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Relation of Melatonin, CoenzymeQ10 and AMP Activated protein kinase in postmenopausal women with cardiovascular diseases

Tafaoul Jaber Hameed[1*], Nehad Nejres Hilal[2], Mohammed Mohsin Abdul-Aziz[3]
1, Dep. of clinical Laboratory Sciences, College of Pharmacy, Tikrit University.
2, Dep. of Pathology, College of Medicine, Tikrit University.
3, Department of Surgery, College of Medicine, Tikrit University.
*Tafaoul_jaber@tu.edu.iq

Abstract:
Background: *Cardiovascular disease (CVD) remnants the important cause of morbidity and death among women internationally.*
Objective: *This study aims to study the relationship between melatonin, coenzyme Q10, and AMP-activated protein kinase (AMPK) in postmenopausal women with CVDs.*
Methodology: *A case-control study was conducted, involving 90 female participants aged between 53 and 70 years. The sample comprised 60 patients diagnosed with CVD and 30 healthy controls. Samples were collected from August 2024 to December 2024 at Tikrit Teaching Hospital in Tikrit city and Al-alam Hospital. The researcher prepared a data collection sheet used during interviews, which included questions about participants' age, weight, height, and medical history. The participants all women aged from 53-70 years. A total 60 postmenopausal women with CVDs versus to 30 healthy controls women participants enrolled in the present study. Blood samples were collected at specific time from 10:00pm to 1:00am and analyzed for measurement of melatonin, coenzymeQ10 and AMP activated protein kinase.*
Results*: Melatonin concentration were significantly lower in the postmenopausal women with CVDs (199.7±80.3 pg\ml) compare to control (366.1±115.1 pg\ml). Coenzyme Q10 level were significantly reduced in postmenopausal women with CVDs (9.7±3.4ng\ml) compare to control (16.7±5.6ng\ml). AMPK level were reduced in postmenopausal women with CVDs (1994.1±881.9pg\ml) compare to control (3236.3±1157.6pg\ml).* ***Conclusions****: In postmenopausal women the risk of CVDs will increase with decrease the level of melatonin, coenzymQ10 and AMP activated protein kinase.*
Keywords*: Postmenopausal, cardiovascular diseases, CVD, Melatonin and CoenzymeQ10, AMP activated protein kinase.*

1-INTRODUCTION

Cardiovascular disease (CVD) is the foremost cause of morbidity and death among women worldwide. Despite the important problem of these diseases, awareness and knowledge of their associated risk factors among women remain limited[(1)]. According to the World Health Organization (WHO), CVD is the leading cause of death worldwide[(2)]. Not only is CVD a significant cause of death, it is increasingly recognized as a significant contributor to long-term disability, especially as survival rates improve thanks to advances in medical care. The WHO projects that by 2030, ischemic heart disease and cerebrovascular disease will account for approximately 9.8% of all disability-adjusted life years (DALYs) lost internationally[(3)].
Menstruation is an important event in women's lives and may contribute to the development of CVD. It is associated with changes in CVD patterns, metabolic health markers and rare CVDs [(4)]. Menopause is associated with increased blood pressure, body mass index (BMI), body weight, and body fat distribution [(5)]. Several cardiovascular changes during menopause, including changes in body fat distribution, changes in lipoprotein levels, and endothelial dysfunction, are associated with an increased risk of CVD. This relationship goes beyond a decrease in testosterone; Although decreased estradiol levels increase the risk of CVD, the mechanism is complex and multifactorial[(6)]. Melatonin is a hormone secreted by the pineal gland, which is responsible for regulating circadian rhythms. It also acts as an antioxidant, scavenges free radicals, delays aging and boosts the immune system [(7)]. Melatonin has antioxidant properties by scavenging reactive oxygen species (ROS) and reducing oxidative stress, two critical factors in the development of atherosclerosis and endothelial dysfunction. Additionally, melatonin influences inflammatory pathways by decreasing pro-

inflammatory cytokine levels, thereby mitigating plaque formation and vascular injury[8]. Melatonin secretion diminishes with age and in the presence of various diseases. Disruptions in sleep patterns, often associated with aging and chronic illnesses such as obesity and diabetes, are linked to decreased melatonin levels. Consequently, melatonin is recommended for handling sleep complaints such as insomnia and jet lag. Its pleiotropic effects include regulation of circadian cycles and sleep, immune modulation, antioxidative actions, and roles in reproductive health, mood regulation, and even transplantation [9].

