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ORIGINAL ARTICLE

IMPACT OF AGE ON BIOCHEMICAL FACTORS IN PATIENTS WITH ANGINA

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ABSTRACT

Background: cardiovascular diseases, particularly angina pectoris, remain a leading cause of morbidity and mortality worldwide. Work-related physical and psychological stress has been recognized as an important contributor to cardiovascular dysfunction, potentially influencing biochemical pathways involved in angina pathophysiology. The aim of this study was to evaluate the effect of occupational stress on selected biochemical markers in patients with stable and unstable angina, with emphasis on age-related differences.

Materials & Methods: This case-control study was conducted at the Emergency and Cardiac Surgery Center of the Imam Al-Hussein Teaching Hospital, from October 2024 to January 2025. A total of 120 male participants, aged 30 to 70 years, were enrolled. They were divided into two main groups: 90 male with angina, subdivided equally into: 45 patients with stable angina, 45 patients with unstable angina and 30 healthy male controls without any history of cardiovascular, metabolic, or chronic diseases. This comparative study included patients diagnosed with stable and unstable angina. Serum levels of visfatin, angiotensin-converting enzyme (ACE), proteinase-3 (PR3), troponin, lipid profile parameters, and oxidative stress markers were assessed. Participants were stratified into two age groups: <50 years and ≥50 years. Biochemical variations between age groups were analyzed to determine age-dependent responses to work-related stress.

Results: Significant differences were observed in several biochemical markers between the two age groups. Patients aged ≥50 years exhibited altered stress-related biochemical responses compared to younger patients, particularly in ACE, PR3, and oxidative stress markers. These findings suggest an age-dependent modulation of biochemical pathways associated with angina under occupational stress conditions.

Conclusion: Age plays a significant role in modifying biochemical responses to work-related stress in patients with angina pectoris. Understanding these age-related variations may aid in early detection, targeted prevention strategies, and improved management of angina, especially among individuals exposed to occupational stress.

KEY WORDS: Angina Pectoris; Angiotensin-Converting Enzyme; Oxidative Stress; Proteinase 3; Troponin; Visfatin

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INTRODUCTION

Cardiovascular diseases (CVDs) represent a major global health burden and are among the leading causes of morbidity and mortality worldwide. According to international epidemiological reports, CVDs account for nearly one-third of all global deaths, with ischemic heart disease being the predominant contributor. Angina pectoris is one of the most common clinical manifestations of ischemic heart disease, affecting millions of individuals and significantly impairing quality of life, work productivity, and functional capacity.[1] Classically, angina has been defined as chest pain caused by myocadiac insufficiently oxygenated predominantly due to coronary artery disease (CAD).[2] Rapid and appropriate diagnosis, and correct differentiation of stable and unstable angina, are important for early and effective management in order to minimize mortality and morbidity.[3]

Biomarkers have been the focus of a tremendous interest in the last couple of decades for use as non-invasive diagnostic modality for the early detection of cardiovascular diseases. Biomarkers can also provide useful data on pathophysiological mechanisms leading to the generation of angina and, thus, aid clinicians in diagnosing and more accurately determining the activity of the disease.[4] Some of the

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most interesting biomarkers for angina are Proteinase 3 (PR3), angiotensin-converting enzyme (ACE), and visfatin. These molecules are involved in inflammatory responses, vascular injury and metabolic disturbances, all of which are critical for the pathogenesis of atherosclerosis and ischemic heart disease.[5] The PR3 enzyme is abundant within neutrophils and is an important mediator of vascular inflammation and degradation of the extracellular matrix, which underpin plaque instability and damage to the endothelium.[6] By contrast, ACE is one of the key enzymes in the renin-angiotensin-aldosterone system (RAAS) and has important functions in regulating blood pressure and fluid homeostasis.[7] Hyper-activity results in increased vasoconstriction, inflammation and vascular remodelling which raised the cardiovascular risks.[8] On the other hand, visfatin is an adipokine synthesized by visceral fat depots that has been characterized as a proinflammatory and metabolism-modulating adipokine. Further, it was known to be involved in atherosclerosis, oxidative stress, vascular inflammation and coronary artery disease.[9]

