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In Memoriam, Salvador Sanchez Alfonso De La Pena, MD, PhD: A Comrade in the Chronousphere (November 14, 1948 - November 2, 2011)

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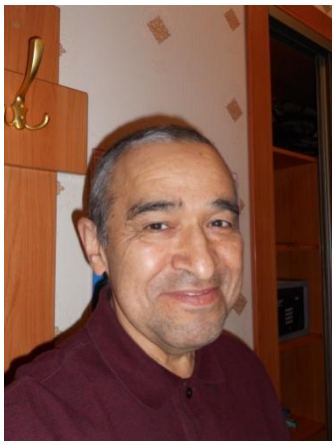
Salvador A. Sánchez de la Peña



Graduated from the National Autonomous University of Mexico (UNAM), September 18, 1973

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Director of Medical Chronobiology Laboratory, 1998-2011

Editor, Revista Internacional Bilingüe: GERONTO-GERIATRICS

Comments by his American mentor and some of his close associates:

It seems that there are no better words to remember Salvador than those written by the Lord of Time - Dr Franz Halberg: For members of the BIOCOS worldwide, including Minnesota friends, Salvador remains an integral part of what we do. After Mexico City, Minnesota was his second home, whether he enthusiastically described what he did to Earl E. Bakken, the developer of the implantable cardiac pacemaker or analyzed data from an Italian woman isolated from society for over 100 days, to find what Earl had described as "free-running". His real home, of course, was and remains worldwide and beyond, the sphere of the human mind, what Edouard Le Roy, Pierre Teilhard de Chardin and above all Vladimir Ivanovich Vernadsky called the noösphere, the sphere of human creativity, complementing Eduard Suess's (the Viennese geophysist) biosphere. Salvador helped take us a step beyond the noösphere by examining both the basic rules and their applications. These were steps toward introducing time (chronos) into the noösphere. By seeking new transdisciplinary cycles to quantitatively assess the otherwise qualitative noosphere, we can measure, apparently for the first time in statistical inferential terms, the domain of the human mind by its mood and its creativity, manifested in the occurrence at about 500-year intervals of prominent historians, poets, and physicians. In classical Greek, "noos" and "nous" both describe the human mind; the Attic Greek "nous" serves to portmanteau it into "chronos", time, and "sphairos", sphere, into a chronousphere. On the basic side, Sal's enthusiasm and his stamina supporting his inquiry into the unknown laid the basis of a time-qualified feedsideward (rather than time-unqualified feedback) in the pineal-hypothalamic-pituitary-adrenal-cellular network first and in the cosmos next. His last contributions were data for examining the role of the cosmos in modulating human blood pressure.

Whatever anybody does in time, by selecting a partial system from the universe for investigation, he/she has to consider contributions by the complementary system of the cosmos and may best account for the latter's cycles. Sal showed that the same dose of the same molecule can enhance or delay the development of a malignancy. He contributed many research articles on chronooncology (e.g., 2-9). His publications assure him a lasting place in science and health care through which he will continue to contribute second to none (1-182). May the premetabolic syndrome, on the applied side be his legacy's highlight (179-181).

Dr. Wilson: Salvador was a steadfast friend who believed in the warmth of friendship. Sal gave his all to those that knew him. He was a shining light that guided us with his happy enthusiasm, visionary chronobiological thinking and his exemplary work ethos and energy.

In the last 12 months, he co-authored an important classic article that has been accepted for publication (1) and he made contributions to presentations in Moscow and earlier in Taipei. He lives in and beyond the noosphere. We will always think of him as a great friend and his parting is a great loss. I knew him for the last 30 years, planned great adventures with him in Mexico on premetabolic syndrome in children and adults and somehow these should be kept alive.

Dr. Sothern: it was truly with great sadness and shock that I learned of Salvador's passing earlier this November. Even though many of us had been in touch quite often over the past several years about mutual research interests, most of us had absolutely no idea that he had a recurrence of non-Hodgkin's lymphoma and was undergoing treatment with cis-platinum that irreparably damaged his kidneys. In an October 15 email from him Sal wrote that he was collecting patient data. He mentioned being in the hospital, but didn't say why, so I assumed something routine (like when he broke his arm in Sept 2010 or wrote in May 2010 that he had some health problems in April 2010 but was better). It was wrong to assume there was nothing to worry about with his recent hospitalization. I did not know about his life-threatening illness.

Sal and I were friends since his days in the late 1970's and into the 1980's in Minnesota in the Chronobiology Laboratory of Franz Halberg and we continued to stay in touch as he followed Bill Hrushesky to Albany, New York and later returned to Mexico City in the 1990s to continue his medical and research career. He was always such an interesting character, always optimistic with grand ideas, a gracious attitude in the face of great pressures, and

eager to engage in as much research as possible, including editing his "modest" (his word!) "International Journal of Geronoto-Geriatrics", serving as a reviewer for several international journals, and collaborating with so many others around the world on research projects.

Along these lines, in July of this year we published a paper together, which may be his last as a first author, but the first (we think) to combine the areas of homeopathy and chronotherapy (chrono-homeopathy), two areas that he was passionate about that each continue to generate a certain amount of skepticism (182). We were very pleased to find a rhythmic aspect of aconite's effect of mouse body temperature and were hoping that this would be of interest to others in the field of homeopathy (i.e., timing is everything, but is still widely overlooked in most fields).

