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Comparison of creatine kinase-MB, troponin-I, troponin-T, Triiodothyronine, Thyroxine, Apoprotein-B and homocysteine between non-smokers, smokers at high altitudes, and smokers at sea level

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ABSTRACT

Earlier diagnosis of heart disease can occur via awareness of biochemical changes. Keeping this in view, we wanted to determine if there was any difference between biochemical heart parameters between non-smokers (the control group), smokers who live at a high altitude, or smokers who live at sea level. There were 180 participants categorised into three groups, A, B, and C, depending upon their smoking/non-smoking classification, or distance from sea level. Blood samples were taken as per requirements to check levels of creatine kinase-MB, troponin-I, troponin-T, Triiodothyronine (T3), Thyroxine (T4), Apolipoprotein B (apo-B), and homocysteine, and subjected to enzyme-linked immunoassay (ELISA) investigations. Creatine kinase-MB, troponin-I, troponin-T, T3, thyroxine, apoprotein-B, and homocysteine all exhibited a noteworthy difference ($p \leq 0.01$) when compared between non-smokers and smokers (either at a high altitude or sea level), but only troponin I and T3 showed a noteworthy difference when compared between smokers at a high altitude versus at sea level ($p \leq 0.01$) as follows: Creatine kinase-MB, $p=0.434$; troponin-I, troponin-T, $p=0.208$; T3, $p \leq 0.01$; thyroxine, $p=0.190$; apoprotein-B, $p=0.008$; and homocysteine, $p=0.039$. It has been found that significant differences exist between smokers and non-smokers regarding cardiovascular (CV) pathology, whether the person resides at a high altitude or sea level. However, additional studies should be performed to find the correlation between smokers at a high altitude versus and smokers at sea level, which can change the treatment methods at high altitudes and pave the way for finding new medicines.

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Introduction

The diagnosis of acute myocardial infarction (AMI) is generally confirmed by several clinical shreds of evidence, electrocardiographic alterations, and the elevations of traditional cardiac enzymes (1). On the contrary, medical indications are likely to be uncommon and an ECG is sometimes difficult to use for a diagnosis. Traditional cardiac enzymes, creatine kinase (CK) and its isoenzyme MB (CKMB) cannot eliminate AMI at the very outset. Cardiac skeletal muscles have troponin. There exist three kinds of troponins— troponin C, troponin I, and troponin T. Troponin C carry the joining areas for Ca2+ which assists in initiating a contraction, troponin I obstructs the interactivity of myosin and actin and troponin T converts to tropomyosin (2, 3). The discharge of troponins occurs as a reaction to a myocardial wound irrespective of any cause. One of the most common causes of cardiac muscle injury is ischemia but an increase in troponins may be due to other factors besides an ischemic injury. A minor preliminary increase happens to take place the moment troponins are discharged out of the cytosolic pool that is recognizable in blood. If the breakage remains for a long time and necrosis continues, additional troponins are discharged from the strained/injured muscle (4).

It has been seen in a study of almost 30,000 participants that there is an inconsistency between troponin and CK-MB data in about one-third of participants. However, it was noticed that participants who had negative results for troponin, but CK-MB was present, had rates of mortality that were not elevated compared to participants who tested negative for both of the heart damage biomarkers. Likewise, in another study, it was reported that inpatient hospital mortality was excessive when both CK-MB and troponin were tested as positive, intermediary in CK-MB-negative/troponin-positive patients, and less likely in patients for whom both of these markers were negative and also decreased in those who were CK-MB positive/troponin negative (5). Thus, an isolated CK-MB elevation is said to have limited prognostic value in patients with non-ST elevation acute coronary syndrome.

T3 and T4 are important hormones that are produced in the thyroid gland. The main clinical manifestations of deficiency of thyroid hormones include decreased contractility of the vasculature, bradycardia, and increased systemic vascular resistance, whereas increased thyroid

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hormones result in increased blood volume and increased contractility due to the activation of the renin-angiotensin-aldosterone axis, tachycardia and pulmonary hypertension (6). It has also been noticed in many studies that T3 accelerates the ageing process by decreasing the proliferation process. However, as an individual age, T3 accelerates the ageing process (partly by decreasing proliferation), diminishing the repair mechanisms and restricting longevity. Some processes like caloric curtailment, which extends the life span, have been proven to deplete the levels of circulating T3, which is additional evidence stressing the important role of T3 in ageing (7). Studies have shown the induction of both maturation and ageing effectors by T3 through the binding of various isoforms to the key regulators, p16Ink4a and Mafa (8).

Cardiovascular (CV) peril can still be monitored by apoB (9). ApoB plays a major role in the transfer of triglycerides and cholesterol from the gut and liver to various utilisation and storage sites. ApoBis considered to be a major parameter in appraising CV peril in patients with diabetes and/or a metabolic syndrome because these patients tend to have minimum amounts of LDL particles i.e., an almost relatively normal LDL-C but with an elevated apoB level. In a study conducted by Johannesen et al., it was found that in patients treated with statins, a correlation existed between elevated levels of apoB and non-HDL-C, which had greater residual peril of all-cause mortality including AMI. However, LDL-C had no such association (10). Homocysteine tests specified for plasma and urine are revealed via the screening and diagnosis of diverse kinds of homocystinuria, vitamin B-12 and vitamin B-6 depletion, and deficiency of folic acid. It is still debatable whether an elevated plasma homocysteine level increases CV peril. Many studies have indicated that smokers who have higher levels of plasma homocysteine are at increased risk of CV diseases (11). Therefore, we took up this study to find out the relationship between these endocrine parameters at high altitudes and sea level.

Materials and Methods

Study design

This research study was a correlational study to determine whether living at a particular elevation (almost 2500 metres) played a role in biochemical parameters which are related to the CV system. The study was conducted for a period of two years, from April 2020 to June 2022. The research hypothesis and objective of the study were "To determine if there was any difference between biochemical heart parameters between non-smokers (the control group), smokers who live at a high altitude, or smokers who live at sea level."