Co enzyme Q10 is a lipid-soluble quinone through a core benzoquinone ring its primary function in the cell to take part in the electron transportation chain in the internal mitochondrial membrane[10]. Coenzyme Q10 is essential for ATP generation and for supplying needs of heart muscle and other tissues because of its antioxidative qualities. Studies on patients with CVDs have revealed that their concentrations of CoQ10 are much lower than those of healthy people[11]. CoQ10 has a protecting effect on the heart muscle and other tissues by preventing the start of lipid peroxidation processes[12]. Research indicates that heart failure is one of several conditions potentially associated with a deficiency in coenzyme Q10. The extent of coenzyme Q10 deficiency has been found to correlate by the strictness of heart failure. Recent studies suggest that patients with heart failure are more vulnerable to the detrimental effects of reactive oxygen species (ROS). Supplementing with coenzyme Q10, owing to its antioxidant properties, may help alleviate these opposing effects and potentially improve clinical results [13].

2-METHODOLOGY

2.1-Study design: The case-control study included 90 female participants a ratio 2:1 (60 patients and 30 control) is used to increase statistical power when a control group is readily available this lead to increase the clinical significance of the results. Participants aged between 53 and 70 years old. Samples were collected at a detailed time, from 10 P.M. to 1 A.M., between August 2024 and December 2024. The collection sites included Tikrit Teaching Hospital in Tikrit city and Al-alam Hospital. The investigator prepared a data collection form used during interviews with the participants, which included questions about their age, weight, height, and medical history.

2.2-Study population

2.2.1-Inclusion criteria: Postmenopausal women with CVDs aged from 53-70 years were included in the study.

2.2.2-Exclusion criteria

- All patients with chronic liver or renal disorders, as well as those with myocardial infarction, were excluded from the study.
- Male participants were also excluded.
- Patients who are taking warfarin or melatonin were not included in the study.

2.2.3-Study groups

-Patients groups included sixty postmenopausal women.
-Control group included thirty healthy women.

2.4-Materials: Serum levels of melatonin, coenzymeQ10 and AMP Activated protein kinase were measures using specific enzyme-linked immunosorbent assay (ELISSA) kits from Sunlong, Bitotech.

2.5-Sampling: Blood samples were obtained between 10:00pm and 1:00am, When the anterior orbital vein is punctured with a disposable syringe, about five milliliters of blood are collected. Pour five milliliters into a tube with a gel separator, which helps to separate the serum by centrifugation at 3000 rpm for 10-15 minutes. The resulting pure serum was placed in a dry and transparent Eppendorf tube and stored at -20 °C until melatonin evaporated, coenzymeQ10 and AMP activated protein kinase levels were measured using ELISA methods.

2.6- Ethical Considerations: According to the research consent form, healthy and sick people have given informed consent to participate in this study. Each participant received a personal interview and completed a questionnaire. The questionnaire includes information such as serial number, name, age, height, weight, place of residence, gender, time of illness and method of treatment.

2.7-Statistical analysis: All statistical analyses were performed using R version 4.4.2 (R Core Team, 2025) and RStudio (RStudio Team, 2025). Before the analysis, data was checked for missing values, outliers and inconsistencies. Descriptive statistics were computed for all variables. Continuous variables were showed as

mean Mean ± SD. Boxplots were used to visualize the association between study groups and characteristic of interest. Group contrasts were achieved using autonomous samples t-tests for unremitting variables, after checking for homogeneity of variance.

3-RESULTS

Melatonin concentration were markedly lower in the CVD group (199.7±80.3 pg\ml vs. control 366.1±115.1 pg\ml; p value : <0.05). Similarly mean of Coenzyme Q10 level were significantly reduced in CVD group compare to control group (CVD: 9.7±3.4ng\ml vs. control: 16.7±5.6ng\ml; p value <0.05). AMPK level were reduced in CVD group compare to control group (CVD: 1994.1±881.9pg\ml vs. control: 3236.3±1157.6pg\ml; P value<0.05).

