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Low physical activity and high homocysteine levels among doctors

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ABSTRACT

Background
Homocysteine is a recognized risk factor for cardiovascular disease. Less is known about the influence of physical activity in homocysteine levels. The aim of our study is to find out the prevalence of high homocysteine levels and low physical activity among doctors and the relationship between them.

Methods
The study included 101 doctors working in a tertiary care hospital in India. Pregnant women and individuals with a known history of cardiovascular and/or cerebrovascular diseases were excluded. The main outcome variables measured were plasma total homocysteine and physical activity, using GPAQ (Global Physical Activity Questionnaire).

Results
Prevalence of a high homocysteine level (≥15µ/l) was 34.7% and the prevalence of low physical activity (<600 MET minutes/week) was 25.7 % in our study population. High homocysteine values were associated with male sex (p=0.00) and smoking (p=0.003). Homocysteine was significantly associated with low physical activity (MET minutes/week) adjusting for age, sex and smoking status (p<0.05). There was no significant association between homocysteine and physical activity with FBS, HbA1c and Lipid Profile.

Conclusion
Homocysteine level is inversely related to physical activity. Hyperhomocysteinemia is a strong risk factor for cardiovascular disease. From a public health viewpoint, it is important to identify the modifiable risk factors that influence homocysteine levels.

Keywords: Homocysteine, Physical activity, Sedentary lifestyle, Cardiovascular risk, Doctors, Workplace, GPAQ

INTRODUCTION
Physical activity is known to have a positive effect on health. The beneficial effects of physical activity in preventing mortality due to cardiovascular diseases and other conditions have been clearly described in the available literature.[1–3] Regular physical activity can improve endothelial function in a number of ways, including synthesis of molecular mediators, changes in neurohormonal release and oxidant/antioxidant balance.[4] In modern society, however, sedentary behaviour – prolonged sitting – has become a part of our lives across many settings, including in the workplace, on transportation and at home. Sedentary behaviour (from the Latin sedēre, to sit), is described as prolonged sitting and the absence of physical activity. Physical activity and sedentary behaviour depend on individual life choices and are influenced by environmental factors including job characteristics. The medical profession is very stressful, with long working hours, giving doctors little time to engage in physical activities. According to the World Health Organization (WHO), physical inactivity is estimated to be the main cause of 21–25% of breast and colon

cancers, 27% of diabetes and 30% of ischemic disease in the Global Burden of Disease.[5] Doctors' personal physical activity practices not only affect their own health but also influence how they counsel patients regarding physical activity, which is a cornerstone in the management of many chronic diseases.[6]

Homocysteine (Hcy) is a sulphur-containing amino acid. It is not obtained from diet; it is synthesized in the human body from methionine, an essential amino acid. Plasma total homocysteine (tHcy) refers to the sum of protein-bound, free-oxidized and reduced forms of homocysteine in plasma[7] and is usually about 5–15µ/l in healthy subjects.[8] An elevated level of tHcy in blood – hyperhomocysteinemia – is emerging as a prevalent and strong risk factor for atherosclerotic vascular disease in the coronary, cerebral and peripheral vessels, and thromboembolism.[9] Recent studies suggest that screening for homocysteine levels may be advised in those with unexplained thrombotic tendencies and in young patients who develop coronary disease without the usual predisposing factors such as hypertension, smoking, hypercholesterolemia or diabetes.[9] Mechanisms by which homocysteine causes vascular injury include endothelial injury, proliferation of smooth muscle cells, increased oxidative stress, DNA dysfunction, reduced activity of glutathione peroxidase and by promoting inflammation.[10] Studies[11–13] have identified moderately elevated concentrations of homocysteine as a potentially modifiable risk factor for coronary artery disease independent of other risk factors.

Hyperhomocysteinemia is caused by genetic and acquired factors. One of the major causes of acquired hyperhomocysteinemia is the deficiency of folates and vitamin B12, which are cofactors in Hcy metabolism. Other determinants include age, sex, smoking, alcoholism, physical activity, renal function and certain drugs such as folate antagonists, antiepileptics and contraceptives.[5] Physical activity has an inverse relationship with Hcy level independent of genotype or plasma B-vitamin status.[14] Physical activity can lower blood homocysteine level and improve overall health. It has been estimated that at least 9% of premature mortality globally could be avoided if everyone adhered to WHO physical activity guidelines.[15] From a public health viewpoint, it is crucial to identify the modifiable factors that influence plasma Hcy levels, as elevated levels are associated with an increased risk of cardiovascular disease.[16,17] In our study we aimed to find out the prevalence of low physical activity and high homocysteine levels among doctors and the relationship between them.