Recruitment of patients

The 180 participants were categorized into three groups, A, B and C, depending upon their smoking/non-smoking status, and the elevation of where they lived. Participants living at an elevated elevation (height) were from the city of Abha (2,470 metres above sea level) and those at sea level were from Guwahati (50 metres above sea level).

Dropouts

In the beginning, we considered taking 75 participants in each group; but due to non-commitment for the study parameters, or some participants having conflicting inclusion criteria or otherwise, we had to restrict our participants in each group to 60.

Inclusion criteria

Adult patients (≥30 years of age and less than 60 years of age) who had smoked for a duration of a minimum of 10 years were included in the smoker's category, and healthy controls were matched using the same age group (≥30 years of age and less than 60 years of age).

Exclusion criteria

Patients were excluded if they were taking medicines for hypertension, if known to be a diabetic on medicines, and had any serious chronic disease including confirmed coronary arterial disease (CAD), previous revascularisation coronary artery bypass grafting (CABG), percutaneous transluminal coronary angioplasty (PTCA), or stenting), other cardiac diseases (e.g., valvular disease or aetiology of cardiomyopathy), unstable angina with elevated serum cardiac biomarkers, ECG changes, etc.; non-ST elevation acute coronary syndromes (NSTE-ACS), non-ST-elevation myocardial infarction (NSTE-MI), ST-elevation myocardial infarction (STE-MI), or confirmed acute coronary syndrome (ACS). Studies in populations with >20% asymptomatic or with known CAD unless data are stratified by symptom status/CAD status are conflicting, so those patients were excluded too. For the smoker's category, individuals who had smoked for less than 10 years were excluded from the study.

Ethical considerations

All ethical aspects were considered while finalising this research from the Research Ethics Committee (HAPO-06-B-001) through Approval No. ECM#2022-5518.

Support

The authors thank the Deanship of Scientific Research, King Khalid University for financial support under grant number RGP.1/356/43. *2.8 General Measurements*

General data points such as age, waist circumference, body mass index, and ethnicity, were collected.

Collection of the biomarkers and performance of investigations

Blood was taken as per requirements for creatine kinase-MB, troponin-I, troponin-T, triiodothyronine (T3), thyroxine (T4), Apolipoprotein B (apo-B) and homocysteine, and subjected to enzyme-linked immunoassay (ELISA) investigations.

Troponin I and troponin T assay

The troponin complex is important for regulating skeletal and cardiac muscle contractions. This complex includes three protein subunits: troponin C, troponin I and troponin T. Troponins I and T have unique cardiac isoforms. The human cardiac troponin I ELISA method is a single-wash 90 minutes sandwich ELISA technique that was utilised for the quantification of cardiac troponin I. For determining troponin T, captured antibodies were conjugated to an affinity tag that is fully recognised by the monoclonal antibody utilised to coat the ELISA plates. This technique allowed the formation of an antibody-analyte sandwich complex in a single step, which significantly reduced the

assay time (11-13).

CK-MB assay

CK-MB was estimated via the kit method. Specific inhibition of CK-M sub-units was the base method. Inhibition was done by anti-CK-M monoclonal antibodies. These antibodies inhibit the M subunits and also the MM isoenzyme which corresponds to CK-MB. Determination of subunit B was achieved by the utilisation of a reactive system which is based on an analytical technique and is optimised by utilising IFCC, with N-acetylcysteine acting as an activator (14).

T3 and thyroxine assay

Competitive binding between T3 in the assayed serum and T3-peroxidase conjugate for a restricted number of binding sites is the main principle; in this assay, wells were coated with anti-T3n (from sheep). Therefore, the amount of T3 peroxidase conjugate which was bound to the respective wells was inversely proportional to the concentration of T4 in the blood. The principle for the determination of T4 is also the same (15, 16).

apoB assay

Plasma for apoB was collected in a lavender top (EDTA) tube. Serum was separated from cells as soon as possible or within two hours of collection. Then a single-wash 90 min sandwich ELISA was utilised. This method also employs capture antibodies conjugated to an affinity tag that is recognised by the monoclonal antibody used to coat the ELISA plates. This technique allows the generation of the antibody-analyte sandwich complex in a single step, significantly reducing the assay time (17).

Homocysteine assay

Homocysteine was also assayed by the ELISA technique utilising the competitive enzyme immunoassay technique of using a polyclonal anti-HCY antibody and its counterpart, the HCY-HRP conjugate (18).

Statistical evaluation

All statistical evaluation was completed with SPSS Version 23, from IBM. Mean and standard deviation, skewness, standard error, and graphical representation were initially completed and then a non-parametric test, i.e., Mann Whitney-U, was done to determine if there were significant differences between smokers at an elevated altitude, smokers at sea level or the non-smoking controls.

Results

Demographic profile

The age for SH was 46.4±6.75 years, whereas, for SSL, it was 48.25±7.5 years. In the case of NP, the age was 45.35±8.85 years. All other characteristics are depicted in Table 1.

Cardiac troponin T

The mean±SD for cardiac troponin_T in the control group was 0.0744±0.10490 ng/mL. At the elevated height, the mean±SD for cardiac troponin_T was 0.9208±0.14184 ng/mL, while at sea level, it was 0.9624±0.19729 ng/mL (Fig.1). The minimum level for cardiac troponin_T in the control group was 0 while the maximum was 0.35 ng/mL. For the smokers at the elevated height, the maximum level was 0.68 ng/mL while the minimum level was 1.21 ng/mL. For smokers at sea level, the minimum cardiac troponin_T was 0.45 ng/mL while the maximum level was 1.34 ng/mL. The median level for cardiac troponin-T was 0.0166 ng/mL, 0.9650 ng/mL and 0.02547 ng/mL in the control group, with elevated height and sea level. Skewness was 1.633 ng/mL for the control group, 0.061 ng/mL at an ele-