As recently as October of this year, Sal mentioned that all the research that he was tirelessly planning to do and/or had already started, including monitoring heart patients who received homeopathy treatment with aconite, and measuring clock genes in these and cancer patients. Of course he had many, many other research interests, including chronomics and the premetabolic syndrome, for which he was honored with lifetime achievement awards for excellence in medicine and health applications by the International Organization for Medical Teaching and Research for all of Latin America, Central America and the Caribbean that he received in Bogota, Colombia in November 2010. He was very happy to receive this recognition and was eager to push forward with his pursuits. Sadly, this was not to be.

With a heavy heart, but a smile from having known such a nice person, my sympathy goes out to all who knew and cared about Sal, including his children Sal Jr. and Amaranda, and Elizabeth, their mother. ”Dost thou love life? Then do not squander time, for that's the stuff life is made of." Benjamin Franklin (1706-1790). Cand. Med. Rito was his student and collaborator for the last 5 years and was very useful in the setting of the Research Laboratory on Chronomics, a critical step beyond Chronobiology since the cosmos, part of chronomics and the chronousphere, is the ever-present control for whatever is being done in time.

Germaine (Professor Cornelissen) and her husband, Francis (Dr Guillaume) to his son: Please accept our heartfelt condolences. We lost a great friend with the passing of your father. Salvador came to the lab soon after I joined Franz's lab, so our friendship dates a long time. We had a very close cooperation not only when we were on the same team but also after he left.

We learned the sad news yesterday but even today it is hard to realize that this was the last good-bye. Your father came to the lab shortly after I did and we shared many fond memories of hard work at the lab and great discussions, excitement at findings that came almost everyday thanks to the hard work of Sal. We traveled to meetings together, eager to present our results and meet new friends who came from the four corners of the world. His mother came to visit him in Minnesota as did my parents, a small family away from home. I can still remember how proud your father was when you were born. And he remained proud of you over the years as you grew up and became the handsome man we saw in the pictures of your wedding. Whereas nothing can replace your father, his legacy will live on.

There were several ongoing projects we had the privilege to cooperate on. Please be sure that we shall do our utmost to complete the tasks so that the efforts he put into these endeavors to the very end, despite his failing health, will come to fruition. The last time we saw your father was on the occasion of Franz's 90th birthday. He was in good spirits then.

Attached are two pictures taken on that occasion, one with Franz at the lab (the orange shirt he is wearing was a special gift from Professor Keiko Uezono on the occasion of his 90th birthday), and one with me (to his right), Miguel Revilla from Spain (to my right), RB Singh from India (to his left) and Doug Wilson whom you may have met at your wedding (far right in the picture).We loved your father. He will be greatly missed. With deepest sympathy, Germaine and Francis.

Dr. Singh met Salvador in 2004 during the 3rd International Congress in Cardiovascular diseases, Taipei, Taiwan, 26-28 Nov 2004 and got the opportunity to be his friend (144). Dr Singh had another opportunity to enjoy his friendship during the 90th birthday of Dr Halberg, when Professor Revilla from Spain, Dr DeMeester from Belgium and Drs

Sergey Chibisov and Radzhesh Agarval from Russia had also come for the celebration, hosted by Franz's daughters Francine and Julia, his wife Othild, and Germaine.

We all in BIOCOS send our deepest condolences to his family herewith - the words do not give justice to Salvador, but the heart is deeply touched and the mind is sorrowful but knows of his great achievements. He has merely moved to another place, where all of us will be moving eventually to greet him.

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Plasma Fibrinogen Levels in Acute Myocardial Infarction

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Abstract

Research evidence suggests that high plasma fibrinogen represents a major risk factor for cardiovascular diseases. The increased occurrence of CVD necessitates the need to analyze fibrinogen levels in ischemic heart disease(IHD) patients and study its relationship with physiological and behavioral risk factors. The present study analyses plasma fibrinogen levels in relation to known cardiac risk factors, in 72 patients (63 men and 9 women) afflicted with myocardial infarction. Parameters studied were anthropometry, plasma fibrinogen and lipid profile. Anthropometric data indicated a lower muscle mass status in majority of the subjects. Although the body mass index (BMI) was normal in majority of subjects, waist-to-hip ratio (WHR) was higher than normal range. Clinical data revealed atherogenic lipid profile in 58% of the subjects. Mean plasma fibrinogen values were 3.8g/L, high normal (>3.0g/L) in 28% and above normal (>4.0g/L) in 30% of the patients. Fibrinogen levels were higher ($p<0.01$) in patients with diabetes, while they were lower in alcohol users ($p<0.05$). Also, mean fibrinogen, cholesterol, LDL, triglycerides, WHR and BMI were higher in smokers than in non-smokers. The results show that fibrinogen level may be the risk factor of IHD in presence of known CVD risk factors. Since most of the risk factors are amenable to changes in lifestyle, it is worthwhile to modulate the levels of these parameters to achieve reductions in plasma fibrinogen.

Introduction

Chronic diseases like cardiovascular disease (CVD), cancer and diabetes are well recognized as major health problems in the world today. The involvement of lipid and thrombotic component in the pathogenesis of ischemic heart disease (IHD) is well known [1,2] . Clinical and epidemiological evidence indicate that the pre-thrombotic state characterized by hypercoagulability, is associated with increased risk of myocardial infarction [3-5]. Components of haemostatic system which could influence IHD due to their thrombotic characteristics have been identified

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viz., plasma fibrinogen, factor VII, coagulant activity, increased platelet aggregation as well as impaired fibrinolysis [3-5].