Oxidative stress is an important aspect of cardiovascular pathophysiology-it is the disruption in the balance of ROS production and the antioxidant defense system of the body. Oxidative stress can be assessed by the measurements of 4-hydroxynonenal (4-HNE) and glutathione peroxidase-1 (GPX-1) which are also used for measurement. Increased oxidative stress exacerbates the increased lipid peroxidation, protein oxidation, and DNA damage, leading to endothelial dysfunction and the development of angina; these effects are potentiated (synergistic effects) by one another on the micro and macro endothelia.[10] In conjunction with oxidative stress and inflammation, lipid dysregulation is always present as a significant predictor of cardiovascular disease. Increased total cholesterol (TC), triglycerides (TG), and low-density lipoprotein (LDL) levels are associated with the formation of atherosclerotic plaque in coronary arteries, causing their stenosis and reduced perfusion of the cardiac muscle. This form of dyslipidemia in the same patients also under work-related stress or intense exercise, which would further increase hemodynamic stress and vascular injury, favors ischemic events.[11]

Occupational stress, whether physical or psychosocial, has been progressively recognized as a cardiovascular disease risk factor.[12] Occupational stress can activate the hypothalamic-pituitary-adrenal (HPA) axis, elevate cortisol levels, and boost sympathetic nervous system activity, thus leading to elevated blood pressure, elevated heart rate, and augmented inflammatory responses.[13] These physiological changes can worsen endothelial function and increase the likelihood of plaque rupture, particularly in individuals with underlying cardiovascular risk factors. Notably, age is critical in specifying the physiological response to cardiovascular stressors. Elderly are prone to developing increased arterial stiffness, endothelial dysfunction, and increased oxidative stress, which tend to amplify the detrimental effect of work-related stress on cardiovascular health.[14] Younger adults may develop greater metabolic responses, including lipid disturbance and inflammatory activation, to work-related stress.[15] Considering the facts above, the current research strives to study the effect of occupational stress on certain significant biochemical parameters of angina in different age groups.[16] Through targeting PR3, ACE, visfatin, troponin, lipid profiles, and oxidative stress markers, the current research will help to add more knowledge on the interaction between age and stress on cardiovascular risk modulation.[17] The rationale of this study is to provide support for developing age-related treatment and diagnostic programs that can achieve early diagnosis and treatment of angina, particularly in people working under high occupational stress.[18] The aim of this study was to evaluate the effect of occupational stress on selected biochemical markers in patients with stable and unstable angina, with emphasis on age-related differences.

MATERIALS AND METHODS

This research was designed as a case-control study conducted at the Emergency and Cardiac Surgery Center of the Imam Al-Hussein Teaching Hospital .The study period extended from October 2024 to January 2025, allowing for comprehensive data collection and analysis. A total of 120 male participants, aged 30 to 70 years, were enrolled. They were divided into two main groups: 90 male with angina, subdivided equally into: 45 patients with stable angina, 45 patients with unstable angina and 30 healthy male controls without any history of cardiovascular, metabolic, or chronic diseases. Each participant underwent structured interviews using pre-designed questionnaires to collect demographic and health-related data, including: Age, Occupational background, Smoking status, History of physical exertion or psychological stress, Family history of cardiovascular disease and Lipid profile history.

Blood samples were collected at different time intervals (1, 5, 6, 10, and 12 hours) to measure biomarkers such as PR3, ACE, visfatin, troponin,while the white blood cells (WBC), glutathione peroxidase-1 (GPX-1), 4-hydroxynonenal (4-HNE), Total cholesterol (TC), triglycerides (TG), and low-density lipoprotein (LDL) levels were measured once during the study period. Enzyme-Linked Immunosorbent Assay (ELISA) was used to measure biomarker levels, and statistical analyses were performed to compare results between patients and controls.

RESULTS

A Total of 120 patients were included in the study, mean age of 30 ± 70 years. Patients were catego-

rized into stable angina (n = 45) and unstable angina (n = 45) groups, along with an age-matched control group (n = 30).Serum levels of visfatin, ACE, and PR3 were significantly elevated in both stable and unstable angina patients compared with controls. Visfatin showed a consistent significant increase ($p \leq 0.01$) at all measured time points (5, 10, and 15 hours) in both angina groups. In patients with stable angina, ACE and PR3 levels were significantly increased ($p \leq 0.01$) at 1 and 5 hours, followed by a significant decrease at 10 hours ($p \leq 0.01$) compared with controls. In contrast, patients with unstable angina exhibited a significant elevation of ACE and PR3 levels ($p \leq 0.01$) at all time points relative to the control group. Age-stratified analysis indicated that these changes were more pronounced in patients aged ≥50 years, suggesting an age-dependent modulation of biochemical responses to angina. Table(1) displays the results acquired for serum visfatin ,ACE and PR3 levels in patients groups with control group, raise significantly ($p \leq 0.01$) in visfatin at three different time points(each 5 hour), in stable and unstable type of angina compared with control group , and show the elevation significantly ($p \leq 0.01$) in ACE and PR3levels in (1 and 5 hour) and decrease significantly ($p \leq 0.01$) in (10 hour) of patients with stable angina in comparison to control , increase significantly ($p \leq 0.01$) in ACE and PR3levels at(Each Time Point) of patients with unstable angina in comparison to control group, according to the age.