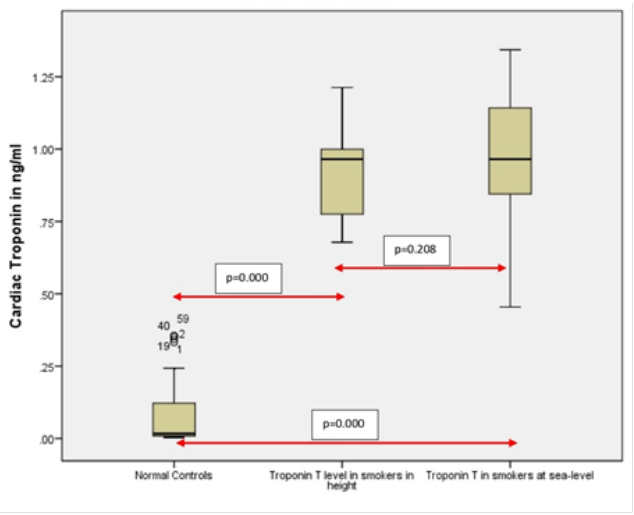

Figure 1. Comparison of troponin_T in normals, smokers at height and smokers at sea level.

Table1. Demographic and clinical characteristics of participants.

	Smokers at Height (SH)	Smokers at Sea Level (SSL)	Non-smokers (NP)
Age (in years)	46.4±6.75	48. 25±7.5	45.35±8.85
BMI (in kg/m^2)	25.1±1.25	26.9±1.15	26.2±0.85
WC (in cm)	93.2±1.4	94.19±1.7	95.4±1.25
SBP (in mmHg)	138±4.2	135±3.9	126±2.6
DBP (in mmHg)	85.35±6.25	81.9±12.6	78.25±4.25
FPG (in mg/dl)	83.25±8.55	87.5±7.25	84.5±9.76
PPPG (in mg/dl)	128±9.25	131±11.15	131±12.50
TC (in mg/dl)	204.8±53.5	188.95±40.25	136.8±38.5
HDL-C (in mg/dl)	28.25±6.25	30.24±5.6	40.25±7.75
TG (in mg/dl)	185.35±46.5	194.5±39.35	127.75±38.65

*BMI-Body mass index; WC-Waist circumference; SBP-Systolic blood pressure; DBP-Diastolic blood pressure; TC-total cholesterol; HDL-C-HDL-cholesterol; TG- triglycerides; FPG-Fasting plasma glucose; PPPG-Postprandial plasma glucose.

vated height and -0.305 ng/mL for sea level (Table 2). The p-value when comparing healthy controls and smokers at an elevated height (H) and also between healthy controls and smokers at sea level (S) using the Mann-Whitney U test, was p≤0.01, which showed that it was significant. However, when smokers (H) and smokers (S) were compared, the p-value became 0.208, which showed an insignificant association (Table 3).

Cardiac troponin I

The mean±SD for cardiac troponin I in the control group was 0.0128±.00576 ng/mL. At an elevated height, the mean±SD for cardiac troponin I was 0.0263±.00427 ng/mL, while at sea level, it was 0.0312±.00807 ng/mL (Fig.2). The minimum level for cardiac troponin I in the control group was 0 while the maximum was 0.02 ng/mL. For the elevated height smokers, the maximum level was 0.03 ng/mL while the minimum level was 0.02 ng/mL. At sea level, the minimum cardiac troponin I was 0.02 ng/mL while the maximum level was 0.05 ng/mL. The median levels for cardiac troponin-I were 0.0142 ng/mL, 0.0277 ng/mL and 0.0298 ng/mL in the control group, with elevated height and sea level. Skewness was -0.097 for the control group, -0.700 ng/mL for an elevated height and 0.126 ng/mL for sea level (Table 2). The p-value when comparing healthy controls and smokers (H) and also between healthy controls and smokers (S), and smokers (H) and smokers (S) using the Mann Whitney U test, was p≤0.01, which showed that it was significant (Table 3).

CK-MB

The mean±SD for CK-MB in the control group was 10.12±3.96 U/L. At an elevated height, the mean±SD for CK-MB was 16.3167±3.68 U/L, while at sea level, it was 16.7167±3.76 U/L (Fig.3). The minimum level for CK-MB in the control group was 4 U/L while the maximum was

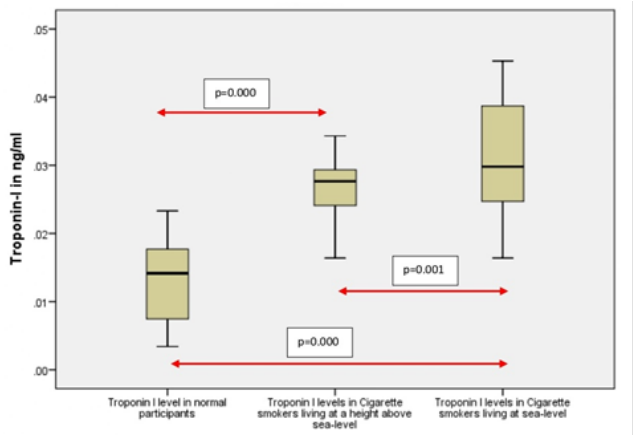

Figure 2. Comparison of troponin_I in normals, smokers at height and smokers at sea level.

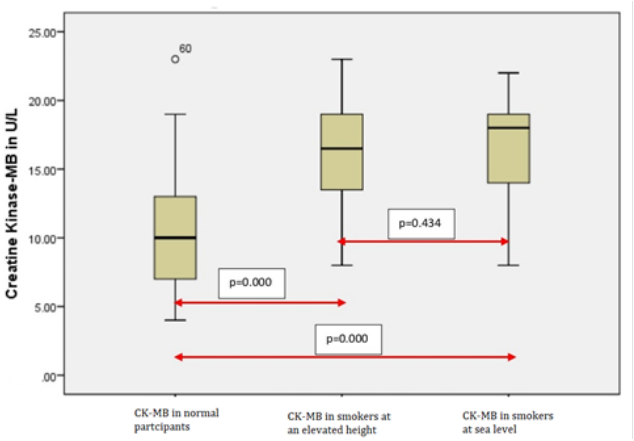

Figure 3. Comparison of CK-MB in normals, smokers at height and smokers at sea level.