Prospective epidemiologic investigations indicate that plasma fibrinogen is a powerful predictor for myocardial infarction and stroke [6]. Clinical findings suggest that hyperfibrinogenemia favors atherothrombotic events of IHD by predisposing to thrombosis and by enhancing atherogenesis [7]. The present study is planned with the objective of analyzing plasma fibrinogen levels in MI patients

Table 1. Prevalence of Classic CVD Risk Factors

Risk factor	%
High Cholesterol (>200mg/dl)	38
Elevated Triglycerides (>160mg/dl)	50
Hypertension	42
Obesity	16
WHR (>0.8)	40
Smoking	56
Alcohol users	41
Diabetes	51

Table 2. Anthropometric measures of the Subjects

Parameters	Male (n= 63)	Female (n=9)
Body Mass Index	24 ± 2.9	24 ± 3.5
MUAC (cm)	28.2 ± 2.7	27.1 ± 3.1
MUAMC (cm)	15.9 ± 4.6	34. 1 ± 3.7
TSF (cm)	12.1 ± 6.0	17. 6 ± 8.7
Body fat (%)	27 ± 6.0	38 ± 3.0

Values are mean ± SD

Normal ranges

BMI : > 18.5-25

WHR : ≤ 0.8

TSF : M = 12.5, F = 16.5 (Triceps skinfold)

MUAC : M = 29.3, F = 28.5

(Mid upper arm circumference)

MUAMC : M = 25.3, F = 23.5

(Mid upper arm muscle circumference)

Methodology

The study included a total of 72 patients (63M, 9W) of acute myocardial infarction(AMI) admitted at the CSI Holdsworth Memorial Hospital, Mysore, over a period of 10 months. The research protocol included general examination and personal history, anthropometric measurements and biochemical tests. The study was approved by the hospital ethical committee.

Personal history – detailed enquiries about past and present complaints, personal and other habits (alcohol use and smoking) and about family history were made using a formulated questionnaire.

Anthropometric measures – Body weight and height were measured in the subjects in minimum

clothing and without shoes on 2 occasions. BMI was calculated as body weight (kg) divided by height squared (m^2). The waist and hip circumference were also measured and waist-to-hip ratio (WHR) was calculated. Skinfold measurements were taken using Lange skinfold caliper at the biceps, triceps, suprailiac and subscapular levels and body fat percentage was calculated according to the method of Durnin and Womersly [8].

Biochemical tests – Plasma fibrinogen was analyzed using Nycotest ™ test (Nycomed Pharma, Oslo) based on the method of Clausse [9]. Other relevant and routine tests including Hb, cardiac enzymes, lipid profile and blood sugars were carried out in each patient using standard diagnostic kits. Serum LDL-cholesterol was calculated by the formula LDL-C = serum cholesterol – HDL-C (serum triglycerides/5). Blood samples for fibrinogen analysis were collected immediately on admission to the ICU, drawn in tubes containing trisodium citrate.

Statistical analysis – The anthropometric and biochemical data is expressed as mean and SD. Linear correlation coefficients between plasma fibrinogen and each of anthropometric and biochemical parameters were calculated.

Results

The age of the subjects ranged from 25-69y. Women comprised a small number in the study group. For majority of subjects the disease had occurred after 40y, the percentage of men being affected was greater in the age-group of 41-50 and 51-60y. The disease history of the patients revealed the occurrence of classical risk factors like hypertension, diabetes in > 40% of the subjects. Also, cigarette smoking and alcohol consumption was quite common among male subjects.

The BMI ranged from 21-29 (mean 24$\pm$ 3.9). Majority of subjects (70%) had BMI within the normal range (18.5-25), only 27% were found to be overweight indicating grade I obesity. WHR was more than 0.8, in both men and women. Female subjects tended to have higher body fat when compared to males.

The mean plasma fibrinogen and lipid profile are given in Table 3. The mean plasma fibrinogen was 3.8 $\pm$ 1.9 g/L, ranging from 1.9 – 6.8 g/L. Although the overall mean value for plasma fibrinogen was well within the normal range (2-4g/L), a majority of subjects had a high normal value ie., > 3.0g/L, while 30% of them had values higher than 4g/L. Data pertaining to the lipid profile, classified according to NCEP Guidelines[10], revealed a distinctive atherogenic profile in majority of subjects. It was observed that mean total cholesterol and triglycerides were higher than the desirable range in > 50% of the subjects, while LDL cholesterol was within the desirable range in only 29% of the subjects. Mean body weight, BMI, %body fat, fibrinogen and lipid profile were higher in subjects with WHR >0.8 (mean 0.95).

