponse. Among individual cardiovascular risk factors, elevated total cholesterol was a significant predictor of treatment nonresponse and lack of remission. They concluded that cardiovascular risk factors may have negative effects on the course of treatment in depression. Thus, it can be concluded that the cholesterol level and the risk of IHD are related to the anxiety more than related to the depression and the treatment of patients with elevated cholesterol level may have anxiety symptoms that needed for treatment and not only treatment of depression.

Studies have revealed a relationship between cholesterol levels and serotonergic function in healthy young adults ⁽⁷¹⁾. While Engstrom *et al* (1995) ⁽⁷²⁾ could not find much support for the hypothesis of association between low cholesterol levels and decreased serotonin activity in the brain. Another important reason for the decrease in serum cholesterol in depressed patients is that, decreasing appetite as a consequence of depression in men would probably lead to both decreasing cholesterol and triglyceride concentrations ⁽⁷³⁾.

Sonawalla *et al* (2002) ⁽⁷⁴⁾ noticed that among 322 depressed outpatients, 51.6% were classified as having elevated serum cholesterol (>200 mg/dL). Furthermore, they found that depressed patients with elevated cholesterol levels were significantly more likely to be non responders to fluoxetine treatment than were depressed patients with non elevated cholesterol levels ⁽⁷⁴⁾. Papakostas *et al* (2003) ⁽⁷⁵⁾ noticed that major depressed patients with elevated cholesterol levels were more likely to have a poorest prognosis for treatment response.

The results of Table (2) showed a significant difference between male and female in control and untreated depressed patients groups while there is no significant difference in between male and female in treated depressed patients. These results can be discussed by different means. The relation between depression and IHD differs between men and women. Patients with IHD—would have a lower prevalence of depression. This is clearly not the case for men with IHD. The difference in the sexes also showed different effects of cholesterol on depression and the risk of IHDs. Men, who are at higher absolute risk of IHD, are more susceptible than women to changes in autonomic nerve activity or changes in the operation of the catecholamine and steroid axes. Secondly, depression may lead to an increase in smoking and a decrease in physical activity that is more pronounced in men than women. It might reflect differences in severity of depression and illness behavior between the sexes—for example, men may be diagnosed with depression only if it is of a certain severity ⁽⁷⁶⁾.

Horsten *et al* (1997)⁽⁷⁷⁾ found that low cholesterol levels in middle aged healthy women were associated with a higher prevalence of depressive symptoms and with lack of social support. Men had an excessive death which was attributed to cardiovascular diseases and suicide⁽⁷⁸⁾. In one research⁽⁷⁹⁾, it is found that there is a slight decrease in serum cholesterol in patients with major depression as compared with healthy control. While other⁽⁸⁰⁾ cited that low serum cholesterol was not associated with depressive symptoms in older men or women. Although there is a decrease in serum cholesterol noticed in older men with depression⁽²⁾.

The risk of IHD was three times higher among men with a recorded diagnosis of depression than among controls of the same age. Men with depression within 10 years were three times more likely to develop IHD than were the controls⁽⁷⁶⁾. Depression may be an independent risk factor for IHD in men, but not in women⁽⁷⁶⁾. Furthermore, Low HDL-cholesterol is significantly associated with suicide attempts in women. Serum cholesterol was unrelated with either suicide ideation or attempts in men⁽⁸¹⁾.

Huang (2001)⁽⁸²⁾ showed no significant differences in serum total cholesterol between patients with mania and major depression, between patients with and without physical violence, or between patients who had and had not made a suicide attempts. Almeida-Montes *et al*(2000)⁽⁸³⁾ found that, there is no significant difference in lipid profiles between patients who had attempted suicide and those who had not. Low total cholesterol and LDL cholesterol levels in persons in the acute period of major depression provided a useful parameter of suicide risk. A significant statistical correlation between the low level of total cholesterol and either suicidal ideation and severity of depression was also found^(41, 84). Other studies have found no association between low or declining concentration of cholesterol and depression^(16, 85, 86). If low cholesterol concentration was related to low mood then it would be expected that a population with a high predicted cholesterol concentration—that is, patients with IHD—would have a lower prevalence of depression. This is clearly not the case for men with IHD⁽⁷⁶⁾.