METHOD AND MATERIALS

Study population

The study was conducted among 101 doctors working in a tertiary care center in Kerala, South India. After obtaining approval from the institutional Ethics Committee and written consent from each person, the following sociodemographic and lifestyle covariates were recorded: age, sex, education level, marital status, menopausal status, smoking status, alcohol use and past medical history. Anthropometric parameters including height and weight were recorded. BMI (Body Mass Index) was calculated according to the formula weight/height (in m^2) and BMI groups were classified according to Asian BMI criteria.[18] Triplicate resting blood pressure was recorded according to standard protocols.[19]

Biochemical parameters

We collected 5ml of fasting blood sample in 0.5M EDTA tubes from each person. Fasting homocysteine was assayed in AU680 Beckmann Coulter. Fasting plasma glucose (FBS) levels were determined by the hexokinase method. Total cholesterol, serum triglycerides and HDL cholesterol were measured by enzymatic methods. HbA1c was assayed by particle enhanced immunoturbidimetric method. All the parameters were assayed in AU680, by Beckman Coulter. From the values of total cholesterol, HDL and triglyceride, the value of Low-Density Lipoprotein (LDL) was determined using Friedewald's formula.[20]

Physical activity

Physical activities were assessed by a self-reported questionnaire based on the Global Physical Activity Questionnaire (GPAQ).[21] The participants were asked about the intensity, frequency and duration of their activities in three domains: 1) at work, 2) during travel and 3) during recreation. According to the GPAQ a metabolic equivalent (MET) value of 4 was assigned for moderately intense physical activity and a value of 8 was assigned for vigorously intense physical activity. The value MET was then multiplied by the number of days per week on which physical activity was undertaken and the duration on a typical day for each domain of physical activity. This gives the amount of physical activity in metabolic equivalent of task-minutes per week (MET-minutes/week). The MET-minutes/week of all the domains were then summed to create an overall physical activity score. According to the WHO, physical activity less than 600 MET-minutes/week is considered insufficient.[22]

Statistical methods

Numerical data were expressed as mean ± standard deviation (SD) if the distribution was normal, or median with an interquartile range if not, and categorical data as frequencies. All variables were tested for normal distribution using the Kolmogorov–Smirnov test. In univariate analysis, categorical variables were tested using the chi-square and Fisher exact test. Continuous variables with and without normal distribution were compared using Student's t-test or the Mann–Whitney U test, respectively. Correlations between continuous variables were tested using Pearson correlation or Spearman correlation coefficient (r) analysis. Variables that were significant at the 0.1 level were included in the multivariate analysis. Multivariate linear regression analysis was used to determine independent predictors for homocysteine.

All statistical tests were two-sided. A p-value <0.05 was considered to be statistically significant. Data analysis was performed using R software (R version 3.6.2 (2019-12-12) and The SPSS statistical package (version 16.0). The diagrams in Fig 1 and 2 are constructed using R software (R version 3.6.2 (2019-12-12)) and Microsoft excel.

RESULTS

General characteristics

The study population was 101 doctors working in the Government Medical College, Kollam, Kerala, South India. Two thirds of the study population (63.4%) were female and 36.6% male.

The mean age of the population was 39 years (Table 1) and more than half fell in the age group 31–40 years; 97% were married and 94% were non-smokers. Around one eighth (16%) of the study population had a history of hypothyroidism.

Table 1 Anthropometric and biochemical parameters of the study group (n=101)

Characteristics	Mean	SD	SE	95% CI for Mean		Median	Minimum	Maximum
				L	U			
Age	39.8	9.2	0.9	38.0	41.6	37.5	27.0	62.0
Height	162.3	8.7	0.9	160.5	164.0	161.0	140.0	186.0
Weight	67.5	10.9	1.1	65.4	69.7	67.5	40.0	106.0
BMI	25.5	3.1	0.3	24.8	26.1	25.0	18.3	35.6
Systolic BP	117.7	11.2	1.1	115.5	120.0	120.0	80.0	142.0
Dystolic BP	77.6	7.0	0.7	76.2	79.0	80.0	60.0	92.0
FBS	98.1	27.3	2.7	92.7	103.5	93.0	70.0	267.0
HbA1c	5.9	1.1	0.1	5.7	6.1	5.7	4.9	13.6
Total cholesterol	203.1	35.0	3.5	196.1	210.0	197.5	128.0	323.0
Triglyceride	123.4	79.4	7.9	107.7	139.2	105.5	45.0	613.0
LDL	128.8	36.5	3.6	121.6	136.1	130.0	38.0	275.0
HDL	42.9	10.8	1.1	40.7	45.0	42.0	16.0	77.0
Homocysteine	10.9	4.4	0.44	10.1	11.8	10	4	30
MET min/week	1165.6	698.0	69.8	1027.1	1304.1	1070.0	40.0	3600.0
Sedentary time	6.9	2.2	0.2	6.5	7.4	7.0	1.0	11.0

****SD – Standard Deviation, SE – Standard Error***

Anthropometric characteristics

The mean height and weight of the study population were 162.3cm and 67.5kg respectively (Table 1).

