

## PROPORTION OF POSITIVE STRESS TEST IN YOUNGER PATIENTS COMING TO TERTIARY CARE HOSPITAL FOR THE EVALUATION OF ISCHAEMIC HEART DISEASE. ARE WE GOING TO LOSE OUR YOUNGER WORKFORCE?

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<https://doi.org/10.47144/phj.v53i1.1724>

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### Contribution

MTF conceived the idea and designed the study. Data collection and manuscript writing was done by NMAS, KIB, MUK, FAS, MNL, and JAS. All the authors contributed equally to the submitted manuscript.

### All authors declared no conflict of interest.

### This article may be cited as:

Farman MT, Siddiqui NMA, Bhatti KI, Khan MU, Siddiqui FA, Lashari MN, Sial JA. Proportion of Positive stress test in younger patients coming to tertiary care hospital for the evaluation of Ischaemic Heart Disease. Are we going to lose our younger workforce?. Pak Heart J 2020;53(01):45-51.

## ABSTRACT

**OBJECTIVE:** To study the proportion of positive exercise stress test in younger patients coming to tertiary care hospital for the evaluation of ischaemic heart disease (IHD). Our secondary objective was to find out the difference of risk profile between the relatively younger and elderly population having IHD.

**METHODOLOGY:** This descriptive cross sectional study was conducted at cardiology department of a tertiary care centre at Karachi, Pakistan during July 1st 2018 to December 31st 2018 (six months). All adult patients whose exercise tests had been turned positive were selected for the study. Patients with history of arrhythmias, conduction defects, valvular heart diseases, co-morbid conditions like cirrhosis, stroke, osteoarthritis, chronic kidney disease were excluded from the study. The risk factors of interest were hypertension, diabetes Mellitus, smoking, lipid disorders and obesity.

**RESULTS:** Total 85 patients were selected for the study. Out of them, 73 (85.9%) were male and 12 (14.1%) were female. Mean age of our patients was  $56.2 \pm 8.7$  years. Out of 85 patients, 33 (38.8 %) were falling into the category of younger (< 55 years) patients, while elderly ( $\geq 55$  years) patients were 52 (61.2%). In comparison to younger population, diabetes mellitus (34.6 vs 15.2 %; P-value = 0.04) and smoking (23.1 vs 6.1%; P-value= 0.03%) were significantly more prevalent in elderly individuals. Prevalence of Hypertension was slightly higher in younger population (78.8 vs 73.1 %; P-value 0.5) as compare to elderly population. Similarly, younger population were found to be more obese (36.4 vs 28.8 %; P-value 0.4) as compared to elderly population. Prevalence of lipid disorder was almost equal between both the groups (40.4 vs 39.4%; P-value=0.9).

**CONCLUSION:** The burden of Ischaemic heart disease is growing in our younger population and every third of our ischaemic patient is among the younger age group. Although proportion of diabetes and smoking is less common in younger population, trend of hypertension and obesity is on rise.

**KEY WORDS:** Ischaemic Heart Disease, Younger Population, Coronary Risk factors

## INTRODUCTION

Ischaemic heart disease (IHD) remains the primary cause of death all over the world.<sup>1</sup> There is general consensus regarding the need for investigation of symptomatic patients suspected of IHD and subsequent investigation of therapies.<sup>2-3</sup> Evaluating asymptomatic individuals, however, is controversial but potentially allows early detection and more precise risk estimation.<sup>4</sup> Estimating risk in any one individual is important not only for implementation of effective management strategies but also for reassurance and psychosocial security. In some cases, the first presentation of IHD may be myocardial infarction (MI) or in worst case scenario unexpected cardiac death.<sup>5</sup> Evaluation may allow detection of occult IHD prior to such devastating events.<sup>6</sup> Among young men, 34(20%) has been shown to have advanced coronary artery lesions.<sup>7</sup> The Framingham Heart Study demonstrated a rate of MI in men and women between the ages of 30–44 of 51.1/1000 and 7.4/1000 respectively.<sup>8</sup> A higher rate of MI of between 4% and 10% among those aged  $\leq 45$  years was reported in other studies and greater number of them being male.<sup>9-11</sup>

The demonstration of developing heart disease at a young age can be psychologically and economically demanding not only for the individual but also for family members and especially siblings who may fear for their own health. Family history of premature CAD is known to be a risk factor for IHD but is lacking in the widely accepted risk scores.<sup>12-13</sup> The widespread presence of family history of CAD in young MI patients has been reported as high as 64%.<sup>11, 14-15</sup> In the Framingham Offspring Study, presence of sibling CAD increases the risk of a cardiovascular event in young adults by almost two fold.<sup>16</sup> It can therefore be hypothesized that siblings of patients who experience MI at a young age may be at increased risk of asymptomatic CAD and future premature MI. Yusuf et al,<sup>13</sup> demonstrated the significance of family history as a risk factor for MI particularly in young patients. With the help of an effective evaluation tool premature CAD could potentially be identified in these individuals.

