

# A COMPARATIVE ANALYSIS OF BODY FAT PERCENTAGE AND INCIDENCE OF ESSENTIAL HYPERTENSION AND TYPE-2 DIABETES MELLITUS IN A VEGETARIAN AND NON-VEGETARIAN POPULATION

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## ABSTRACT

**Background:** Obesity is identified as a complex multifactorial disorder and a notable growing global problem. Body fat percentage (BFP) is more reliable method as compared to BMI for assessing the risk of developing disease. Essential hypertension and Type-2 diabetes mellitus are both associated with adiposity.

**Aims & Objective:** In this study, we planned to observe the association, if any, of raised BFP levels in strict-vegetarians and comparatively analyzed with non-vegetarians in context to the indicated diseases.

**Materials and Methods:** After getting approval from ethical review committee of the Aga Khan University for this Random, Cross sectional and population based study, 563 subjects were selected randomly (males 295, females 268, strict-vegetarians n= 324 (58.0%), non-vegetarian n=235 (42.0%) in 2012 from Tharparker, Pakistan. We recorded demographic and anthropometric data, presence of blood pressure, type-2 diabetes mellitus and co-morbidities. Analysis of BFP was carried out by Deurenberg formula. Level of BFP >20 in males and > 25 in females was taken as raised/abnormal. Data was analyzed descriptively and categorically by using SPSS-21 for comparative analysis of prevalence of the essential hypertension (EHTN) and Type-2 Diabetes Mellitus (T2DM). Comparative analysis of association of raised levels of BFP was carried out in context to EHTN and T2DM in vegetarian and non-vegetarian population. A p-Value of < 0.05 was considered significant.

**Results:** Vegetarian subjects, n= 324 (58.0%), showed minimum age as 15 years; maximum 82 (mean 39.6, Std. Deviation 16.6). Non-vegetarian subjects, n= 235 (42.0%), had minimum age 10 years; maximum 76 years (mean 33.7, Std. Deviation 15.5). More male subjects had raised BFP (270 = 94.7%) than females (129 = 49%), p-Value 0.000. Despite positive association of raised BFP levels with EHTN and T2DM, the comparative analysis of association of raised BFP levels among the vegetarian and non-vegetarian cohort in relation to both EHTN and T2DM showed non-significant p-Values (0.105 and 0.347 respectively).

**Conclusion:** Raised body fat percentage in the strict-vegetarian and non-vegetarian cohorts showed a non-significant association to produce essential hypertension and type-2 diabetes mellitus. Findings point to some other risk factors which could be responsible to produce the disease in the studied cohorts. Doing exercise and reducing caloric intake is strongly advised as the best measure to maintain a normal phenotype.

**Key Words:** Body Fat Percentage; Deurenberg Formula; Essential Hypertension; Type 2 Diabetes Mellitus; Vegetarian; Non-Vegetarian

## Introduction

The value of body fat percentage (BFP) over 20 in the males is considered as above normal/raised, in the females this level is considered normal up to 25. Other than adipose tissue, skeletal muscle mass is the largest adult body compartment. The subject variability in muscularity is often cited as a reason for the non-specificity of BMI.<sup>[1-5]</sup> The prevalence of obesity is increasing progressively<sup>[6]</sup> and it is identified as a complex multifactorial disorder and a growing global problem. It has reached at its epidemic level worldwide, affecting more than one billion adults identified as overweight, with at least 300 million being obese.<sup>[7]</sup>

In the developing countries the incidence of such conditions is increasing at an alarming state. This is due to an increased income and progressive urbanization

trend.<sup>[7,8]</sup> Overweight and obesity are well known causative factors for the genesis of co-morbidities like type 2 diabetes, hypertension, cerebrovascular accidents and osteoarthritis etc. Apart from health related physical, psychological and social problems in the society, the obesity carries 2% to 7% of total health care cost.<sup>[7,9]</sup> The burden of related disorders, including cerebrovascular and cardiovascular diseases, makes the morbidity and mortality of hypertension highest among all diseases. Coronary artery disease is also a notable cause of morbidity and mortality in Americans, South Asians and African Americans.<sup>[10]</sup>