Brown and Salive (1994)⁽¹⁶⁾ findings do not support the hypothesis that increased mortality from external causes in people with a lower cholesterol concentration is due to their having more severe depressive symptoms, which might lead to suicide or violence⁽¹⁶⁾. Furthermore, doctors should not be deterred, therefore, from seeking to lower cholesterol concentration in elderly patients whose concentrations are high.

Although there have been contradictory results, several situations that are perceived as stressful can raise cholesterol levels^(87, 88, 89, 90, 91). Chen *et al* (2001)⁽⁹²⁾ showed that total serum cholesterol concentration lower than (160 mg/dL) are commonly noticed in persons with anxiety, hostility and phobias. In a study carried out on samples (100 cases) from the same population of this study, the correlation was highly positive between anxiety symptoms and IHD and about 48% of patients had these anxiety symptoms before the attack. While low correlation was found between depression and IHD although 10% of the patients showed symptoms of depression⁽⁹³⁾. Hence, obtaining a complete agreement and one acceptable explanation of the results from different sources is not applicable.

Yeragani *et al* (1989)⁽⁶³⁾ cited that imipramine treatment leads to an increase in serum cholesterol level in treated depressed patients. In one study serum total cholesterol, high density lipoprotein cholesterol, were significantly lower in subjects with major depression than in normal controls and the treatment with antidepressants did not significantly alter either high density lipoprotein or total serum cholesterol⁽⁹⁴⁾. This result is encountered by the result of the present work and the results of Vinokur and Gubachev (1994)⁽⁹⁵⁾ who found that antidepressant administration results in lowering of total blood cholesterol and atherogenic lipoproteins.

Depression has been shown to be proarrhythmogenic in patients with established IHD^(28, 30). This is thought to be due to an increase in sympathetic nerve activity or a decrease in

parasympathetic nerve activity, or both of these. This mechanism might operate in depressed patients without established IHD, increasing their risk of developing it or accelerating its onset^(28, 30). Depression may lead to coronary events directly or indirectly via poorer health behaviors, such as increased smoking or decreased activity⁽³¹⁾. Such behavior changes may lead to higher cholesterol concentration or blood pressure. Furthermore, depression might result in an unfavourable lipid profile resulting from an interaction between the catecholamine and steroid axes⁽³⁰⁾.

Low plasma cholesterol concentration (<4.14 mmol/L) were much more common in patients with affective disorders (20%) than in urban healthy peoples, but there is no evidence that low plasma cholesterol could cause or worsen affective disorders. Yates and Wallace (1987)⁽⁹⁶⁾ found similar cholesterol levels in the healthy population and depressed patients^(15, 96).

Acute mental stress is associated with an increase in serum cholesterol levels⁽⁹⁷⁾. McCann *et al*(1995)⁽⁹⁸⁾ have suggested the stress-induced lipolysis model as a mechanism for the increase in sympathetic activity and the associated increase in serum cholesterol levels in response to acute mental stress. According to this model, epinephrine stimulates the release of free fatty acids from lipoproteins. These free fatty acids become available to the liver for the synthesis and secretion of very low density lipoprotein particles that containing cholesterol⁽⁹⁹⁾, which undergo modification in the circulation to become low density lipoprotein particles^(100, 101). Furthermore, a correlations have been observed between free fatty acids levels and magnitude of epinephrine increases in response to psychological stress⁽⁹⁸⁾.

Bajwa *et al* (1992)⁽¹⁰²⁾ compared cholesterol levels of patients with panic disorder, major depression and normal controls matched for age and gender. They found that patients with panic disorder had significantly higher serum cholesterol levels than normal controls and those with major depression. This study and other⁽¹⁰³⁾ hypothesized that higher cholesterol levels could be a result of noradrenergic activity, placing these patients at greater risk for the development of cardiovascular disease. Lacerda *et al* (2000)⁽³⁹⁾ noticed that the mean \pm standard deviation cholesterol level was low for major depression despite the fact that the later were older. This hypothesis however has been challenged by Feder (1993)⁽¹⁰⁴⁾ who called attention to the fact that cholesterol levels are much strongly influenced by genetics and diet than by psychological stress.