The simple exercise treadmill test (ETT) is a mainstay to discover patients suspected of IHD, but it has also been utilized as a screening tool due to the association demonstrated between asymptomatic or silent ischemia and IHD mortality.<sup>17,18</sup> These studies showed the likelihood of a positive ETT to predict the risk of cardiac death.<sup>17-18</sup> IHD is considered to be prevalent in relatively younger age group in south east population but we do not know the exact proportion in our local population. The purpose of this study is to find out the prevalence in our population. Secondly, we want to specifically focus on our younger population because of significant socioeconomic impact from the consequences of IHD in this sub-group. The application of an effective screening strategy to the younger population may lead to

large clinical and social successes due to their increased potential life expectancy.

## METHODOLOGY:

This descriptive cross sectional study was conducted at Dow Institute of Cardiology, Dow University of Health Sciences Karachi. We collected the data of exercise tests performed in our department from July 1st 2018 to December 31st 2018. Data of all adult patients whose exercise tests had been turned positive were selected. Patient's data with history of arrhythmias, conduction defects, valvular heart diseases, co-morbid conditions like cirrhosis, cerebrovascular stroke, osteoarthritis, chronic kidney disease were excluded from the study. The data was collected in predesigned questionnaire. The risk factors of interest were hypertension, diabetes Mellitus, smoking, lipid disorders and obesity.

Numerical data was presented in mean  $\pm$  standard deviation (SD) where categorical presented in frequencies and percentages. Stratification was done in age to determine the association of study variables between young ( $<55$  years) and older ( $\geq 55$  years) age groups. Independent t and chi-square tests were applied as appropriate and  $p \leq 0.05$  was considered statistically significant value. SPSS version-22 was used for analysis.

## RESULTS:

Total 85 patients were selected for the study. Out of them, 73 (85.9%) were males and 12 (14.1%) were females. The mean age of the patients was  $56.2 \pm 8.7$  years. Out of 85 patients, 33 (38.8 %) were falling into the category of younger patients. While elderly patients were 52 (61.2%). In comparison to younger population, diabetes mellitus (34.6% vs 15.2 %; P-value = 0.049) and smoking (23.1% vs 6.1%; P-value= 0.039%) were significantly more prevalent in elderly individuals (Table-3). Proportion of Hypertension was slightly higher in younger population (78.8% vs 73.1 %; P-value 0.552) as compared to elderly population (Table-3). Similarly, younger population were found to have more obese (36.4% vs 28.8 %; P-value 0.468) as compared to elderly population (Table-3). Proportion of lipid disorder was almost equal between both the groups (39.4% vs 40.4%; P-value=0.971). Total exercise time ( $6.2 \pm 2.1$  vs  $5.2 \pm 2.1$  minutes; P-value=0.042) and METS ( $7.3 \pm 2.1$  vs  $6.1 \pm 1.7$ ; P-value=0.004) were significantly higher among younger population that is understandable. Hypertensive hemodynamic response was observed higher among elderly population (21.2% vs 6.1%; P-value= 0.060).

**Table -1: Study demographics and characteristics (n=85)**

Variables	Mean $\pm$ SD / n (%)
Age (years)	56.2 $\pm$ 8.7
Age Groups (years)	
<55 years	33 (38.8%)
$\geq$ 55 years	52 (61.2%)
Gender	
Male	73 (85.9%)
Female	12 (14.1%)
Indication for ETT	
Screening for CAD	78 (91.7%)
Post Intervention Assessment	3 (3.5%)
Post MI Assessment	4 (4.7%)
Hypertension	64 (75.3%)
Diabetes Mellitus	23 (27.1%)
Current Smoker	14 (16.5%)
Obesity	27 (31.8%)
Dyslipidemia	34 (40%)
Medication History	
Beta Blocker	38 (44.7%)
Anti-diabetic	21 (24.7%)
Statins	37 (43.5%)
Aspirin	41 (48.1%)