There are a large number of techniques available for the assessment of body fat percentage, but many of these techniques are not applicable in epidemiological studies for various reasons.<sup>[11-13]</sup> Unfortunately, the most accurate techniques such as densitometry, isotope

dilution or dual energy X-ray absorptiometry (DXA) are expensive and/or need specific skill of the operator and/or adequate cooperation of the subject.<sup>[14]</sup> The calculation of the body fat percentage by using Deurenberg formula is quite reliable method in the epidemiological and clinical studies. This method utilizes the weight-height index, age and sex of the subject in its formula and requires minimum expenses and equipment.<sup>[15]</sup>

Essential hypertension (EHTN) is a complex, multifactorial and polygenic disorder. EHTN and other cardiovascular diseases are associated with progressively increasing morbidity and mortality all over the globe.<sup>[16]</sup> In the US alone, 50 million people are under treatment for elevated blood pressure.<sup>[17]</sup> EHTN is very common worldwide with 972 million cases. In 2000, hypertension affected 26.4% of the adult population.<sup>[18]</sup> It is expected to increase by about 60%, up to 1.56 billion by 2025.<sup>[17]</sup> An estimated 7.1 million deaths per year are attributed to hypertension worldwide.<sup>[19]</sup>

Prevalence of hypertension is reported with variance around the world. It is lowest in the Indo-Pak subcontinent (rural India, 3.4% in men and 6.8% in women) and the highest in Poland (68.9% in men and 72.5% in women).<sup>[20]</sup> The mortality rates from coronary arterial disease in South Asians are reported to be two to three times higher than those in Caucasians irrespective of gender, religion, social class, dietary practices or country of residence.<sup>[21,22]</sup>

Although lack of preventative measures contribute toward the high incidence of EHTN, yet in some ethnicities and sub-ethnicities these factors appear to be insignificant suggesting that a particular genetic makeup of individuals may be favouring the diseases. For example, South Asian migrants to the UK are found to have a higher incidence of coronary artery disease than the Western population.<sup>[23]</sup>

According to the last National Health Survey of Pakistan, every third person over the age of 45 years was hypertensive and only 3% of all persons classified as hypertensive had blood pressures below 140/90 mmHg.<sup>[24]</sup> Hypertension and dyslipidaemia cluster more often than any other common cardiovascular diseases, i.e. myocardial infarction, congestive heart failure and stroke.<sup>[25]</sup> South Asians and US populations are found related to a higher prevalence of metabolic syndrome which has become increasingly common among them.<sup>[26,27]</sup>

Notable factors in development of EHTN are calorie excess (as manifested by obesity), high salt intake, low potassium intake, decreased physical activity, heavy alcohol consumption and psychosocial stress.<sup>[28]</sup> Health status of teenagers is progressively at an alarming state due to cigarette smoking, obesity, sedentary lifestyle, computer related entertainments and decreased participation in physical activity programs.<sup>[29-31]</sup> Present day strategies towards decreasing hypertension and thereby decreasing the cardiovascular diseases emphasize awareness and practice of non-pharmacological interventions especially physical activity and exercise.<sup>[32]</sup>

It is observed that exercise decreases blood pressure in about 75% of hypertensive individuals. Women may decrease more blood pressure by exercise than men. There are data from different world regions to support this aspect viz. Asian and Pacific Island patients reduce more blood pressure with exercise than Caucasian patients.<sup>[33]</sup> These findings show that the effect of exercise appears to be controlled genetically.<sup>[33]</sup> With exercise, patients also improve other important parameters like lipoproteins and lipid levels as well as insulin sensitivity. There is also evidence of exercise induced improvement of left ventricular hypertrophy in hypertensive subjects and thereby prevention to develop myocardial infarction.<sup>[33]</sup>

In this study, our main aim was to compare the elevated body fat percentage levels in the strict-vegetarian and non-vegetarian cohorts in context to the presence of essential hypertension and type-2 diabetes mellitus. To achieve this aim we carried out this study based on the objectives for observing the subjects with the normal and raised levels of the body fat percentages, prevalence of normotensives and hypertensives; and the normoglycemic and diabetics in both cohorts.