In a study carried out on samples from the same population of this study, the correlation was highly positive between anxiety symptoms and IHD and about 48% of patients had these symptoms before the attack. While low correlation was found between depression and IHD although 10% of patients showed symptoms of depression⁽⁹³⁾. Hence, a complete agreement and explanations of the results from different sources is not available. In another study; leptin and cholesterol levels were low in patients with major depressive disorder, but high in schizophrenic patients; an inconsistently positive correlation between mean leptin levels, cholesterol, and body mass index among different groups. It is concluded that the leptin and cholesterol might play differently important pathophysiological roles in major depression and schizophrenia⁽¹⁰⁵⁾. Even there are many limitations, the results of Roy and Roy (2006)⁽¹⁰⁶⁾; failed to show any significant relationship between serum cholesterol levels and either total Beck Depression Inventory (BDI) scores or current suicidal ideation⁽¹⁰⁶⁾.

Conclusions:

From the results of this research and the review, it can be concluded that:

1. High serum cholesterol is consistent risk factor for IHD.
2. Depression is not yet a consistent risk factor for IHD.

3. Low cholesterol in suicide patients (usually severely depressed) can be predicted by a severe decline in appetite and cease of food ingestion before the test of suicide ideation in patients or before the suicide attempt. Therefore, cholesterol levels in their serum should be expected to be decreased.
4. Many researches were carried out according to the Diagnostic and Statistical Manual of Mental Disorders 4th version (DSM-IV) published by American Psychiatric Association. This type of classification cited that, there is a decrease or increase in appetite in depressed patients. Therefore, those patients who had had an increase in appetite were included in many papers and therefore they affected positively the results of serum cholesterol.
5. Treatment with TCAs results in improvement in depression symptoms, including appetite, but has bad side effects on heart. Hence, the diagnosed depressed patients, who already under treatment, have a higher risk of IHD than control. In those groups of depressed patients, serum cholesterol will be normal or higher than the baseline, but they have a higher risk of IHD.

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Table (1): Significance and p-values of the comparison in serum cholesterol in treated depressed patients, untreated depressed patients, and control groups.

Comparison groups	p-value	Significance
Control vs. Treated Depressed Patients	0.2110	Non-Significant
Control vs. Untreated Depressed Patients	0.0140	Significant
Treated vs. Untreated Depressed Patients	0.0086	Significant

Table (2): Significance and p-values of the comparison between males and females in serum cholesterol in treated depressed patients, untreated depressed patients, and control groups.

groups	Male vs. Females (p-value)	Significance
Control	0.0423	Significant
Untreated Depressed Patients	0.0255	Significant
Treated Depressed Patients	0.128	Non-Significant