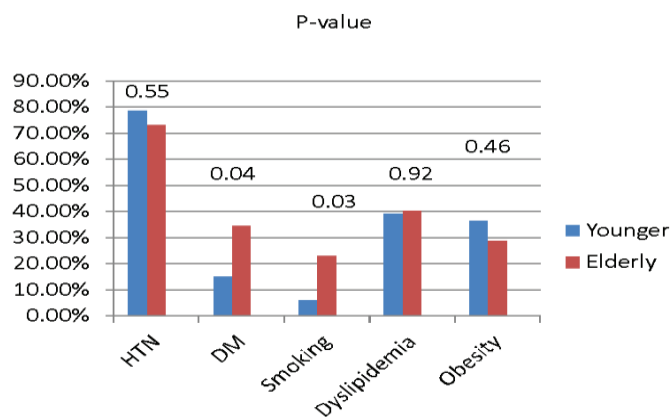
**Table-2 Exercise test findings**

Variables	N (%)
Reason for Exercise Termination	
Fatigue	36 (42.4%)
Chest Pain	33 (38.8%)
ECG Changes	16 (18.8%)
Mean Exercise time (minutes)	5.6 $\pm$ 2.1
Exercise time Groups (minutes)	
<5 minutes	31 (36.5%)
$\geq$ 5 minutes	54 (63.5%)
Metabolic Equivalent	6.6 $\pm$ 1.9
DTS Score	-5.7 $\pm$ 6.2
DTS Groups (score)	
$\geq -11$	20 (23.5%)
-10 to +4	55 (64.7%)
> +4	2 (2.4%)
0	8 (9.4%)
Type of ECG Changes	
Down-sloping	82 (96.5%)
Up-sloping	3 (3.5%)
Hemodynamic Response	
Normal or Adequate	71 (83.5%)
Hypertensive	13 (15.3%)
Hypotensive	1 (1.2%)
Exercise Effort Test	
Good	57 (67.1%)
Poor	28 (32.9%)

**Table -3: Comparison of Study Variables between younger and elder Age Groups**

Variables	Age Groups		P-value
	<55 years n=33; (%)	≥55 years n=52; (%)	
Indication for ETT			0.109
Screening for CAD	32 (96.9%)	46 (88.4%)	
Post Intervention Assessment	0	3 (5.7%)	
Post MI Assessment	1 (3%)	3 (5.7%)	
Hypertension	26 (78.8%)	38 (73.1%)	0.552
Diabetes Mellitus	5 (15.2%)	18 (34.6%)	<b>0.049</b>
Current Smoking	2 (6.1%)	12 (23.1%)	<b>0.039</b>
Obesity	12 (36.4%)	15 (28.8%)	0.468
Dyslipidemia	13 (39.4%)	21 (40.4%)	0.928
Medication History			
Beta Blocker	16 (48.5%)	22 (42.3%)	0.577
Anti-diabetic	5 (15.2%)	16 (30.8%)	0.104
Statin	13 (39.4%)	24 (46.2%)	0.540
Aspirin	16 (48.5%)	25 (48.1%)	0.971
Reason for Termination			0.450
Fatigue	16 (48.5%)	20 (38.5%)	
Chest Pain	13 (39.4%)	20 (38.5%)	
ECG Changes	4 (12.1%)	12 (23.0%)	
Exercise time (minutes)	6.2 ±2.1	5.2 ±2.1	<b>0.042</b>
Metabolic Equivalent	7.3 ±2.1	6.1 ±1.7	<b>0.004</b>
DTS Score	-5.2 ±6.7	-5.9 ±6.1	0.627
Hemodynamic Response			0.060
Normal or Adequate	30 (90.9%)	41 (78.8%)	
Hypertensive	2 (6.1%)	11 (21.2%)	
Hypotensive	1 (3%)	0	

Figure-1: Diabetes and Smoking are significantly higher in elderly population; Dyslipidemia is equivalent; while Hypertension and Obesity is relatively higher in younger population.



## DISCUSSION

Exercise treadmill test is the most widely used test for both the diagnosis and prognosis of Ischaemic Heart Disease.<sup>19</sup> We observed in our study that every third of our patient was young who had positive stress test for myocardial ischaemia (38.8 vs 61.2 %). This is the most alarming situation and we must focus to our younger population to help them out of this potentially deadly disease. We also identified that among the traditional risk factors like DM and Smoking which was although more common among the elderly population (34.6 vs 15.2 %; P-value = 0.04 and 23.1 vs 6.1% ; P-value= 0.03% respectively), other traditional risk factors like Hypertension, dyslipidemia and obesity either equally common or on the rising trend among younger population (Table-3).