## Materials and Methods

After getting an ethical approval from the Ethics Review Committee (ERC) of the Aga Khan University (AKU), Karachi, we carried out preliminary visits to Tharparker to recruit the subjects. The consent form was approved by AKU-ERC and was explained and distributed to the subjects. We included known hypertensives and newly diagnosed hypertensives as cases and normotensive individuals as controls.

A signature of the participant was obtained while a thumb impression was used in case of the illiterate

participants. In case of children, guardian's signature or thumb impression was also obtained. This study was carried out at Tharparker, Sindh, Pakistan (location: 24° 42' 0" North and 70° 11' 0" East coordinates) during 2012.

This area was selected because it is quite famous historically for strict-vegetarian population. The strict-vegetarians in this case due to social and religious reasons did not consume eggs, fish, sea foods and meat of any kind since birth. They practice this trend since historic past. This area has people who consume non-vegetable diet also. Exclusion and inclusion criteria were set.

We included individuals from both genders i.e. males and females from 10 years to 82 years of age. We recruited the lower age group down to 10 years so as to look at the presence of hypertension in the young age group. Due to electronic age the children have sedentary life style and play computer games rather than playing games physically. Due to modern trend of eating baked items, creamed chocolates, ice cream, soft drinks and cakes, this age group is also liable to grow overweight.

We excluded the subjects below 10 years of age due to lack of cooperation because of small age group and due to the less incidence of hypertension. We excluded all the subjects who were not willing to continue study and who showed non-compliance. We recruited subjects from both the populations and recorded the demographic and anthropometric data, presence of essential hypertension (EHTN) and co-morbidities (i.e. diabetes, stroke and ischemic heart disease).

We carried out a population based, random and cross sectional study. Total N= 563 subjects (295 males and 268 females) were selected randomly – after screening, n= 324 from vegetarian population and n= 235 from non-vegetarian population i.e. a total of 559 subjects were finally taken in the study. We studied 559 subjects instead of 563 due to unavailability of the responses as to whether they are strict-vegetarians or non-vegetarians although the blood pressure and other variable data were available.

Sample size was calculated statistically with confidence level of 95% by assuming 20% prevalence of hypertension among our study population; and we have also incorporated 10% design effect in sample size. We performed analysis for prevalence of EHTN in the total population and calculated the prevalence of EHTN in

both cohorts. We calculated the body fat percentage by using the Deurenberg formula for both sexes and performed a comparative analysis of the association of the vegetarian diet and non-vegetarian diet with the EHTN and T2DM.

We recorded height, weight; and the blood pressure by taking three blood pressure measurements from the left arm at 15-minute intervals in the resting state from each participant. Any individual with systolic blood pressure >140mmHg and diastolic blood pressure >90mmHg on all the three occasions was diagnosed and labelled as hypertensive.

The subjects were labelled as normo-glycemic or diabetic by taking past history and looking at the clinical and the lab investigation reports and the physician's consultation files. The levels of the fasting sugar > 110mg/dL and the two hours post prandial random blood sugar levels > 180mg/dL were considered abnormal/raised. The fasting sugar levels between 110mg/dL and 125mg/dL were considered as pre-diabetic and the fasting glycaemia > 125mg/dL was taken as a definite case of diabetes mellitus.

Calculation of the BMI were done by using the formula given in WHO Website for Global Database on BMI viz.  $BMI = \text{weight in Kg} / \text{Height in meter squared}$ . Body fat percentage calculation was carried out by using Deurenberg Equation obtained from e-Medicine Endocrinology website:  $\text{Body fat percentage (BFP)} = (1.20 \times BMI) + (0.23 \times \text{Age}) - (10.8 \times \text{gender}) - 5.4$ . The Sex Codes used were: M = 1, F = 0. The values of body fat percentage >20 in males and >25 in females were taken as above normal or raised.

For each of the indicated strategies, the data was analyzed descriptively and categorically by using the statistical software SPSS-21. Similar variables were grouped to facilitate the out puts and to ease out correlation with status of hypertension and T2DM. Association of raised body fat percentage with the essential hypertension in both cohorts (i.e. vegetarians and non-vegetarians) was tested. Chi squired p-values < 0.05 were considered significant.