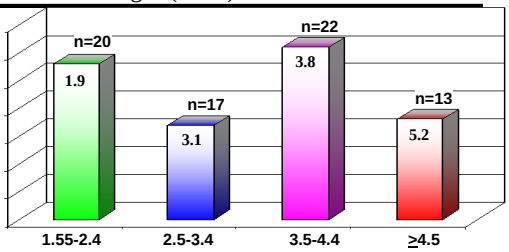
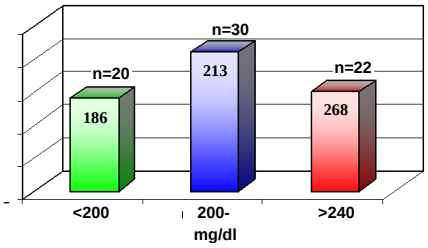
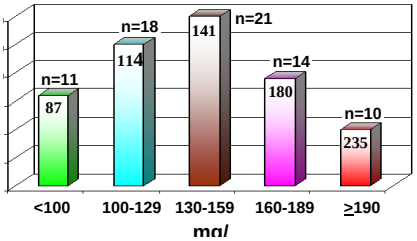
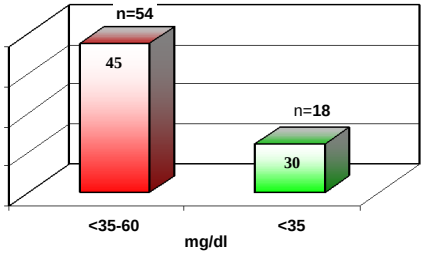
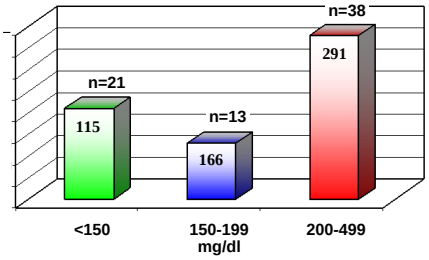
The influence of smoking and alcohol consumption in men on plasma fibrinogen is shown in table 4. In this study, IHD developed in 70% of current smokers, compared to ex-smokers and non-smokers. Mean plasma fibrinogen in smokers was significantly higher than in non-smokers. As expected, plasma fibrinogen in alcohol users was significantly lower ($p<0.05$) compared to non-alcohol users. Alcohol consumption appears to lower fibrinogen.

Comparison of mean fibrinogen levels between different groups is shown in Figure 1. It was observed that subjects with diabetes and hypertension had significantly ($p<0.01$) higher levels compared to non-diabetic and normotensive IHD subjects. Significant correlation between fibrinogen and age of the subjects, body fat % and triglyceride levels were observed (table 5).

Discussion

The results demonstrate that fibrinogen was a risk factor in subjects with at least one of the known CVD risk factors. Fibrinogen was higher in these subjects compared with subjects having no previous history of diabetes, hypertension and lipid abnormalities. The presence of well known CVD risk factors might contribute to increased risk of IHD through increases in plasma fibrinogen. Fibrinogen has been reported to be positively associated with the incidence of IHD in epidemiological studies [3,5,7].

Table 3. Plasma fibrinogen and lipid profile data of the subjects

Biochemical parameter overall mean Population within ranges (n=72) and their mean values	
1. Plasma fibrinogen 3.8 ± 1.9 (g/l)	
2. Total cholesterol 211.6 ± 30.4 (mg %)	
3. LDL cholesterol 110. ± 30.3 (mg %)	
4.HDL cholesterol 39.3 ± 7.4 (mg %)	
5. Triglycerides 210 ± 53.1 (mg %)	

Several studies have reported increases in fibrinogen with age [11-13]. These studies, however, were based on >200 patients. Although the total number was small (n=72), the results indicate an age effect. It is reported that moderate alcohol consumption is protective against heart disease [2,13]. In this study, maximal beneficial effect on fibrinogen were observed in subjects with moderate levels of alcohol consumption.

Obesity is associated with elevated fibrinogen levels [2, 12-14]. Although, the obese subjects had higher values than non-obese group, the correlation did not reach statistical significance. Elevated fibrinogen was more closely related to body fat than

to the degree of obesity expressed as BMI. This observation is in agreement with reported data [12].

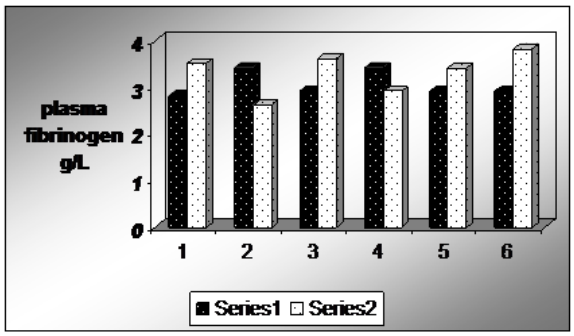
Table 4. Influence of smoking habit and alcohol consumption on plasma fibrinogen

Smoking Habit		Alcohol consumption	
n	Fibrinogen g/L	n	Fibrinogen g /L
Non smokers	22 2.86	Non drinkers	33 3.0
Ex smokers	7 2.92	Very light	5 4.2
Light smokers	18 3.41	Light	8 2.6
Heavy smokers	16 3.82	Moderate	9 2.0
		Heavy	8 2.2

Values are mean ± SD, $p < 0.05$.

Table 5. Correlations between fibrinogen , somatic and biochemical parameters

Parameters	*Fibrinogen*
	r	*P level*
1. Somatic		
BMI	0.20	NS
WHR	0.03	NS
MUAC	0.07	NS
TSF	1.75	NS
Body fat	0.39	<0.05
2. Biochemical		
Cholesterol	0.03	NS
HDL-C	0.17	NS
LDL-C	0.05	NS
TG	0.37	<0.05
3. Others		
Age	0.31	<0.05
Blood pressure (systolic)	0.02	NS



Series 1 Series 2

1- Non smoker Smoker
2- Non alcohol user Alcohol user
3- Non obese Obese
4- Non vegetarian Vegetarian
5- Normotensive Hypertensive
6- Non diabetic Diabetic

Figure 1. Comparison of fibrinogen in different subject groups.