Only 16.8% of the study population falls in the normal range of BMI and the mean BMI is 25.5 (Table 1).

Biochemical characteristics

The prevalence of high homocysteine level (more than 15 μ/l) was found to be 34.7% in the study population (Figure 1). The prevalence of low physical activity (less than 600 MET minutes) was found to be 25.7 % in the study population (Figure 2).

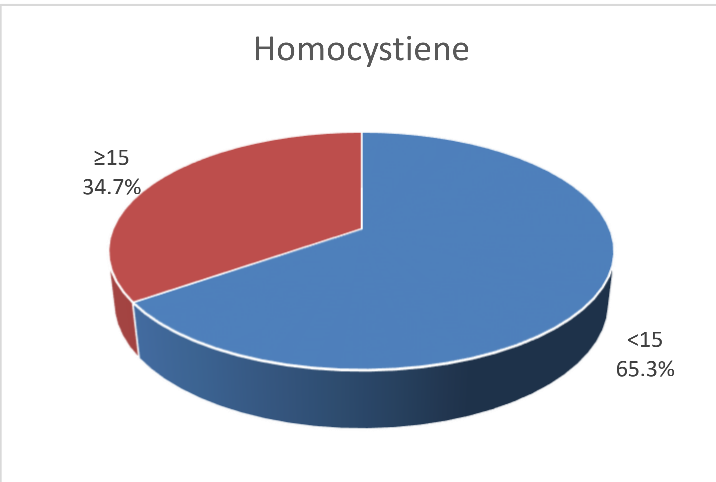

Fig 1: Distribution of homocysteine levels among the study population

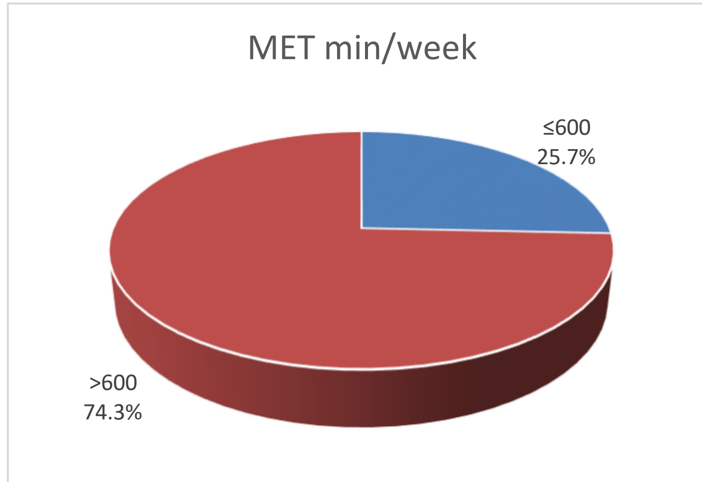

Fig 2: Distribution of physical activity among the study population

Women were more physically active than men (Fig 3). There was a significant association between high homocysteine values and male sex (Figure 4) and smoking (Table 2). The regression model reveals that homocysteine was significantly associated with MET minutes adjusting for age, sex, smoking status and hypothyroidism. A 38% (R^2=0.380) variation in homocysteine was explained by these predictors. The model fitness was good as the ANOVA p<0.05 (Table 3). Also, high homocysteine values were correlated with low physical activity (low MET minutes/week). (Table 4) There was no significant association of homocysteine with other biochemical parameters such as FBS, HbA1c and Lipid profile (Table 4).