## Results

After getting the approval from the Aga Khan University's ethical review committee (ERC), the recruited 563 subjects for this study displayed (males 295, females 268) from the Non-vegetarian and strict

Vegetarian population. From 559 screened subjects, we took n= 324 (58.0%) from vegetarian population and n= 235 (42.0%) from non-vegetarian population, p-Value 0.179 (Table 1). The minimum age in case of vegetarian subjects was 15 years; maximum 82 (mean 39.6, Std. Deviation 16.6). The minimum age in case of non-vegetarian subjects was 10 years; maximum 76 years (mean 33.7, Std. Deviation 15.5).

Out of 548 studied subjects, majority of individuals were found to have the raised levels of BFP i.e. 399 (72.8%), (Table 2). More male subjects had raised BFP 270 (94.7%) than females 129 (49%), p-Value 0.000 (Table 1). More female subjects were found to have normal BFP levels 134 (51.9%) as opposed to males 15 (05.3%), (Table 1). The comparative analysis of the normal and raised levels of BFP among the vegetarian and non-vegetarian cohort generated a non-significant p- Value (0.427), (Table 1).

Comparative analysis of prevalence of essential hypertension in the vegetarians and non-vegetarians with the status of BFP values was carried out. The entire population of N= 563 subjects showed the incidence of EHTN as 81 (14.4%). Vegetarians affected with EHTN were n= 40 (12.3%) as opposed to non-vegetarians affected with EHTN n= 40 (17.0%), p-Value 0.119, (Table 3).

Although generally, it was found that the raised levels of BFP were more associated with essential hypertension viz. more males had raised BFP levels 39 (14.4%) as compared to males with normal BFP 00 (00.0%), p-Value 0.126, (Table 4); similarly, more females had raised BFP levels 34 (87.2%) as compared to females with normal BFP 05 (12.8%), p-Value 0.000, (Table 4). But, when the comparative analysis of vegetarian versus non-vegetarian cohorts with the association of raised BFP status in context to EHTN was carried out, it generated non-significant p-Values (0.105), (Table 3).

Similarly the raised values of the BFP were positively associated with type-2 diabetes mellitus. But comparative analysis for the presence of the diabetes mellitus among both the vegetarian and non-vegetarian cohorts with raised BFP also gave a non-significant p-Value of 0.347, (Table 3).

We also studied the stratification of the other co-morbidities showing almost matching prevalence among the vegetarian and non-vegetarian cohorts. It was found

that in n= 557 subjects 57 (10.2%) were positive for asthma, vegetarian asthmatics were 38 (11.9%) as opposed to non-vegetarian asthmatics 19 (8.1%). Out of 234 subjects, a positive history of stroke was obtained in 04 (0.7%) subjects, vegetarians with stroke 3 (0.9%) and non-vegetarians with stroke 01 (0.4%).

**Table-1: Basic variables related to the vegetarian and non-vegetarian cohorts, (N=559\*, Males = 293, females = 266)**

Characteristics			p-Value
	Veg.	Non Veg.	
Participants	324 (58.0%)	235 (42.0%)	0.179
BFP in Veg & Non-Veg.	Veg.	Non Veg.	
(<20 / <25)	83 (25.9%)	65 (29.0%)	0.427
(>20 / >25)	237 (74.1%)	159 (71.0%)	
BFP Gender wise	Males*	Females*	
(<20 / <25)	015 (05.3%)	134 (51.9%)	0
(>20 / >25)	270 (94.7%)	129 (49.0%)	
EHTN Gender wise	Males	Females	
Yes	40 (13.6%)	41 (15.3%)	0.557
No	255 (86.4%)	227 (84.7%)	
T2DM Gender wise	Males	Females	
Yes	23 (7.8%)	18 (6.7%)	0.615
No	270 (92.2%)	249 (93.3%)	

\* Disparity in matching with total number is due to missing values; BFP: Body Fat Percentage; EHTN: Essential Hypertension; T2DM: Type-2 Diabetes Mellitus; Veg: Strict-vegetarian; Non-Veg: Non-vegetarian