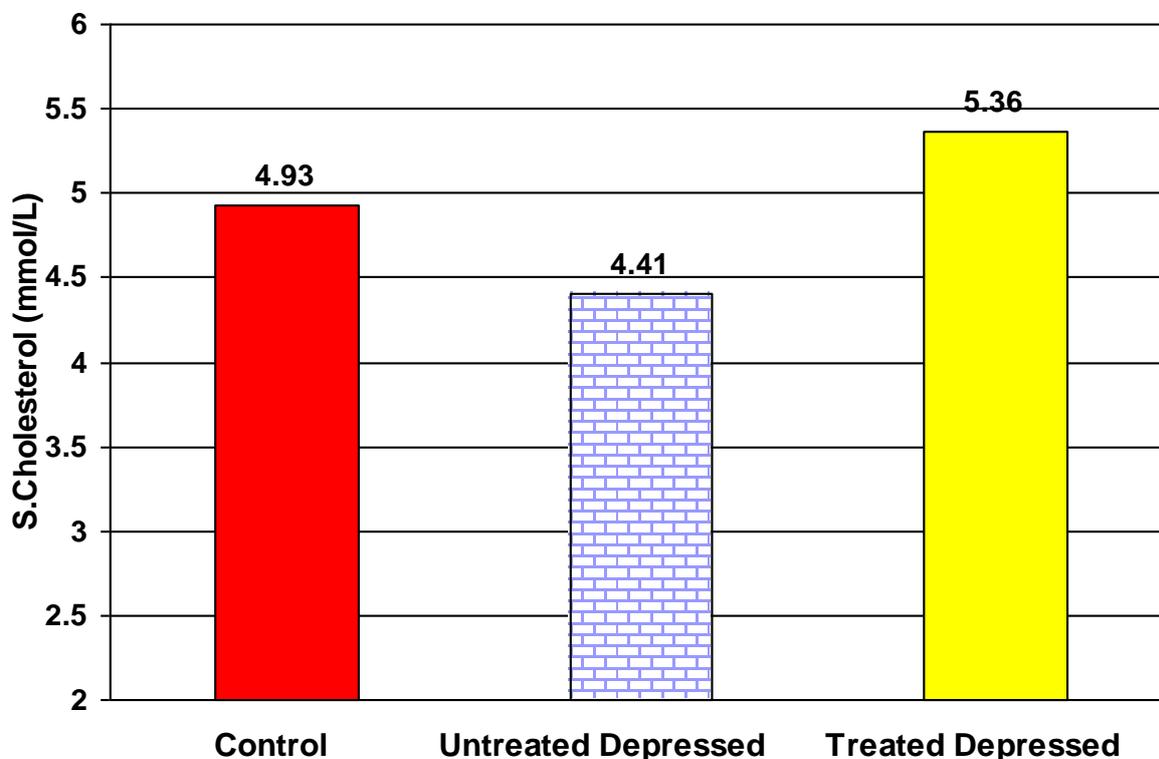


Figure (1): Serum cholesterol in treated depressed patients, untreated depressed patients, and control groups.

EFFECT OF FENUGREEK SEEDS AND GARLIC POWDER ON PLASMA CHOLESTEROL AND TRIACYLGLYCEROL IN MEAT TYPE CHICKS

S.J. hamodi

A.S. Ahmed

Dept. of Animal Resources , College of Agriculture , Baghdad University , Fax : 00 (+9641) 5112009 .

M.A. Al-Qayim

Dept. of Physiology and Pharmacology , College of Veterinary Medicine , Baghdad University

تأثير بذور الحلبة ومسحوق الثوم في كوليسترول وكليسيرينات الدم الثلاثية

- دراسة في فروج اللحم -

Abstract:

The objective of this study was to investigate the effect of different levels of fenugreek seeds and garlic powder on plasma cholesterol and triacylglycerol of broilers . Two hundred and fifty one – day old chicks were assigned to 5 treatments with 3 replicates each. The birds were fed either basal diet or basal diet supplemented with two levels of fenugreek seeds (1 and 3%) or basal diet supplemented with two levels of commercial garlic powder (0.5 and 1%) from one-day through 49 days of age .

An obvious significant ($P < 0.001$) decline in plasma cholesterol and triacylglycerol were observed in birds fed diet containing fenugreek seed or garlic powder as compared with the other groups. On the other hand , Rations containing 0.5% garlic powder enhanced feed conversion ratio of birds .

Keywords : fenugreek seeds , garlic powder , cholesterol , triacylglycerol , meat chicks

الخلاصة:

استهدفت هذه الدراسة معرفة تأثير استخدام مستويات مختلفة من بذور الحلبة ومسحوق الثوم على كوليسترول وثلاثي كليسيرينات الدم في فروج اللحم. نفذت الدراسة على تجربتين ، التجربة الاولى استخدمت مجموعة من الافراخ (135 فرخ) بعمر يوم واحد وزعت على ثلاث معاملات كل معاملة بثلاث مكررات بواقع 15 فرخاً للمكرر الواحد. غذيت الافراخ منذ اليوم الاول ولغاية 49 يوماً على عليقة موحدة مع اضافة مسحوق بذور الحلبة بالمستويات (0 ، 1 ، 3%) . وفي التجربة الثانية غذيت مجاميع الافراخ (135 فرخ) باضافة مسحوق الثوم التجاري بالمستويات (0 ، 1 ، 0.5%) ومنذ اليوم الاول وحتى نهاية التجربة عند عمر 49 يوماً. اظهرت نتائج التجريبتين حصول انخفاض معنوي ($P < 0.001$) في تركيز كوليسترول وثلاثي كليسيرينات الدم في مجاميع الطيور التي غذيت على علائق تحتوي بذور الحلبة ومسحوق الثوم بالمقارنة مع مجموعة السيطرة. كما سجلت مجاميع الطيور التي غذيت على علائق مسحوق الثوم بنسبة (0.5%) افضل كفاءة تحويل غذائي بالمقارنة مع بقية مجاميع الطيور في التجربة.