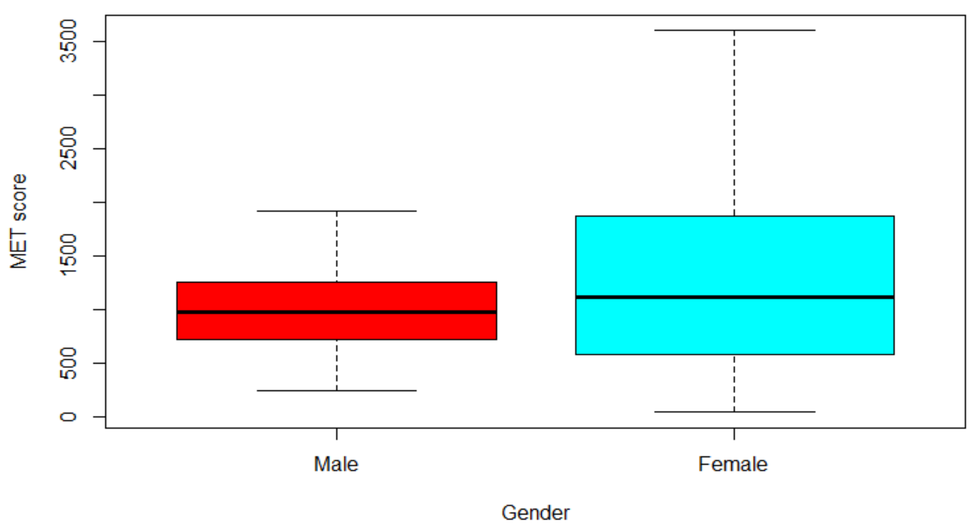

Fig 3: Boxplot diagram describing physical activity according to gender

Lower and upper end of the whisker represents minimum and maximum value of MET minutes/week. The lower border of the box represents the 25th percentile and the upper border of the box represents 75th percentile. The middle horizontal line represents the median value.

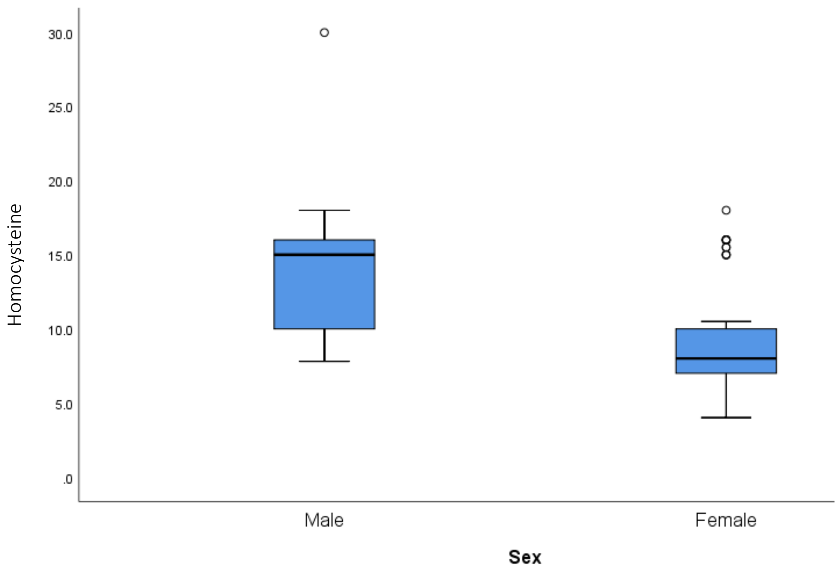

Fig 4: Boxplot diagram describing homocysteine according to gender
Lower and upper end of the whisker represents the minimum and maximum value of homocysteine. Lower border of the box represents the 25th percentile and the upper border of the box represents the 75th percentile. The middle line represents the median value.

Table 2 plasma homocysteine levels by age, sex, smoking status and past medical history

Characteristics		n	Homocysteine Mean	Homocysteine SD	P
Sex	Male	37	14.05	4.24	0.000
	Female	64	9.12	3.35	
Age	≤ 30	12	9.40	4.28	0.15
	31 - 40	52	10.80	4.59	
	41 - 50	20	10.47	4.16	
	>50	17	12.94	3.69	
Smoking	No	95	10.60	3.94	0.003
	Yes	6	16.08	7.71	
Past history of hypothyroidism	No	84	11.07	4.54	0.48
	Yes	17	10.24	3.60	
Past history of hypertension	No	91	10.87	4.49	0.72
	Yes	10	11.40	3.47	
Past history of diabetes mellitus	No	94	11.04	4.45	0.33
	Yes	7	9.36	3.30	

Table 3 Regression model for the estimation of homocysteine with predictors as age, MET minutes/week, smoking and sex

	Unstandardized coefficients B	Unstandardized coefficients SE	Standardized coefficients Beta	T	P
(Constant)	1.676	4.209		0.398	0.69
Age	0.088	0.037	0.184	2.383	0.019
Sex	-1.659	1.05	-0.183	-1.58	0.12
MET min/week	-0.001	0	-0.188	-2.391	0.019
Smoking	2.645	1.521	0.143	1.738	0.08