**Table-2: Distribution of Body Fat Percentage (BFP) as Normal and Raised in the studied population**

Body Fat Percentage (BFP)		Frequency	(%)
Total Population N=548*	Normal**	149	27.20
	Raised***	399	72.80
Total Males N=284	Normal**	15	5.30
	Raised***	270	94.70
Total Females N=263	Normal**	134	51.00
	Raised***	129	49.00
Non-vegetarian N=224*	Normal**	65	29.00
	Raised***	159	71.00
Vegetarian N=320*	Normal**	83	25.00
	Raised***	237	74.10
Vegetarian Males N=159*	Normal**	6	3.80
	Raised***	153	96.20
Vegetarian Females N=161*	Normal**	77	48.00
	Raised***	84	52.00
Non- vegetarian Males N=123*	Normal**	8	6.50
	Raised***	115	93.50
Non- vegetarian Females N=100*	Normal**	56	56.00
	Raised***	44	44.00

\* Disparity in matching with total number is due to missing values among various strata; \*\* Normal: <20 M & <25 F; \*\*\* Raised: >20 M & >25 F

**Table-3: Analysis of prevalence of essential hypertension and type-2 diabetes mellitus in normal and raised status of body fat percentage (BFP) in vegetarian and non-vegetarian subjects**

Body Fat Percentage		Vegetarians		Non-vegetarians		p-Values
		Total N (%)	Affected N (%)	Total N (%)	Affected N (%)	
EHTN	Normal**	83 (100)	02 (2.4)	65 (100)	04 (6.2)	0.252
	Raised***	237 (100)	37 (15.6)	159 (100)	35 (22.0)	0.105
	Total*	324 (100)	40 (12.3)*	235 (100)	40 (17.0)*	0.119
DM-2	Normal**	82 (100)	02 (2.4)	65 (100)	00 (0.0)	0.205
	Raised***	236 (100%)	20 (8.5)	159 (100)	18 (11.3)	0.347
	Total*	321* (100)	22 (6.9)	235 (100)	18 (7.7)	0.716

\* Disparity in matching with total number is due to missing values among various strata; \*\* Normal: <20 M & <25 F; \*\*\* Raised: >20 M & >25 F

**Table-4: Gender distribution of essential hypertension in normal and raised status of body fat percentages (BFP) in total population (N=547\*)**

Variables	Total N (%)*	Affected N (%)	p-Value
Males with BFP < 20	14 (4.9%)	00 (0.0%)	0.126
Males with BFP > 20	270 (95.1%)	39 (14.4%)	
Females with BFP < 25	134 (51.0%)	5 (12.8%)	0
Females with BFP > 25	129 (49.0%)	34 (87.2%)	

\* Disparity in matching with total number is due to missing values among various strata