Table (1): Contrast of biochemical markers between CVD and control groups.

Group	Mean ± SD		
	Melatonin(pg/ml)	CoenzymeQ10(ng/ml)	AMPK(pg/ml
Patient	199.7±80.3	9.7±3.4	1994.1±881.9
Control	366.1±115.1	16.7±5.6	3236.3±1157.6
P value	<0.05	<0.05	<0.05

Mean±SD, Welch Two Sample t-test, Significant results (P<0.05) are bolded.

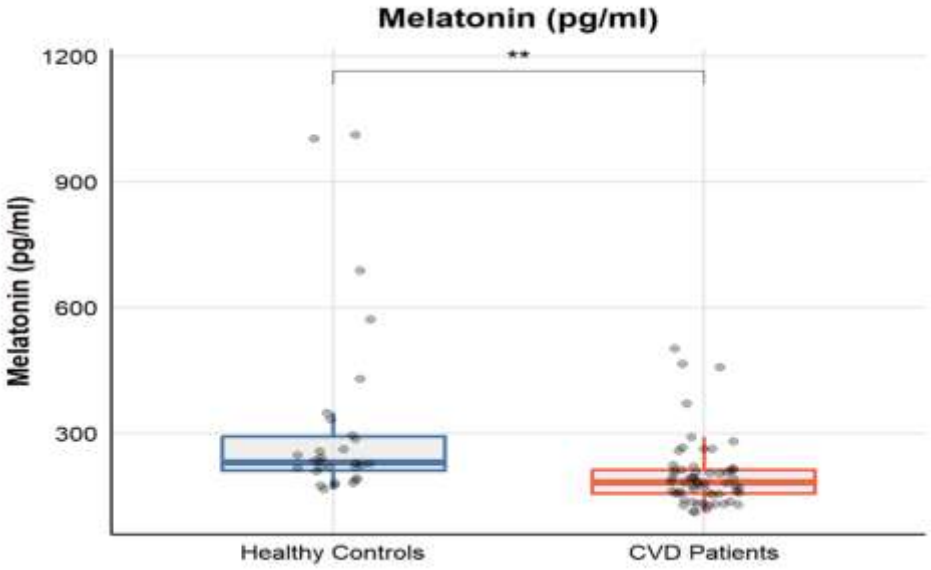

Fig. (1): Contrast between patients and control in Melatonin.

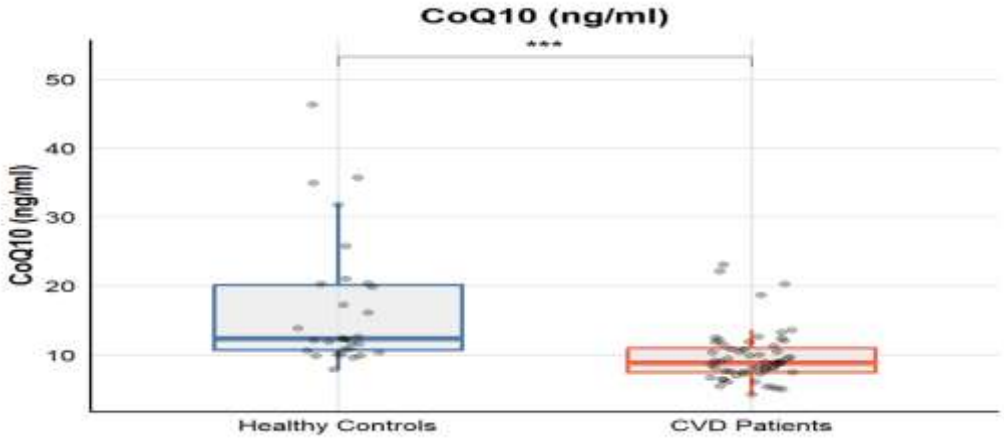

Fig. (2): Contrast between patients and control in CoQ10.