Introduction

Coronary heart and peripheral arterial disease have been associated with high levels of serum cholesterol . Some studies suggest that elevated serum triglycerides may also be a risk

feature especially in individuals with diabetes (8). Scientific reports indicated that fenugreek (*Trigonella foenum graceum* L.) have therapeutic properties that may be beneficial in treating hypercholesterolaemia. The seeds have been shown to possess hypocholesterolaemic effect in humans (9 , 18) , rats (5 , 16 , 19 , 20) , dogs (24) , rabbits (1) and Chickens (2).

It was reported that essential oils of garlic (*Allium sativum*) can prevent fat-induced hyperlipemia (3). A marked reduction in serum cholesterol level was observed in rats fed a diet supplemented with 2 or 3% garlic powder . Various garlic extracted exhibited hypocholesterolemic effects in chickens , mainly through the inhibition of the key enzymes in cholesterol and lipid synthesis (13). Feeding male (Ross x Ross) chickens with diets supplemented with different levels of garlic powder induces reduction in plasma cholesterol and triacylglycerols , in addition to reduction in liver and breast muscle cholesterols (6). Chicken were chosen for this study as a model because of their cholesterol biosynthesis in similar to that of humans (7). The aim of this study was to examine the effects of varying levels of fenugreek seeds or garlic powder on plasma cholesterol and triacylglycerol levels , as well as their effects on broiler performance .

Materials and Methods

Two hundred and twenty five one-day old male of Fawbro distributed into 5 treatments , each consisted of 3 replicates with 15 birds in each replicate . The birds were reared under a continuous light schedule . Feed and water were provided *ad libitum* (Table 1) . At the end of the experiment (49 days) , birds were weighted and their feed intake was determined. The birds were fed either basal diet or basal diet supplemented with two levels of fenugreek (1 and 3%) or basal diet with two levels of commercial garlic powder (0.5 and 1%) from one up to 49 days of age.

Two birds from each pen were randomly chosen for blood collection. Blood samples were collected from the jugular vein using tubes containing EDTA. Total plasma cholesterol and triacylglycerols (mg/dl) were determined by enzymatic method using a commercial kit (Biomerax Sa ref 61224) with spectrophotometer under a wave length of 560 nm and 570 nm respectively .

Data were analyzed statistically by analysis of variance (21). Treatment means were tested for differences using Duncan's multiple range test at $P < 0.05$ (4).

Table 1 : Composition of the basal diet

Composition	Content (g/100 g)
Ground yellow corn	60.0
Soybean meal	30.0
Wheat	5.8
CaCO ₃	1.2
*Vitamin Troumix	3.0
<u>Calculated composition (% dry matter)</u>	
Metabolizable energy (Kcal / kg)	2860
Crude protein (%)	19.0
Calory : protein ratio	154

* Vitamin Troumix provides (per kilogram) : Vit. A , 467 IU ; Vit. D₃ , 100IU ; Vit. E, 1.667 mg ; Vit. K, 134 mg, Vit. B₁ , 100 mg ; Vit. B₂ , 500 mg ; Vit. B₆ , 200 mg ; Vit. B₁₂ , 1.33 mg ; Ca , 170 gm.

Results and Discussion

Body weight , body weight gain , feed consumption and conversion were compared between treated and control birds (Table 2).

There were no significant differences between treatments in all parameter .

On average experimental birds fed 1 or 3% fenugreek attained body weight gains of 1442 and 1567 , feed consumption 3981 and 4269 g respectively . Furthermore , birds fed 0.5 , 1.0% garlic attained body weight gains of 1630 and 1606 g consumption 3727 and 3990 g of feed respectively .