Also, it emphasizes the importance of body fat in the development of metabolic abnormalities. Similarly, significant correlation between fibrinogen and triglycerides (TG) reiterates the involvement of hypertryglyceridemia in atherosclerosis. Increase in TG may be diet induced or due to genetic and metabolic defects. Also, it is well known that carbohydrate rich diets increase production of triglycerides. Elevations in TG levels may have an effect on fibrinogen synthesis through increases in free fatty acids. Lipolysis of TG liberates fatty acids and it is known that free fatty acids (FFA) stimulate hepatic fibrinogen synthesis [2,15]. This biosynthetic control manifested by FFA appears to provide a connecting metabolic link between TG metabolism and thrombosis in the genesis of atherosclerosis. Indians are reported to have high levels of TG [16], which may be due to habitual high carbohydrate diets and / or genetic susceptibility [14]). In the present study, the carbohydrate intake of the subjects was high, contributing >75% of total calories. The clinical presentation of diseases, environmental conditions and nutritional status of Indians are quite different compared to Western population [17-19]. Indians may also have higher lipoprotein(a) which enhances the atherogenecity of LDL cholesterol and more thrombogenic [19]. Increased intake of Western diet is known to cause rise in triglycerides and free fatty acids which are precursors of fibrinogen. Increased

concentration of fibrinogen can occur in between 6.00 AM to 12.00 noon as circadian rhythm which may become worst in patients with ACS [19]. Thus, the excess risk of Indians to IHD also results from diet and lifestyle related conventional risk factors. Furthermore, few population based studies have mainly focused on the relation of plasma fibrinogen with single metabolic abnormalities [1-3].

In conclusion, the results of this observational study show that fibrinogen increased the risk of IHD in presence of known CVD risk factors. Since most of the risk factors are amenable to changes in lifestyle, it is worthwhile to reduce the levels of these parameters to achieve reductions in plasma fibrinogen.

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Synergistic Antilipidemic and Antihepatotoxic Action of *Gongronema Latifolium* and *Nauclea Latifolia* in Streptozotocin Diabetic Rat Models

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Abstract

Purpose: The combination effect of *Gongronema latifolium*(GL) and *Nauclea latifolia* (NL), promising vegetables used in traditional management of metabolic disorders on serum lipid components and some liver marker enzymes was investigated in diabetic rat models. *Method:* The study design consisted of thirty six (36) rats divided into 6 groups of 6 rats each. Whereas groups 1 and 2, non diabetic and diabetic controls received placebo treatment, groups 3-5 respectively received 200mg/kg b.w. of GL, NL, and 100mg/kg b.w. each of GL and NL per day, for 21 days. The 6th group received subcutaneous insulin, 5IU/kg b.w. per day. Thereafter, the animals were sacrificed, and serum prepared from blood collected was used to assay lipid components and liver function enzymes, using standard analytical kits. *Result:* Measured blood glucose in diabetic animals decreased significantly from initial by 66.34%, 18.12% and 67.73% respectively upon treatment with GL, NI and GL plus NI. Whereas diabetes induction caused significant increases ($p<0.05$) in total cholesterol (TC), 54.42% and low density lipoprotein (LDL), 55.0% compared to the normal control (NC), treatment with extracts of GL or NI significantly decreased ($p<0.05$) these by (58.70% and 24.79%, TC) and (71.70% and 33.38%, LDL) respectively. However, the combined extracts produced more steady reduction (59.70% and 70.26, TC and LDL), similar to the NC. Also the amino transferases (ALT and AST) activities which increased by 66.83% and 72.87% in the DC rats indicating hepatotoxicity, secondary to hyperglycemia, became reduced upon treatment with GL, NI and GL plus NI. Again, the extent of reduction was better with combined extracts (85.58% and 53.77%), and compared favorably with NC. *Conclusion:* Lower dosages of the two extracts when combined provides higher efficacy in protection against atherosclerosis and hepatotoxicity in diabetes. Hence the need to adopt this strategy in bio-prospecting for antidiabetic natural products.

Keywords: Synergism, diabetes mellitus, lipid profile, aminotranaminases, *Gongronema latifolium*, *Nauclea latifolia.*

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Introduction

Diabetes mellitus is a multifactorial disease, which is characterized by hyperglycemia and glucosuria (Atangwho, 2008) among others. Diabetes mellitus is also a non-communicable disease, which is considered as one of the five leading cause of death in the world. About 100 million people around the world have been diagnosed with diabetes and by the year 2010, it was projected that 215 million people will have the disease (Zimmet, 1999).

Recently, the search for appropriate hypoglycemic agents has been focused on plants used in traditional medicine partly because of leads provided by traditional medicine to natural products that may be better treatments than currently used drugs (Rates, 2001). Many minor components of foods such as secondary plant metabolites have been shown to alter biological processes, which may reduce the risk of chronic disease in human (Nwanjo et al. ,2006). Polyherbal therapy, sometimes called polyherbalism a combination of herbs or phytochemicals from more than one source, a concept originally peculiar to Ayurveda (Singh, 2005) has today been accepted as an effective therapeutic approach in sourcing medicament for degenerative ailments. The herbs are selected according to the disease and have several advantages over monotherapies namely; reduced toxicity and side effects, and maximum/synergistic therapeutic efficacy (Singh, 2005 and Tiwari and Rao, 2002). Singh et al have succesfully used commiphora mukul, fruits and vegetables, fenugreek and stargooseberry in the management of patients with hyperlipidemia in 1990s.