Table (1): The Comparison of groups at Each Time Point Separately according to the age groups.

Parameters	Time	Age Group	Control		Stable		Unstable		P. value
			Mean	Std. D.	Mean	Std. D.	Mean	Std. D.	
Visfatin	In 1 hour	Less than 50	0.782	0.431	7.102	1.886	15.075	0.826	0.00006**
		Greater & equal than 50	0.659	0.325	8.878	1.407	12.883	2.275	0.00005**
	After 5 hours	Less than 50	0.782	0.431	9.800	1.185	22.175	2.081	0.00003**
		Greater & equal than 50	0.659	0.325	9.964	0.930	19.261	2.360	0.00006**
	After 10 hours	Less than 50	0.782	0.431	10.802	1.156	27.650	4.502	0.00001**
		Greater & equal than 50	0.659	0.325	10.503	1.040	26.995	4.622	0.00001**
ACE	In 1 hour	Less than 50	2.818	0.792	8.540	1.016	11.475	1.087	0.00003**
		Greater & equal than 50	3.254	0.389	8.700	1.058	10.385	1.126	0.00008**
	After 5 hours	Less than 50	2.818	0.792	20.000	2.042	26.650	5.725	0.00007**
		Greater & equal than 50	3.254	0.389	20.478	2.423	26.483	3.663	0.00001**
	After 10 hours	Less than 50	2.818	0.792	2.340	0.744	51.175	10.225	0.00007**
		Greater & equal than 50	3.254	0.389	2.440	0.594	54.637	7.716	0.00007**
PR3	In 1 hour	Less than 50	96.865	7.942	399.880	65.162	352.425	40.045	0.00004**
		Greater & equal than 50	99.008	3.218	371.678	39.721	480.049	725.710	0.04984**
	After 5 hours	Less than 50	96.865	7.942	530.960	76.700	580.075	53.661	0.00007**
		Greater & equal than 50	99.008	3.218	531.018	42.718	557.944	44.349	0.00002**
	After 10 hours	Less than 50	96.865	7.942	93.900	3.953	740.450	69.595	0.00003**
		Greater & equal than 50	99.008	3.218	94.703	4.196	720.024	85.233	0.00004**

**The mean difference is significant at the 0.01 level.

Table(2) shows the results increased for Troponin h.s level in patients groups with control group, at three different time points(each 6 hour) , and according to the type of angina , rise significantly (p≤0.01) in Troponin h.s levels in (1 and 6 hour) and decrease significantly (p≤0.01) after (12 hour) in comparison at (1and 6 hour) of patients with stable angina in comparison to control group, and enlargement significantly (p≤0.01) in Troponin h.s level in patients with unstable angina compared with control group, at three different time points (each 6 hour), according to the age groups.

Table(3) shows the results added for TC,TG and LDL level s in patients groups with control group, according to the type of angina , escalation significantly (p≤0.01) in TC,TG and LDL levels of patients with stable and unstable angina in comparison to control group, according to the age groups.

Table(4) display rise significantly (p≤0.01) in WBC and 4-HNE levels and decrease significantly (p≤0.01) in GPX-1 of patients with stable and unstable angina in comparison to control group, according to the age groups.

Table 2: The comparison of groups at each time point separately according to the age groups.

Parameters	Time	Age Group	Control		Stable		Unstable		P. value
			Mean	Std. D.	Mean	Std. D.	Mean	Std. D.	
Troponin	In 1 hour	Less than 50	8.900	2.123	75.180	25.840	113.025	10.361	0.00002 **
		Greater & equal than 50	9.731	2.009	83.918	19.587	115.688	30.114	0.00001 **
	After 6 hours	Less than 50	8.900	2.123	163.040	74.125	280.675	33.290	0.00004 **
		Greater & equal than 50	9.731	2.009	186.213	51.184	244.290	57.926	0.00003 **
	After 12 hours	Less than 50	8.900	2.123	10.200	1.010	586.725	89.523	0.00005 **
		Greater & equal than 50	9.731	2.009	10.805	1.825	549.190	99.634	0.00001 **

**The mean difference is significant at the 0.01 level.

Table 3: The comparison of lipid profile at each time point separately according to the age groups.