Table 2. Characteristic features of the investigated parameters.

Parameters	Normal range	Minimum	Maximum	Median	Skewness	Kurtosis
Cardiac troponin_T (N)_ng/mL		00	0.35	0.017	1.633	1.667
Cardiac troponin_T (H)_ng/mL	< 0.1	0.68	1.21	0.97	0.061	-0.626
Cardiac troponin_T (S)_ng/mL		0.45	1.34	0.025	-0.305	-0.422
Cardiac_troponin_I_(N)_ng/mL		0.00	0.02	0.014	-0.097	-1.315
Cardiac_troponin_I_(H)_ng/mL	< 0.03	0.02	0.03	0.028	-0.700	-0.211
Cardiac_troponin_I_(S)_ng/mL		02	0.05	0.0298	0.126	-1.126
CK-MB_(N)_U/L		4	19	9.5	0.327	-0.642
CK-MB_(H)_ U/L	5-25	8	23	16.5	0.023	-0.335
CK-MB_(S)_ U/L		8	22	18	-0.432	-0.877
Apo_B_(N)_ mg/dL		38	86	58.0	0.506	-0.394
Apo_B_ (H)_ mg/dL	<130	66	137	85.5	0.919	0.401
Apo_B (S)_ mg/dL		54	112	80.5	-0.109	0.380
T3 (N)_ ng/dL		74	167	96	1.145	1.575
T3 (H)_ ng/dL	40-205	88	224	165.5	-0.222	-0.661
T3 (S)_ ng/dL		95	191	144.5	0.021	-0.401
Thyroxine (N) ng/dL		0.66	1.90	1.234	0.335	-0.651
Thyroxine (H) ng/dL	0.7-1.9	1.11	2.45	1.556	0.552	-0.706
Thyroxine (S) ng/dL		1.11	2.54	1.722	0.327	-1.187
Homocysteine (N)_ µmol/L		4	19	11	0.139	0.45.5
Homocysteine (H)_ µmol/L	4-14	4	35	14.5	0.724	0.681
Homocysteine (S)_ µmol/L		8	33	18	0.734	0.430

Table 3. Comparison of creatine kinase-MB, troponin-I, troponin-T, Triiodothyronine, Thyroxine, Apoprotein-B and homocysteine between non-smokers, smokers at high altitudes, and smokers at sea level.

Parameters	Situation	p-value
Cardiac troponin_T	Smokers (H) Healthy controls	≤0.01
	Smokers (S) Healthy controls	≤0.01
	Smokers (H) Smokers (S)	0.208
Cardiac troponin I	Smokers (H) Healthy controls	≤0.01
	Smokers (S) Healthy controls	≤0.01
	Smokers (H) Smokers (S)	≤0.01
CK-MB	Smokers (H) Healthy controls	≤0.01
	Smokers (S) Healthy controls	≤0.01
	Smokers (H) Smokers (S)	0.434
Apo_B	Smokers (H) Healthy controls	≤0.01
	Healthy controls Smokers (S)	≤0.01
	Smokers (H) Smokers (S)	0.008
T3	Smokers (H) Healthy controls	≤0.01
	Smokers (S) Healthy controls	≤0.01
	Smokers (S) Smokers (H)	≤0.01
Thyroxine	Healthy controls Smokers (H)	≤0.01
	Healthy controls Smokers (S)	≤0.01
	Smokers (H) Smokers (S)	0.190
Homocysteine	Healthy controls Smokers (H)	≤0.01
	Healthy controls Smokers (S)	≤0.01
	Smokers (H) Smokers (S)	0.039

19 U/L. For smokers at an elevated height, the maximum level was 23 U/L while the minimum level was 8 U/L. At sea level, the minimum CK-MB was 8 U/L while the maximum level was 22 U/L. The median level for cardiac CK-MB was 9.5 U/L, 16.5 U/L and 18 U/L in the control group, with elevated height and sea level. Skewness was 0.023 U/L for the control group, 0.023 U/L at an elevated height and -0.432 U/L for sea level (Table 2). The p-value when comparing healthy controls and smokers (H) and also between healthy controls and smokers (S), and smokers (H) and smokers (S) using the Mann Whitney U test, was p≤0.01, which showed that it was significant (Table-3).

Apo-B

The mean±SD for apoB in the control group was 59.02±13.15 mg/dL. At an elevated height, the mean±SD for fasting insulin was 88.83±16.06 mg/dL, while at sea

level, it was 80.0±11.55 mg/dL (Fig.4). The minimum level for apoB in the control group was 38 mg/dL while the maximum was 86. For smokers at an elevated height, the maximum level was 137 mg/dL while the minimum level was 66. At sea level, the minimum apoB was 54 while the maximum level was 112 mg/dL. The median level for apoB was 58 mg/dL, 85.5 mg/dL and 80.5 mg/dL in the control group, with elevated height and sea level. Skewness was 0.506 mg/dL for the control group, 0.919 mg/dL at an elevated height and -0.109 mg/dL for sea level (Table 2). The p-value when comparing healthy controls and smokers (H) and also between healthy controls and smokers (S) was p≤0.01, which showed that it was significant. However, when smokers (H) and smokers (S) using the Mann Whitney U test, were compared, the p-value became 0.008, which showed an insignificant association (Table-3).