Gongronema latifolium (Asclepiadaceae) is a tropical rainforest plant primarily used as spice and vegetable in traditional folk medicine (Ugochukwu and Babady, 2002 and Ugochukwu et al., 2003). Reports from various authors show that it contains essential oils, saponins and pregnans among others (Schneider et al., 1993; Morebise and Fafunwa, 1998 and Morebise et al., 2002). The leaves of *Gongronema latifolium* have protective role against diabetes, hypertension, stomach upsets and pains, typhoid fever (Etim et al., 2008).

Nauclea latifolia (Rubiaceae) commonly known as Pin cushion tree is a strangling shrub or small tree native to tropical Africa and Asia. It grows in Akwa Ibom and Cross River states of Nigeria and is called "Mbom-mbong" whilst in the Northern Nigeria; it is called "Tabasiya. Parts of the plant are commonly prescribed traditionally as a remedy for diabetes mellitus and hypertension (Akpanabiatu et al 2005; Nworgu et al ., 2008 and Okwori et al., 2008).

However, there are no empirical data or scientific reports to support the antidiabetic effect of the combined administration of the two plants. This present study was designed to test the hypoglycemic effect of polyherbal therapy of ethanolic extracts of *Nauclea latifolia* and *Gongronema latifolium* in normoglycemic and STZ-induced diabetic rats.

Materials and Methods

Plant material: Fresh *Gongronema latifolium* leaves were collected from a cultivated land at Ibiaku Itam in Itu Local Government Area of Akwa Ibom State, Nigeria while *Nauclea latifolia* was collected by the fence of Industrial Training Fund office in Calabar, Cross River State of Nigeria. The sample was authenticated by Dr. E. G. Amanke, a Botanist in the Department of Botany, University of Calabar, Nigeria and voucher specimen deposited at the Department of Botany herbarium, University of Calabar.

Preparation of ethanol extract of plants: The ethanol extract was prepared using the wet method of extraction. One kilogramme of the fresh leaves of the plants were cut into pieces separately, blended in1.5litres of ethanol (96%) with an electric blender and transferred into amber coloured bottle and kept in cool (4^oC) dark compartment for 72hours. The mixture/blend was filtered using a cheese material and thereafter with Whatman No 1 filter paper. The extract was concentrated *in vacuo* using a rotary evaporator at 37-40^oC and dried completely in a desiccator containing a self-indicating silica gel.

Animals

Albino Wistar rats of (150-250g) of both sexes obtained from the animal house of the Department of Pharmacology and Toxicology, Faculty of Pharmacy of the University of Uyo, Nigeria were used. They

were kept in clean cages (wooden bottom and wire mesh top), maintained under standard laboratory conditions (Temperature 25± 5oC, Relative humidity 50-60%, and a 12/12h light/dark cycle) and were allowed free access to standard diet (Vital Feed from Grand Cereals and Oil Mills Limited, Jos, Plateau State of Nigeria) and water ad libitum. Animals were acclimatized for 14 days in the animal house of the Department of Biochemistry, University of Calabar, Nigeria before each of the experiments.

Experimental Induction of Diabetes

The diabetes was induced in the overnight fasted animals by a single intraperitoneal injection of freshly prepared solution of streptozotocin (Sigma, USA) $50mgkg^{-1}$b.w. in 0.1M cold sodium citrate buffer pH 4.5 (Ghoraishian, 2006 and Rao and Naidu, 2010). The animals were considered as being diabetic if the blood glucose value were >200mg dl^{-1} on the third day after streptozotocin injection and were used in the experiment. This was estimated using One Touch Glucometer (Lifescan, inc 1995 Milpas, Califonia, USA) with blood obtained from the tail vein of the overnight fasted rats.

Experimental Protocol

Albino rats weighing 150-250g were used in this study. All the rats were kept at an average room temperature 0f 30^{o}C in the animal room of Biochemistry Department, University of Calabar, Nigeria. They were allowed free access to water and feed (product of Pfhizer Nigeria, ltd, Jos) throughout the experimental period.

Thirty (30) rats included in the study were divided into six (6) groups of six (6) animals each (five diabetic and one non diabetic). Diabetes induction was done by intraperitoneal injection of 50mg/kg.b.w of Streptozotocin (STZ) (Sigma, St. Loius, MO, U.S.A) dissolved in sodium citrate buffer (0.01M, pH 4.5).

Diabetes was confirmed by the determination of fasting blood glucose concentration on the third day of post administration of STZ, showing glucose levels above 200mg/dl.

The experimental groupings were as follows: G.l = Diabetic rats treated with 200mg/kg.b.w. of *Gongronema latifolium* twice daily, N.l = Diabetic rats treated with 200mg/kg.b.w of *Nauclea latifolia* twice daily, G.l/N.l = Diabetic rats treated with 200mg/kg.b.w of Nauclea latifolia and Gongronema latifolia, morning and evening respectively.

Insulin = diabetic rats treated with 5 units/kg.b.w of insulin, DC = diabetic control; diabetic rats given placebo, NC = non-diabetic rats given placebo treatment.

At the end of twenty one days, the body weights, and fasting blood glucose of the animals were again determined.

Blood was collected on every 3 days through the rat's tail vein for glucose estimation. At the end of the experimental period, food was withdrawn from the rats and they were fasted overnight but had free access to water. They were then euthanized under chloroform vapor and sacrificed.

Immediately, overnight fasting blood samples were collected for sera preparation by cardiac puncture into sterile plain tubes. Serum samples were separated from the clot by centrifugation at 3,000rpm for 10 minutes using bench top centrifuge (MSE Minor, England) and stored frozen until needed for analysis. All analysis was completed within 24 hours of sample collection.