Parameters	Age Group	Control		Stable		Unstable		P. value
		Mean	Std. D.	Mean	Std. D.	Mean	Std. D.	
TC	Less than 50	137.529	12.329	356.400	76.153	435.750	70.073	0.00001**
	Greater & equal than 50	130.285	16.490	360.580	58.859	468.756	46.572	0.00002**
TG	Less than 50	116.629	6.622	248.000	21.366	270.500	21.237	0.00006**
	Greater & equal than 50	119.385	8.332	244.370	30.239	237.780	26.817	0.00009**
LDL	Less than 50	101.241	11.827	218.960	23.348	277.675	59.266	0.00005**
	Greater & equal than 50	97.392	11.049	216.375	47.772	250.073	46.304	0.00003**

**The mean difference is significant at the 0.01 level.

Table 4: The comparison of groups at each time point separately according to the age groups.

Parameters	Age Group	Control		Stable		Unstable		P. value
		Mean	Std. D.	Mean	Std. D.	Mean	Std. D.	
WBC	Less than 50	6216.512	880.279	16464.740	3041.032	17025.250	2410.647	0.00001**
	Greater & equal than 50	5906.877	964.040	15911.008	2310.888	16101.424	2461.538	0.00002**
GPX-1	Less than 50	38.371	5.811	15.840	2.745	11.650	1.816	0.00002**
	Greater & equal than 50	40.192	6.361	14.443	3.384	11.976	2.808	0.00006**
4-HNE	Less than 50	2.729	0.625	12.420	0.589	12.525	1.482	0.00004**
	Greater & equal than 50	3.185	0.570	11.080	1.191	12.673	1.214	0.00003**

**The mean difference is significant at the 0.01 level.

DISCUSSION

This study provides compelling evidence that work-related stress, manifested through physical exertion and psychological strain, significantly influences the biochemical profiles of angina patients, with age emerging as a crucial modulating factor. The elevated levels of visfatin, ACE, and PR3 observed in unstable angina, especially among younger individuals, underscore the complex interplay between inflammation, oxidative stress, and metabolic dysregulation in the pathogenesis of acute coronary syndromes.[19] These observations accord with previous reports highlighting the participation of adipokines (e.g., visfatin), inflammatory enzymes (e.g., PR3), and regulators of the angiotensin system (e.g., ACE) in the causation of cardiovascular disease.[20]

Younger patients (<50 years) had more biochemical changes in the form of higher lipid levels, heightened oxidative stress, and chronic elevation of inflammatory markers. This may either have been due to : firstly, greater metabolic demands and greater sympathetic activity in young patients with occupational stress [21], secondly and less vascular adaptation or arterial remodeling in younger patients compared to older patients, thus rendering them more susceptible to acute endothelial injury. Thirdly, Lifestyle factors such as smoking and physical inactivity increase oxidative stress and lipid imbalance. [22] Temporal dynamics of ACE and PR3 levels in stable and unstable angina support the hypothesis that unstable plaques are maintained by endothelial dysfunction and chronic inflammation Normalization of biomarker levels to near baseline levels in stable angina suggests that patients experience intermittent ischemia with little or no vascular damage.[23] These findings highlight the need for age-specific treatment and biomarker-based monitoring of patients with occupational stress, especially for younger individuals at risk for unstable angina.

CONCLUSIONS

This study shows that occupational stress significantly increases biochemical risk factors for angina, especially in young people. Elevated levels of visfatin, ACE, PR3, troponin, and lipids reflect increased inflammatory, oxidative, and metabolic stress in unstable angina, and age plays an important role in modulating these effects.

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CONFLICT OF INTEREST
Authors declare no conflict of interest.
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AUTHORS' CONTRIBUTION

The following authors have made substantial contributions to the manuscript as under:

Conception or Design:	HKR, RKA
Acquisition, Analysis or Interpretation of Data:	HKR, RKA
Manuscript Writing & Approval:	HKR, RKA

All the authors agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.