## Discussion

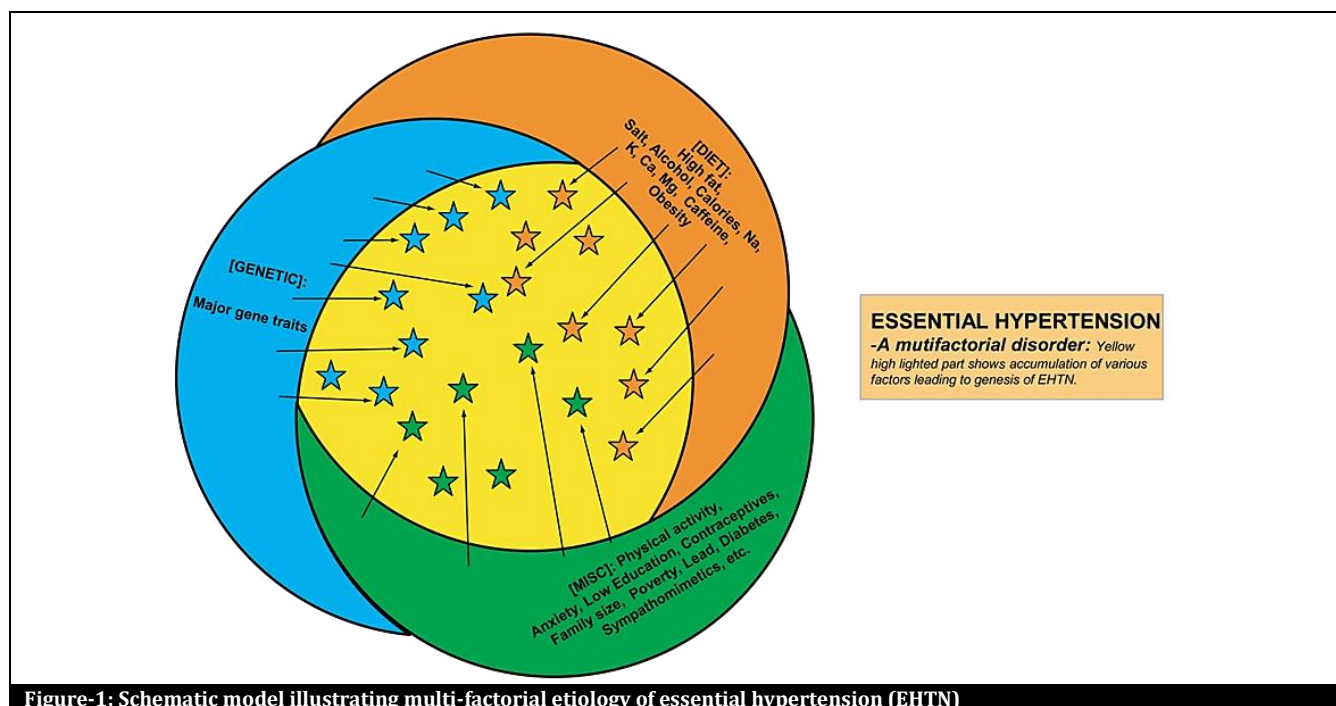
The obesity is associated with increased risk of diabetes, hypertension, heart disease, stroke, cancer, dyslipidaemias, liver and gallbladder disease; sleep apnoea and respiratory problems, osteoarthritis, abnormal menses and infertility.<sup>[34]</sup> With increasing age, the prevalence of overweight and obesity is also increasing in elderly people who, as expected, are more prone to diseases.<sup>[35]</sup> The clinical detection of obesity is of immense importance due to these reasons as well as due to its psycho-social, national health and cost perspectives in patient care related to the management of its complications.

Most common method of detection of obesity is through usage of height and weight parameters because it is convenient, safe and cheaper, despite that it does not distinguish lean body mass from fat mass.<sup>[36]</sup> The BMI calculation formula is quite old as it was developed about 200 years ago by Quetelet and it does not measure the adiposity, hence it is a kind of an imprecise mathematical

estimation of the body mass index.<sup>[37-43]</sup> The assessment of body composition (i.e. mainly the body fat percentage) by using height and weight parameters, age and sex data through Deurenberg formula provides more accurate estimates.

The BMI has been mentioned usually as a sensitive parameter to assess the risk of morbidity and mortality; but BMI by itself has less significance than the body fat percentage because it is the amount of fat itself which is more related to mortality and morbidity. Moreover, the young male and female adults may have the similar values of BMI as those observed in older subjects so the body fat percentage is more reliable indicator and notable risk factor as compared to BMI.<sup>[44]</sup> Relative obesity increases with advancement in age but, the underlying mechanisms for this are not yet fully understood.<sup>[45]</sup>

As the greater fat content with the old age carries the risk of morbidity and mortality, so now the experts are of the opinion that measurement of the body fat percentage is more important for the assessment of such risks than the BMI alone. The biochemical parameters indicating the deranged lipid values are more important for the therapeutic intervention to reduce the risk of morbidity and mortality. But the body fat percentage values are also considered as notable and important indicator for the subjects to start earlier voluntary weight reduction programmes to avoid the indicated risks.



**Figure-1: Schematic model illustrating multi-factorial etiology of essential hypertension (EHTN)**

This way, the subjects can prevent themselves till genesis of dyslipidaemias needing actual commencement of medication. The values of the body fat percentage > 20 in males and > 25 in females are considered as values above normal. The values of body fat percentage to be defined as cut off particularly for obesity are > 25 for males and > 30 for the females. These values are clinically significant for commencement of therapy if the lipid profile values are also simultaneously deranged. There is an immense role of exercise to reduce the weight yet, a moderate reduction of calories is even more important to get a significant weight loss. More intakes of cold water and adequate sleep daily are other methods believed to achieve weight reduction.