Biochemical Assays

Assay kits used for the biochemical assays were obtained from Randox Laboratories Ltd., Admore Diamond Road, Crumlin, Co., Antrim, United Kingdom, Qt 94QY: Lipid profile- Triglycerides (TG), Total cholesterol (TC), High density lipoprotein (HDL), Low density lipoprotein (LDL) and Very low density lipoprotein (VLDL), Aspartate aminotransferase (AST), and Alanine aminotransferase (ALT and were determined using Reitman and Frankel method, 1956., Glucose concentration were determined by the use of One Touch Glucometer (Lifescan, Inc., 1995 Milpitas, Califonia 95035, USA).

Statistical Analysis

All data were expressed as mean ± SD of the number of experiments. The results were analysed for statistical significant by one way ANOVA using the SPSS statistical program of Post Hoc Test (LSD) between groups using MS excel program. P values < 0.05 were considered significant.

Results

The effects of *Gongronema latifolium* (G.l) and *Nauclea latifolia* (N.l) treatment on blood glucose, serum lipid profile and some enzymes of diabetic and non-diabetic rats are shown on tables 1-3 respectively.

Table 1. Effect of Plant Extracts on Blood Glucose levels (mgkg^{-1}) of Streptozotozin-induced Diabetic Rats

	Initial	Final	% change
GL	504.00±30.54*, [a]	169.67±16.62[a]	66.34
NL	406.67±27.68*, [a, c]	333.00±23.08*, [a, c]	18.12
GL + NL	502.67±2.76*, [a]	164.33±32.76[a]	67.73
Insulin (SD)	578.00±6.34*	77.33±10.36*	86.62
DC	292.00±21.05	214.67±14.42	26.43

*p<0.05 vs DC; a = p<0.05 vs SD; c = p<0.05 vs GL+NL.

Table 2. Effect of Plant Extracts on serum lipid profile of Streptozotozin-induced Diabetic Rats

	TG(mg/dL)	TC(mg/dL)	HDL(mg/dL)	LDL(mg/dL)	VLDL(mg/dL)
GL	66.20±7.57[d]	105.07±5.74[a, b]	60.20±2.94*,[a,b,d]	58.10±5.36[a, b]	13.24±1.51[d]
NL	61.07±4.60[d]	191.34±21.70*,[b, d]	66.83±0.14*, [d]	136.72±20.79[b]	12.21±0.92[d]
GL +NL	25.57±0.78*,[a, b]	102.54±2.18[a, b]	46.61±1.00*,[b]	61.04±2.95[a, b]	5.11±0.16*, [a, b]
Insulin	82.86±9.91	448.59±36.04*	66.36±0.15*	398.80±38.17*, [a]	16.57±1.98
DC	75.23±14.56	254.40±29.84*	64.22±2.33*	205.23±31.01*	15.05±2.91
NC	76.41±9.65	115.95±14.59	8.26±1.04	92.40±15.06	15.28±1.93

*P<0.05 vs NC; a = P<0.05 vs DC; b = P<0.05 vs Insulin; d = P<0.05 vsGL+NL.

Table 3. Effect of Plant Extracts on some Serum Enzymes in Streptozotozin-induced Diabetic Rats

	AST (U/L)	ALT(U/L)	AMYLASE(U/L)
GL	41.33±2.01*, [a, b]	18.27±5.01*, [a, b]	261.19±36.52[b, d]
NL	50.33±12.23*, [a, b]	14.33±1.38*, [a, b]	216.37±5.74[a, b]
GL +NL	32.67±1.17*, [a, b]	10.00±0.73*, [a, b]	171.371±9.97[a, b]
DC	70.67*±0.42*	69.33±18.09	254.14±45.41
NC	19.17±2.52	83.00±4.02	166.59±26.65

*P<0.05 vs NC; a = P<0.05 vs DC; b = P<0.05 vs Insulin; d = P<0.05 vsGL+NL.

Measured blood glucose in diabetic animals decreased significantly from initial by 66.34%, 18.12% and 67.73% respectively upon treatment with GL, NI and GL plus NI. Whereas diabetes induction caused significant increases (p<0.05) in total cholesterol (TC), 54.42% and low density lipoprotein (LDL), 55.0% compared to the normal control (NC), treatment with extracts of GL or NI significantly decreased (p<0.05) these by (58.70% and 24.79%, TC) and (71.70% and 33.38%, LDL) respectively. However, the combined extracts produced more steady reduction (59.70% and 70.26, TC and LDL), similar to the NC. Also the amino transferases (ALT and AST) activities which increased by 66.83% and 72.87% in the DC rats indicating hepatotoxicity, secondary to hyperglycemia, became reduced upon treatment with GL, NI and GL plus NI (Figure 1).