Body weight gain and feed conversion efficiency were slightly reduced by fenugreek supplementation . While body weight gain and feed conversion were elevated in birds fed diets containing (0.5 , 1.0%) in comparison with birds fed basal diet (Table 2).

Although plasma total cholesterol and triacylglycerol concentrations were markedly lower in birds fed diets containing fenugreek or garlic , plasma cholesterol level was inversely related to the dietary level of fenugreek or garlic. (Table 3) .

Table 2 : Influence of dietary fenugreek (F) or garlic (G) on mean body weight , body weight gain , feed consumption and feed conversion efficiency

Diet	Body weight (g/bird)	Body weight gain (g/bird)	Feed consumption (g/bird)	Feed conversion efficiency (kg diet/kg gain in weight)
Basal diet	1583	1538	4147	2.696
Basal + 1% F	1487	1442	3981	2.760
Basal + 3% F	1612	1567	4269	2.786
Basal + 0.5% G	1675	1630	3727	2.229
Basal + 1.0% G	1650	1606	3990	2.485

- Means of 3 replicates
- No significant difference between treatments .

Table 3 : Influence of dietary fenugreek (F) or garlic (G) on plasma cholesterol and triacylglycerols

Diet	Cholesterol (mg/dl)	Triacylglycerols (mg/dl)
Basal diet	195 a	321 a
Basal + 1% F	128 b	276 b
Basal + 3% F	113 c	195 c
Basal + 0.5% G	129 b	294 b
Basal + 1.0% G	125 b	277 b

- Means of 6 birds .
- Different letters within a column denote significant difference between means (P < 0.01)

The results of the present experiment (Table 3) showed that the supplementation of fenugreek affected lipid and cholesterol metabolism (reduced plasma cholesterol and triglycerides) .

Earlier studies suggested that half of the hypocholesterolaemic effect of fenugreek is from saponin and the other half from the gum fiber (14 , 17) . fenugreek seeds saponins are of steroidal nature with diosgenin as the main sapogenin (10).

Diosegenin have various effects on cholesterol metabolism , one of the most important being the capacity to lower plasma cholesterol concentration in chickens (11). This hypocholesterolaemic effect has been suggested to be dependent on the capacity of diosgenin to inhibit cholesterol absorption , decrease liver cholesterol concentration , increase biliary cholesterol secretion and increase faecal excretion of neutral steroids (15 , 20 , 23 , 24) . The mechanisms that cause this effect are still not clear. One possibility is that large mixed micells are formed containing bile salts conjugated with cholesterol and saponins , and those large molecules are not available for absorption (15 , 20) .

The observed decrease in plasma triacylglycerols induced by feeding birds fenugreek diet could be due to a lesser synthesis of very low density lipoprotein (VLDL) in the liver (1) , since fenugreek seeds are known to affect insulin secretion (12 , 17) which in turn regulates VLDL and triacylglycerol concentration. Similarly , average plasma triacylglycerol levels were lowered in 42 wk – old laying hens fed fenugreek diet (2).

The decreased plasma total cholesterol and triacylglycerol in birds fed diets supplemented with garlic observed in the present experiment confirms the findings of others (6 , 13) who found about 40% reduction in the activities of the cholesterol biosynthesis limiting enzyme (HMG coA – reductase) in birds fed garlic , which further suggests that garlic alters lipid and cholesterol metabolism (6) .

The insignificant decrease in body weight obtained with 1,3% fenugreek diet may be due to the effect of the fenugreek seeds components in lowering the digestibility of feedstuffs. The analysis of fenugreek seeds components revealed that it contained a considerable propotion of fibers , saponins and viscosity (14) and the role of fibers , saponins and viscosity in reducing feedstuff digestibility was mentioned (22) .

In conclusion , results of the present study demonstrate a therapeutic property of fenugreek seeds and garlic powder , that could be beneficial in treating hypercholesterolemia. Furthermore , reduction of plasma cholesterol and triacylglycerol induced by 3% fenugreek

diet suggests that fenugreek diet can prevent fat induced hyperlipemia and make chicken meat with low lipid content possible .

Acknowledgement

The authors wish to thank Dr. Lazim Al-Taai in appreciation for providing valuable technical assistance .

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