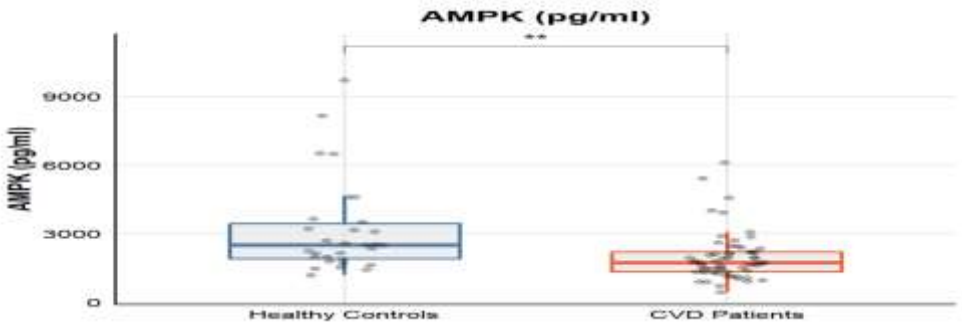

Fig. (3): Contrast between patients and control group in AMPK.

4-DISSCUSION

The fifth decade of life in women is related through an increased risk of CVD. Menopause is a major physiological transition attended by various cardiometabolic variations, counting changes in body configuration, elevated blood pressure, and increased insulin resistance. This study showed that advancing age is related with a higher incidence of CVD among postmenopausal women. Melatonin is the primary hormone responsible for circadian rhythms and controlling the sleep-wake cycle. Melatonin production declines with age. After 40–45 years of age, melatonin levels gradually decline, and by age 70, they represent only 10% of their prepubertal level[14]. Melatonin is a natural antioxidant that has been proven to suppress oxidative stress and maintain stable endothelial function, thereby protecting the cardiovascular system (15). Oxidative stress is increasingly considered an important factor influencing the development and progression of CVDs. Therefore, efforts to treat CVDs should focus on improving the safety and effectiveness of antioxidant therapy and identifying patients who are most likely to benefit from it (16). Coenzyme Q10 (CoQ10) is a common component present in cell membranes and mitochondria, and exists in reduced (ubiquinone) and oxidized (ubiquinonic acid) forms. The antioxidant and anti-inflammatory properties of CoQ10 are beneficial in preventing free radical damage and activating inflammatory signaling pathways (17). Studies conducted at Ibn Sina University Hospital and Al-Salam General Hospital in Iraq showed that, compared with the control group, the average serum levels of CoQ10 in patients with myocardial infarction and angina pectoris were significantly reduced[18]. Similarly, research by Litaro, Tiano et al. suggests that serum CoQ10 levels are low in patients with heart disease. Oxidative stress resulting from myocardial infarction can increase the demand for CoQ10, which can lead to its depletion[19].

AMP-activated protein kinase (AMPK) has a cardioprotective effect, restores cellular metabolic function by interaction with many target proteins, regulates gene expression and regulates protein levels. AMPK improves mitochondrial function and increases the energy status of cells by promoting the use of energy substrates[20]. A recent 2023 study focused on the role of AMPK in cardiac aging, highlighting its importance in maintaining normal metabolic levels and redox homeostasis, especially under oxidative stress and inflammatory conditions. The study found a significant association between age and heart disease, suggesting that AMPK activation may improve cardiac function. He also highlighted the need to enhance AMPK activity in different cardiac tissues and to investigate the advantages and disadvantages of different methods of AMPK activation[21]. Another study suggests that the response to AMPK signaling declines with age. This decreased sensitivity damages metabolic instruction, increases oxidative stress, and reduces endogenous permission. These age-related variations activate essential immunity, leading to mild infections and metabolic disorders[22].

Study limitation: There are few limitations of this study, like difficulties during sample collection when taking the blood sample at night and some patients refuse to give blood for the research. Also, the limited number of participants reduce the reliability of results. Therefore, future studies should include large and more diverse samples to enhance statistical power and improve sample size, thereby increasing the statistical significance of the findings.

CONCLUSIONS:

CVD is the foremost cause of death among women, with a significant increase in risk following menopause. Postmenopausal women generally develop coronary heart disease several years later than men. This study concluded that postmenopausal women with CVDs tend to have lower levels of melatonin, coenzyme Q10, and AMP-activated protein kinase. Therefore, in managing cardiovascular health in postmenopausal women, it may be beneficial to consider incorporating melatonin and coenzyme Q10 into the preventive and therapeutic strategies for heart disease.

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