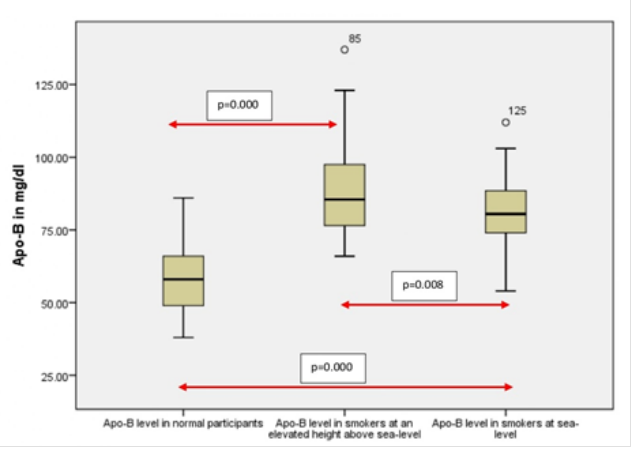

Figure 4. Comparison of Apo-B in normal participants, smokers at height and smokers at sea level.

Triiodothyronine

The mean±SD for T3 in the control group was 100.6167±18.97 ng/dL. At an elevated height, the mean±SD for fasting insulin was 161.2833±34.66 ng/dL, while at sea level, it was 146.9333±24.49 ng/dL (Fig.5). The minimum level for T3 in the control group was 74 ng/dL while the maximum was 167 ng/dL. For smokers at an elevated height, the maximum level was 224 ng/dL while the minimum level was 88 ng/dL. At sea level, the minimum T3 was 95 ng/dL while the maximum level was 191 ng/dL. The median levels for T3 were 96 ng/dL, 165.5 ng/dL and 144.5 ng/dL in the control group, elevated height and sea level. Skewness was 1.145 ng/dL for the control group, -0.222 ng/dL at an elevated height and 0.021 ng/dL for sea level (Table 2). The p-value when comparing healthy controls and smokers (H), smokers (H) and smokers (S) and also between healthy controls and smokers (S) using the Mann-Whitney U test, was p≤0.01, which showed that it was a significant association (Table-3).

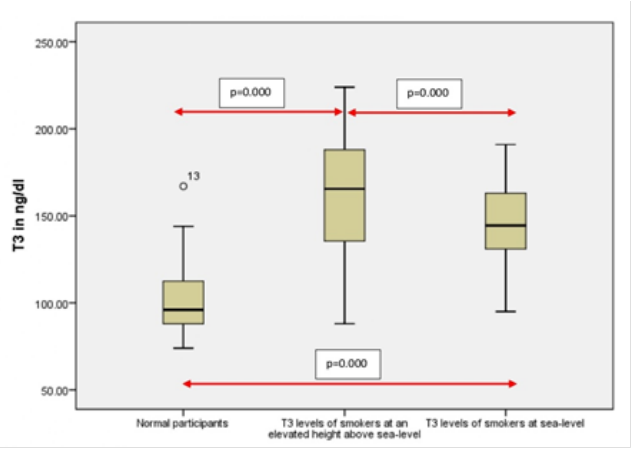

Figure 5. Comparison of T3 in normal participants, smokers at height and smokers at sea level.

Thyroxine

The mean±SD for thyroxine in the control group was 1.2609±.31942 ng/dL. At an elevated height, the mean±SD for thyroxine was 15.3833±6.56 ng/dL, while at sea level, it was 17.7167±6.14263 ng/dL (Fig.6). The minimum level for thyroxine in the control group was 0.66 while the maximum was 1.90 ng/dL. For smokers at an elevated height, the maximum level was 2.45 ng/dL while the minimum level was 1.11 ng/dL. At sea level, the minimum thyroxine was 1.11 while the maximum level was 2.54 ng/dL. The median levels for thyroxine were 1.234 ng/dL, 1.556 ng/dL, and 1.722 ng/dL in the control group, at an elevated height and sea level. Skewness was 0.335 ng/dL for the control group, 0.552 ng/dL at an elevated height and 0.327 ng/dL for sea level (Table 2). The p-value when comparing healthy controls and smokers (H) and also between healthy controls and smokers (S) was p≤0.01, which showed that it was significant. However, when smokers (H) and smokers (S) were compared using the Mann-Whitney U test the p-value became 0.190, which showed an insignificant association (Table 3).

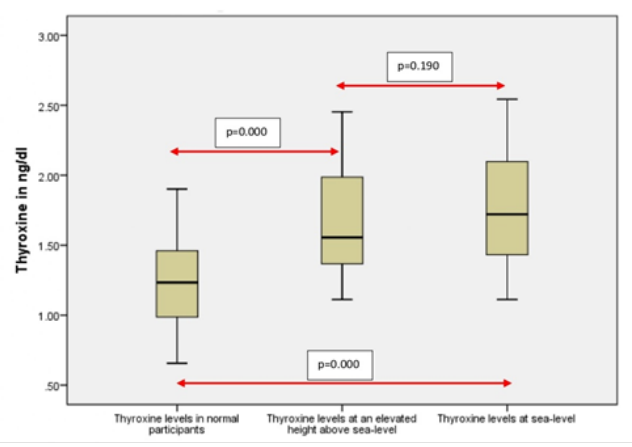

Figure 6. Comparison of Thyroxine in normal participants, smokers at height and smokers at sea level.

Homocysteine

The mean±SD for homocysteine in the control group was 10.6500±4.2018 µmol/L. At an elevated height, the mean±SD for homocysteine was 15.3833±6.56 µmol/L, while at sea level, it was 17.7167±6.14263 µmol/L (Fig.1). The minimum level for homocysteine in the control group was 4 µmol/L while the maximum was 19 µmol/L. For the smokers at an elevated height, the maximum level was 35 µmol/L while the minimum level was 35 µmol/L. At sea level, the minimum homocysteine was 8 µmol/L while the maximum level was 33 µmol/L. The median levels for homocysteine were 11 µmol/L, 14.5 µmol/L and 18 µmol/L in the control group, with elevated height and at sea level.