Table 4 Correlation of homocysteine with other parameters

Correlation of Homocysteine with other parameters	Pearson Correlation r	p
MET min/week	-.280**	0.005
Sedentary time	-0.026	0.79
Age	0.165	0.09
BMI	0.11	0.27
Systolic BP	.249*	0.012
Diastolic BP	.211*	0.034
FBS	-0.113	0.26
HbA1c	-0.074	0.46
Total cholesterol	0.092	0.35
Triglyceride	0.107	0.28
LDL	0.058	0.57
HDL	-0.164	0.101

P<0.05 is significant

DISCUSSION

The study aimed to determine the prevalence of high homocysteine levels and low physical activity among doctors and the relationship between the two. The majority of participants in our study group were physically active and had relatively low homocysteine levels. This finding can be attributed to the predominance of young people in the study population (>50% of the population fell in the age group 31–40 years). We found a significant association between high homocysteine levels and low physical activity. Other studies[14,23] confirm our findings.

The Hordaland Homocysteine Study[24] was the first to demonstrate that plasma tHcy level is inversely related to physical activity. Other studies have demonstrated a dose-dependent reduction in the risk of coronary artery disease with physical activity. This effect cannot be fully explained by changes in other established risk factors.[25] The beneficial effect of physical activity on coronary artery disease risk is probably contributed to by decreased plasma tHcy.[25] Our study demonstrated that plasma tHcy levels are significantly higher in men, which is similar to findings from many previous studies.[24,26,27] This may be explained by the effects of different rates of homocysteine synthesis between the sexes due to larger muscle mass and increased synthesis of creatine phosphate in men, and a lowering effect of the female sex hormone (estrogen).[28] Smokers had significantly higher homocysteine than non-smokers. Several studies[24,29,30] have shown higher tHcy concentrations in smokers. The possible mechanisms for this may be that smoking can cause changes in plasma thiol redox status[31] due to higher formation of reactive oxygen species.[32]

In our study, there was no significant correlation between plasma tHcy and total cholesterol, triglyceride, HDL or LDL. Many Indian[33] and Western studies show similar findings and suggest that homocysteine is not correlated with parameters of Lipid Profile and that it can act as an independent risk factor for cardiovascular disease. There was no significant association between tHcy and FBS or HbA1c in our study, which is different from the findings of a study by Passaro et al on diabetic patients.[34] Although we could not find any correlation between tHcy and BMI, the BMI values were above normal in more than 50% of the study population. This is of great concern considering the age group and ethnicity. Higher body fat percentages and greater abdominal and visceral fat deposition are observed in Asians with the same BMI as Western counterparts.[35] As there is increased cardiometabolic disease risk at an even lower BMI among South Asian populations,[36] India has adopted lower BMI cut-off points.[37] Between 1990 and 2020, the increase in ischemic heart disease (120% in women and 137% in men) in developing countries has been much greater than in developed countries (30% and 60%, respectively).[38] Changes in lifestyles are contributing to the increases in CVD.

Physical activity (MET min/week) was inversely correlated to sedentary time. The mean sedentary time in our study population was 6.9 hours (SD-2.2). Sedentary behaviour is not just physical inactivity by another name: it is defined as any waking behaviour characterized by an energy expenditure ≤1.5 METs while in a sitting, reclining or lying posture.[39,40] Physically inactive is defined as not getting enough physical activity or not meeting physical activity guidelines.[41] According to WHO, physical inactivity is partly due to insufficient participation in physical activity during leisure time and an increase in sedentary behaviour during occupational and domestic activities. Minimizing sedentary time is recommended for promoting health.

CONCLUSION

An elevated level of total homocysteine (tHcy) in the blood is a strong risk factor for atherosclerotic vascular diseases. Physical activity has an inverse relationship with homocysteine level. Doctors' work involves long uninterrupted periods of sitting which may be hazardous to health, contributing to the growing chronic disease burden. Doctors should modify work patterns to include more stretch breaks to have a positive impact on health. Many organizations are now providing stretch breaks in workplaces as a part of combating sedentarism in the workplace. It is also important to impart healthy habits that lower plasma tHcy levels, including the inclusion of naturally vitamin-rich foods in the diet, such fruits and green leafy vegetables, as well as exercise.

LIMITATIONS

The sample size of our study is small. Further studies with larger sample sizes are needed to assess the outcome of increased workplace physical activity.

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