The proportion of positive stress test which was 38.8 % in our study is almost similar to other studies conducted in south East Asia like Ahmedabad, Gujarat, India where 40% of patients were found to have positive stress test from the age group 41-50 years.<sup>20</sup> This is understandable if we consider the genotype and phenotype similarities among the population of both the countries along with socioeconomic and cultural similarities.

Moderate-to-severe obesity is an important risk factor for heart diseases, directly or indirectly through involving risk factors, like hypertension, dyslipidemia, and diabetes. Obesity represents one of the most important independent CVD risk factor. Positive association between CVD mortality and BMI has been shown in many large-scale studies.<sup>21</sup> This is a rapidly growing problem that is associated with an increased risk of premature death and causes many detrimental health effects, including CVD. The rising trend of obesity in our younger patients rings the alarm bells to save our younger work force from the deadly disease of IHD. Besides the specific genotype of south East Asian population where central obesity is common, several factors are contributing to obesity like increasing urbanization, sedentary life style, decreasing opportunities of sporting, increasing trends of taking junk foods etc. Obesity has many deleterious effects on cardiovascular function and structure. The total blood volume and cardiac output have been increased in obesity and cardiac workload becomes usually greater.<sup>22</sup> The adipocyte acts as an endocrine organ, and plays a crucial role in the pathogenesis and complications of obesity.<sup>23, 24</sup> Increased levels of leptin, an adipocyte derived hormone that controls food intake and energy metabolism, may be specifically related with cardiovascular disease and has been reviewed in detail elsewhere in the literature.<sup>24, 25</sup> C-reactive protein (CRP) may play a role in the development of leptin resistance, which is important because endogenous hyperleptinemia does not decrease appetite or increase

energy expenditure.<sup>26</sup> Recently, increased concentrations of both CRP and leptin were associated with an increased risk of major CV events, but leptin seems to be a more powerful predictor.<sup>27</sup> In a multivariate version, leptin was an independent predictor of CV events, whereas CRP was not. Clearly, the increase in inflammatory markers is associated with insulin resistance, obesity, and CV events.<sup>25</sup>

The rising trend of hypertension among younger population is another important finding that needs to be addressed. Hypertension attributes to 4.5 percent of the current global disease burden.<sup>28</sup> In Asian urban adult populations, the prevalence of hypertension has shown an upward trend, and at present varying between 15-35 percent, with hypertension and stroke occurring at a relatively younger age.<sup>29</sup> Young adults have been considered to be lower risk in their development of hypertension, with resultant gaps in the literature on hypertension which typically target older adults and the elderly. The widespread presence of hypertension among younger individuals, however, is on a constant rise. This may be attributed to several factors such as considerable changes in lifestyle and stress patterns, improved recognition rates due to better screening,<sup>30</sup> and a high prevalence of metabolic and dietetic coronary risk factors among adolescents of the middle- and upper-middle class.<sup>31</sup> Whatever the case may be, the higher prevalence of this major coronary risk factor among younger population is a harbinger of increased incidence of Coronary artery disease in near future. Hence, health authorities, health care professionals and civil society should create awareness at mass level and must focus on preventive side so that these deleterious risk factors can be controlled among general and specifically younger population.

In summary, our study shows the growing prevalence of ischaemic heart disease in our younger population. Rising prevalence of hypertension and obesity may be the most important and differentiating contributing factors. While addressing this growing issue and making effective strategies to control the hypertension and obesity in younger population, we also have to investigate the other novel risk factors among younger population.

## LIMITATIONS

Being a single arm study the cause and effect cannot be determined as exposure and outcome measured at the same point in time. Secondly, it's a single centre study therefore the results cannot be generalized to general population. Moreover, the sample size was small, so more studies with a larger sample size and analytical design studies are required to validate the findings.

## CONCLUSION

The burden of Ischaemic heart disease is growing in our

younger population and every third of our ischaemic patient is among the younger age group. Although proportion of diabetes and smoking is less common in younger population, trend of hypertension and obesity is on rise. However larger randomized studies on national level are required to assess the exact magnitude of the problem.

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