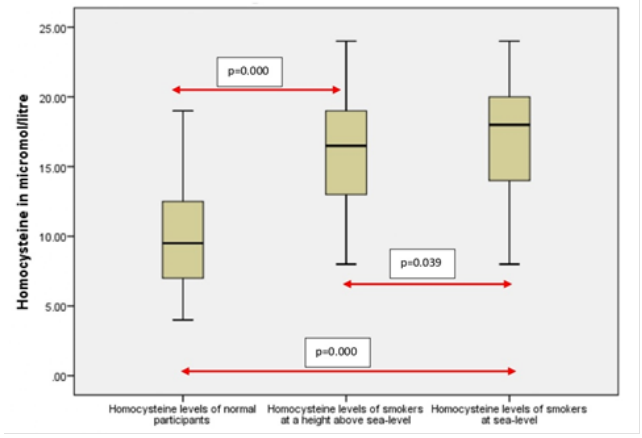

Figure 7. Comparison of Homocysteine in normal participants, smokers at height and smokers at sea level.

Skewness was 0.139 µmol/L for the control group, 0.724 µmol/L at an elevated height and 0.734 µmol/L for sea level (Table-2). The p-value when comparing healthy controls and smokers (H) and also between healthy controls and smokers (S) was p≤0.01, which showed that it was significant. However, when smokers (H) and smokers (S) were compared, the p-value became 0.039, which showed an insignificant association (Table 3).

Discussion

Recent medical studies have suggested investigating troponins as soon as 6-12 hours after the first evaluation and after 24 hours of the inception of any symptoms. In cases of suspected subendocardial non-ST-segment elevation (NSTEMI) or AMI, the volume of troponin may likely be assessed earlier than 3-4 hours due to the possible detectability of the markers. Both troponin T and troponin I are opposed to each other with dis-similar molecules and diverse functions. Due to an increase in either of their myocardial damages, their numerical values change. In cases with severe deterioration of a congestive cardiac disorder owing to aetiologies instead of AMI, the amount of troponin may be increased due to the incapability of the ailing heart to continue proper coronary perfusion (19, 20). In our case, the increased levels of troponin detected might have been due to these causes. Serum CKMB is capable of support from the muscles related to the skeleton and heart. CKMB can consist of nearly 2% of the entire CK in the muscle whereas CKMB constructs 20-40% of overall CK (21, 22). It is possible to separate myocardial from skeletal muscle injury by exhibiting the CKMB outcome in terms of the overall CK ratio. As CKMB is presented in units of mass (ug/l) and overall CK in the units of activity(U/l), the terminology "relative index" (RI) instead of ratio should be employed to explain the proportion of CKMB to overall CK. RI seems not to be proper for all patients, specifically those who have lower overall CK outcomes where the complete CKMB mass outcome bears the effective meaning (23, 24). Since in our study, CK-MB has been increased, myocardial injury is probably the main factor, and most likely due to damage from cigarette smoke.

It has been seen that both excess and deficiency of thyroid hormones elevate the risk of cardiac failure. The more indefinite variations in the status of thyroid hormone associated with subclinical thyroid dysfunction, have been correlated with incident cardiac failure. In other words, many studies have found that patients in cardiac failure will not have enough cardiac capacity to countenance minor changes in the number of thyroid hormones. Some studies have also been conducted in outpatients having pre-existing cardiac failure, but the relationship between subclinical thyroid dysfunction and mortality has not been properly correlated and understood due to the lack of measurement of T3 or T4 levels (25). Our preceding conclusions suggested that smoking influence the prevalence of subclinical hypothyroidism (SCH). Other studies in various countries also reported that low serum TSH concentrations were habitually perceived in some cigarette smokers (26, 27). Furthermore, it has been reported that cigarette smoke exerts inhibitory as well as stimulatory effects on the function of the thyroid and is a crucial risk constituent for the evolution of thyroid disease. For example, Grave's disease, thyroid hormone abnormalities and Graves ophthalmopathy have all been related to smoking (28, 29). As to how or why serum TSH levels are decreased, we still do not fully understand. Many mechanisms have been considered regarding the depletion of thyroid hormones. It was seen in the fifth Tromso study, that the levels of blood-free T3 levels and free T4 were conspicuously elevated in smokers when compared to non-smokers (30). The depletion in TSH amounts may be secondary to the elevation in blood-free T3 and free T4 levels, where it is presumed that short exposure to cigarette smoke elevates blood-free T3 and free T4 levels; however, it was seen that this was not accompanied by a significant depletion in blood TSH levels (31). Therefore, it has been suggested that smoking may elevate thyroid hormone synthesis and subsequent release via pathways that are TSH-independent.

The American College of Cardiology/American Heart Association guidelines confirms the fact that apoB is a reliable marker of CV distress (32). Many epidemiological studies have also suggested the authenticity of apoB as a more reliable marker in CV conditions than non–HDL-C (33). Our research that confirmed that smokers have a higher apoB supports these studies. Whether triglyceride particles by themselves are atherogenic remains a controversial issue since Mendelian randomisation results indicate that triglycerides added a significant amount to LDL-C and did not consider apoB (34). Furthermore, many studies have expressed those triglyceride-enriched but cholesterol-depleted apoB particles seemed to be much less atherogenic when compared to cholesterol-enriched, triglyceride-depleted apoB particles (35). Thus, verification from other studies promotes that Lp(a) adds independent information to the CV risk (36). Nowadays, few therapies are accessible to deplete the concentration of Lp(a), but it still remains unclear if depleting Lp(a) will ameliorate the outcomes of CV problems (37, 38). Although conflicting evidence has been received from various epidemiological studies, the correlation between Lp(a) and major coronary events seemed to be strong-er than its correlation with stroke. One interesting aspect was that it was reported that Lp(a) confers CV risk mainly when LDL-C levels are increased. However, O'Donoghue et al. found that the interrelation between coronary risk and Lp(a) persisted relationship with CV peril in patients having established CV disease and is independent of accessory baseline or otherwise achieved LDL-C levels. Multiple pieces of research on epidemiology have confirmed that the volume of plas-

ma homocysteine is higher in cases with a cardiac disorder, stroke, peripheral vascular diseases, or thromboembolic diseases; but contemporary meta-analysis presents that an everlasting and average homocysteine increase generates only a slight or no effect on any coronary cardiac disorder. Various postulated mechanisms have been suggested by different researchers which may imply some possible mechanisms regarding these changes derived in the present study. Cyanide, organic nitrites, nitrous oxide (NO) and hydrogen sulphide, which are constituents of tobacco smoke, interact with vitamin B12 coenzymes and folic acid and convert them into various biologically inactive compounds. This results in the prevention of remethylation of homocysteine and elevates its concentration in the blood in smokers (35, 39), as has also been confirmed in our study.