Primary or Essential Hypertension (EHTN) comprises 95% of total cases of hypertension. In these cases, no obvious cause is identified. Due to this aspect, EHTN is said to result from complex interactions between multiple genetic and environmental factors (Figure 1). Onset of primary or essential hypertension is not common before 20 years of age. It commences usually between 25 and 55 years. Present accepted view about the origin of essential hypertension is attributed to its multifactorial and polygenic nature. Etio-pathogenesis of EHTN encompasses combined effects of genetic factors (nature) and many environmental factors (nurture) to get elevated blood pressure.<sup>[46]</sup>

Hypertension and atherosclerosis are associated with the inflammatory mechanisms operating at the intima of vascular walls. The c-reactive proteins (CRP) are indicators of inflammatory process operating in the body. They are synthesized in the liver and the complexed-CRP activates complement to initiate opsonization and phagocytosis of invading cells. Their main function is to detoxify endogenous toxic substances produced as a result of tissue damage.<sup>[47-49]</sup>

With respect to inflammation and cardiovascular disease, pro-inflammatory cytokines raise markers such as C-reactive protein, increase coagulation and also cause an unfavorable lipid profile of a peculiar form, with decreased total cholesterol, decreased HDL cholesterol, and increased triglycerides.<sup>[50-53]</sup> It becomes mandatory to explore various populations affected by the raised body fat percentage and obesity. For the people with overweight, high body fat percentage and obesity, it is highly indispensable to follow various means to reduce the bodyweight.

Essential hypertension (EHTN) and adult onset diabetes (T2DM) both have multifactorial etiologies, so we were interested to look at the role of strict-vegetarian diet to prevent these diseases in this population. In this study, it was generally observed that the raised status of the body fat percentage was positively related with both EHTN and T2DM. But; when the vegetarian and non-vegetarian cohorts were comparatively analyzed it manifested a non-significant p-Value. This indicates that in the studied cohorts there are some other etiological factors which are at work in producing the pathological traits.

In our previous publications, we indicated that the effect size of the genetic component (worked up for the serene threonine kinase-39 single nucleotide polymorphism rs35929607) had least involvement in elevating blood pressure in this population. All of these findings point up to a greater cumulative role due to other environmental factors to cause blood pressure. In the studied population, such factors might be sedentary life style, not doing exercise, consuming more calories in diet etc. On clinical examination and history taking from the vegetarian cohort it was noticed that the male and female members of this group were neither found practicing exercise nor had developed habit of daily walking.

Moreover, consumption of fried and baked items was also a common finding in this community. This shows that although these individuals had restricted themselves to consume the vegetarian diet they manifested more body fat percentage (74.0%) as compared to non-vegetarians (70.1%). These findings clearly point up to the exposure of other environmental risk factors. Although these subjects are strict-vegetarians yet they were not benefitted from that diet until or unless they change their life style and the pattern of food from high to a low caloric value.

Looking at the findings obtained from both of these cohorts, two things should be noted with an obviously great importance i.e. doing exercise and curtailing the caloric intake to moderate levels for achieving a normal and healthy phenotype. In future, it is important to look at the effect of sedentary versus active life style and doing or not-doing exercise in this population; and this data needs to be analyzed to see the prevalence of essential hypertension, cardiovascular diseases and comorbidities in both the cohorts.

## Conclusion

A comparative analysis of prevalence of essential hypertension (EHTN) and type-2 diabetes mellitus in the strict-vegetarian as opposed to non-vegetarian cohorts in context to the raised body fat percentage showed a non-significant association indicating some other risk factors to be responsible for producing these diseases in the studied population.

Generally, the raised levels of body fat percentage manifested a positive association with EHTN and T2DM. It is recommended that performing exercise and reducing the caloric intake to moderate levels are strongly indicated to acquire cardio-protection and a healthy phenotype.

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