Limitations of the study: Our study has many limitations. Although we have included cigarette smokers with a habit of more than 10 years duration, we could not track their dietic habits over the same time frame. The amount of daily exercise they conducted was also not considered. Another limitation in our study was the sampe size. We were unable to get more participants in our study. The study participants were not able to be followed up. The number of cigarettes smoked was taken as a daily average only, and no differences between monthly or weekly smoking were taken into the history. Genetic abnormalities, like familial hypertension or CV abnormalities in families, were also not tracked

It has been found that noteworthy differences exist between smokers and non-smokers, when we compared some cardiac markers (as stated above), regarding CV pathology, whether the person resides at an elevated height or at sea level. However, more similar studies should be performed to elucidate the correlation between smokers at an elevated altitude and smokers at sea level since troponin-I and T3 came as significant markers. A lack of oxygen might be one of the factors which play a role at and increased altitude along with gravity, which can change the treatment methods at high altitudes and pave the way for finding new medicines.

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Conflicts of interest

The authors declare no conflict of interest in the manuscript, and in the decision to publish the results.

Consent

Patient consent was obtained.

References

1. Ojha N, Dhamoon AS. Myocardial Infarction. 2022 Aug 8. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2022 Jan–. PMID: 30725761..
2. Barrett KE In: Barrett KE, Barman SM, Brooks HL, Yuan JJ. eds. Ganong's Review of Medical Physiology, 26e. McGraw Hill; 2019. Accessed January 13, 2023. https://accessmedicine.mhmedical.com/content.aspx?bookid=2525&sectionid=204289956
3. Pagana K, Pagana T, Pagana T. Mosby's Diagnostic and Laboratory Test References. St. Louis: Elsevier. 2019.
4. Park J, Lee S-H, Min JJ, Lee J-H, Kwon JH, Lee JE, et al. Association between high-sensitivity cardiac troponin I measured at emergency department and complications of emergency coronary artery bypass grafting. Sci Rep 2019;9(1):1-9.
5. Hachey BJ, Kontos MC, Newby LK, Christenson RH, Peacock WF, Brewer KC, et al. Trends in use of biomarker protocols for the evaluation of possible myocardial infarction. J Am Heart Assoc 2017;6(9):e005852.
6. Bozkurt B, Colvin M, Cook J, Cooper LT, Deswal A, Fonarow GC, et al. Current diagnostic and treatment strategies for specific dilated cardiomyopathies: a scientific statement from the American Heart Association. Circulation. 2016;134(23):e579-e646.
7. Teixeira PdFdS, Dos Santos PB, Pazos-Moura CC. The role of thyroid hormone in metabolism and metabolic syndrome. Ther Adv Endocrinol Metab 2020;11:2042018820917869.
8. Aguayo-Mazzucato C, Lee TB, Matzko M, DiIenno A, Rezanejad H, Ramadoss P, et al. T3 induces both markers of maturation and aging in pancreatic β-cells. Diabetes. 2018;67(7):1322-31.
9. Johannesen CDL, Mortensen MB, Langsted A, Nordestgaard BG. Apolipoprotein B and non-HDL cholesterol better reflect residual risk than LDL cholesterol in statin-treated patients. J Am College Cardiol 2021;77(11):1439-50.
10. Pirouzpanah S, Taleban F-A, Mehdipour P, Atri M, Foroutan-Ghaznavi M. Plasma total homocysteine level in association with folate, pyridoxine, and cobalamin status among Iranian primary breast cancer patients. Nutr Cancer 2014;66(7):1097-108.
11. Zhang F, Li X, Dong Q, Wang Y, Zhang H. Risk of acute cerebral infarction and plasma asymmetrical dimethylarginine and homocysteine levels: a clinical correlation analysis of Chinese population. J Stroke Cerebrovasc Dis 2014;23(9):2225-32.
12. Gerhardt W, Ljungdahl L. Detection of myocardial damage by serial measurements of cardiac troponin T, CK MBmass, and TROPT rapid test. Cardiovasc. Drugs Ther 1997;11(1):227-40.
13. Lee H, Youn H, Hwang A, Lee H, Park JY, Kim W, et al. Troponin Aptamer on an Atomically Flat Au Nanoplate Platform for Detection of Cardiac Troponin I. Nanomaterials 2020;10(7):1402.
14. Anderson JL. ST segment elevation acute myocardial infarction and complications of myocardial infarction. Goldman's Cecil Medicine: Elsevier; 2012. p. 434-48.
15. Al-wageeh S, Ahmed F, Nikbakht HA, Al-shami E, Askarpour MR, Chowdhury U. An Investigation of the Histopathological Pattern of Thyroid in Patients Undergoing Thyroid Operations: A Cross-Sectional Study. Open Access Surg 2020;13:47-52 https://doi.org/10.2147/OAS.S25310916.Caldwell G, Gow S, Sweeting V, Beckett G, Seth J, Toft A. Value and limitations of a highly sensitive immunoradiometric assay for thyrotropin in the study of thyrotroph function. Clin Chem 1987;33(2):303-5.
17. Shearn AI, Aday S, Ben-Aicha S, Carnell-Morris P, Siupa A, Angelini GD, et al. Analysis of neat biofluids obtained during cardiac surgery using nanoparticle tracking analysis: Methodological considerations. Front. Cell Dev Biol 2020;8:367.
18. Selhub J, Jacques PF, Bostom AG, D'Agostino RB, Wilson PW, Belanger AJ, et al. Association between plasma homocysteine concentrations and extracranial carotid-artery stenosis. N Engl J Med 1995;332(5):286-91.
19. Rallidis LS, Sakadakis EA, Tympas K, Varounis C, Zolindaki M, Dagres N, et al. The impact of smoking on long-term outcome of patients with premature (≤ 35 years) ST-segment elevation acute myocardial infarction. Am Heart J 2015;169(3):356-62.
20. Zethelius B, Berglund L, Sundström J, Ingelsson E, Basu S,

Larsson A, et al. Use of multiple biomarkers to improve the prediction of death from cardiovascular causes. N Engl J Med 2008;358(20):2107-16.

21. Fernández-Cisnal A, Valero E, García-Blas S, Pernias V, Pozo A, Carratalá A, et al. Clinical History and Detectable Troponin Concentrations below the 99th Percentile for Risk Stratification of Patients with Chest Pain and First Normal Troponin. J Clin Med 2021;10(8):1784.
22. Cediel G, Rueda F, García C, Oliveras T, Labata C, Serra J, et al. Prognostic value of new-generation troponins in ST-segment–elevation myocardial infarction in the modern era: the RUTI-STEMI study. J Am Heart Asso 2017;6(12):e007252.
23. Ota T, Hasegawa Y, Murata E, Tanaka N, Fukuoka M. False-Positive Elevation of CK-MB Levels with Chest Pain in Lung Adenocarcinoma. Case Rep Oncol 2020;13(1):100-4.
24. Mitchell JE, Hellkamp AS, Mark DB, Anderson J, Johnson GW, Poole JE, et al. Thyroid function in heart failure and impact on mortality. JACC: Heart Failure 2013;1(1):48-55.
25. Biondi B, Cappola AR, Cooper DS. Subclinical hypothyroidism: a review. JAMA. 2019;322(2):153-60.
26. Biondi B, Bartalena L, Cooper DS, Hegedüs L, Laurberg P, Kahaly GJ. The 2015 European Thyroid Association guidelines on diagnosis and treatment of endogenous subclinical hyperthyroidism. Eur Thyroid J 2015;4(3):149-63.
27. Bartalena L, Baldeschi L, Boboridis K, Eckstein A, Kahaly GJ, Marcocci C, et al. The 2016 European thyroid Association/European group on Graves' orbitopathy guidelines for the management of Graves' orbitopathy. Eur Thyroid J 2016;5(1):9-26.
28. Nakajima Y, Yamada S, Nishikido A, Katano-Toki A, Ishida E, Akuzawa M, et al. Influence of smoking on thyroid function in Japanese subjects: longitudinal study for one year of on-off smoking. J Endocrine Society 2019;3(12):2385-96.
29. Zhang Y, Shi L, Zhang Q, Peng N, Chen L, Lian X, et al. The association between cigarette smoking and serum thyroid stimulating hormone, thyroid peroxidase antibodies and thyroglobulin antibodies levels in Chinese residents: A cross-sectional study in 10 cities. PloS one. 2019;14(11):e0225435.
30. Grundy SM, Stone NJ, Bailey AL, Beam C, Birtcher KK, Blumenthal RS, et al. 2018 AHA/ACC/AACVPR/AAPA/ABC/ACPM/ADA/AGS/APhA/ASPC/NLA/PCNA guideline on the management of blood cholesterol: executive summary: a report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines. J Am College Cardiol 2019;73(24):3168-209.
31. Sniderman AD, Robinson JG. ApoB in clinical care: pro and con. Atherosclerosis 2019;282:169-75.
32. Sniderman AD, Couture P, Martin SS, DeGraaf J, Lawler PR, Cromwell WC, et al. Hypertriglyceridemia and cardiovascular risk: a cautionary note about metabolic confounding. J Lipid Res 2018;59(7):1266-75.
33. Hai Q, Smith JD. Acyl-Coenzyme A: Cholesterol Acyltransferase (ACAT) in Cholesterol Metabolism: From Its Discovery to Clinical Trials and the Genomics Era. Metabolites 2021;11(8):543.
34. Willeit P, Ridker PM, Nestel PJ, Simes J, Tonkin AM, Pedersen TR, Schwartz GG, Olsson AG, Colhoun HM, Kronenberg F, Drechsler C, Wanner C, Mora S, Lesogor A, Tsimikas S. Baseline and on-statin treatment lipoprotein(a) levels for prediction of cardiovascular events: individual patient-data meta-analysis of statin outcome trials. Lancet. 2018 Oct 13;392(10155):1311-1320. doi: 10.1016/S0140-6736(18)31652-0. Epub 2018 Oct 4. PMID: 30293769.
35. O'Donoghue ML, Fazio S, Giugliano RP, Stroes ES, Kanevsky E, Gouni-Berthold I, et al. Lipoprotein (a), PCSK9 inhibition, and cardiovascular risk: insights from the FOURIER trial. Circulation 2019;139(12):1483-92.
36. van Capelleveen JC, van der Valk FM, Stroes EG. Current therapies for lowering lipoprotein (a). J Lipid Res 2016;57(9):1612-8.
37. Gencer B, Kronenberg F, Stroes ES, Mach F. Lipoprotein (a): the revenant. Eur Heart J 2017;38(20):1553-60.
38. Parish S, Hopewell JC, Hill MR, Marcovina S, Valdes-Marquez E, Haynes R, Offer A, Pedersen TR, Baigent C, Collins R, Landray M, Armitage J; HPS2-THRIVE Collaborative Group. Impact of Apolipoprotein(a) Isoform Size on Lipoprotein(a) Lowering in the HPS2-THRIVE Study. Circ Genom Precis Med. 2018 Feb;11(2):e001696. doi: 10.1161/CIRCGEN.117.001696. PMID: 29449329; PMCID: PMC5841847.
39. Smith AD, Refsum H. Homocysteine - from disease biomarker to disease prevention. J Intern Med. 2021 Oct;290(4):826-854. doi: 10.1111/joim.13279. Epub 2021 Apr 6. PMID: 33660358.