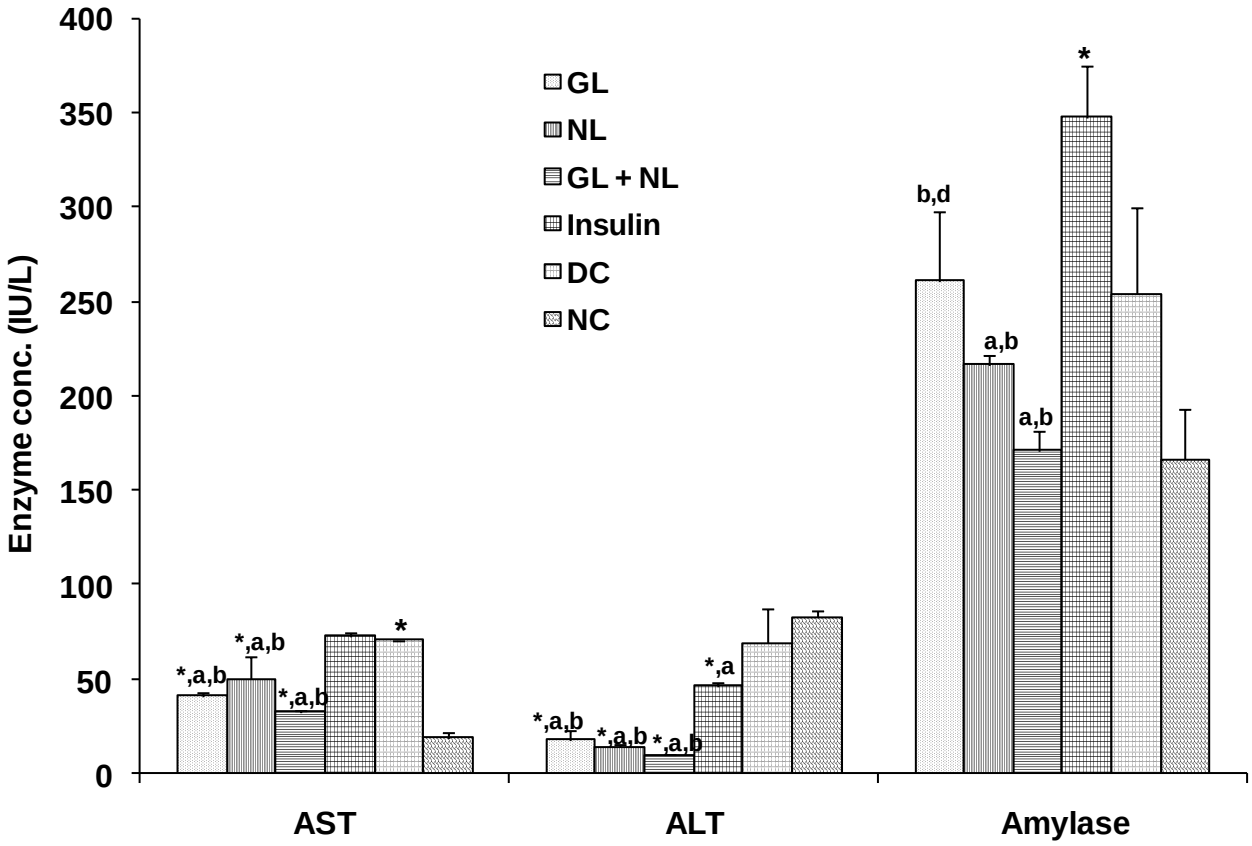

Figure 1. Effect of treatment on some serum enzymes (U/L) in diabetic rats. Values are mean ±SEM, n=6. *p<0.05 vs NC; a=P<0.05 vs DC; b=P<0.05 vs Insulin; d=P<0.05 vs GL+NL.

Again, the extent of reduction was better with combined extracts (85.58% and 53.77%), and compared favorably with NC.

The result shows that induction of diabetes with STZ caused a significant increase in TC and LDL as seen in the DC rats. Intervention with individual extract of G.l and N.l however reduced these indices but was better impacted when the extract were combined, indicating a positive synergy. This observation was also seen in blood glucose levels, lipid profile and the enzyme activities.

Discussion

The presence of high amount of cholesterol in the diet has been shown to increase plasma cholesterol and may elevate aortic atherosclerosis (Lipid Research Clinical Program (LRCP), 1984). Many investigations have shown that diet treatment or drug therapy to regulate cholesterol can decrease subsequent cardiovascular disease (CVD) associated mortality and morbidity (Kwiterovich, 1997). On the basis of this, great effort have been made to reduce the risk of CVD through the regulation of cholesterol, thus the therapeutic benefits of plant foods have been focused of many extensive dietary studies (Yoko-Zawa et al., 2006 and Zhang et al., 2007). Traditional plant remedies have been used for centuries in the treatment of diseases (Akhan and Ali, 1984), but only a few have been scientifically evaluated. Therefore, the effects of G.l and N.l leaves extracts on the lipid profile of rats were studied. The two plants reduced the serum TC and LDL-C levels but a combined administration of the two plants further reduced it better than in individual plant treatment.

Nwanjo, 2005 has shown that the administration of aqueous leaf extract of *Vernonia amygdalina* produced hypoglycaemic, hypolipidaemic and antioxidant effects in rats which is similar to the

observation of this finding. The result is also in line with the findings of Ugochukwu et al., 2003) and Adaramoye et al., (2000). The cholesterol lowering effects of these plant extracts could be beneficial in preventing lipid abnormalities which may arise in certain metabolic disorders (Cho et al., 2002). Ezekwe and Obidoa (2001) have reported that flavonoids, tannins and saponins may play some roles in the hypolipidaemic effect of some plants. The mechanism of hypocholesterolaemic action of these plant leaves may be due to inhibition of the absorption of dietary cholesterol in the intestine or its production by the liver (Ahmed-Raus et al., 1991) or stimulation of the biliary secretion of cholesterol and cholesterol excretion in faeces (Anderson et al., 1991).

Serum enzymes in this case viz. alanine aminotransferase, (ALT), Aspartate aminotransferase (AST), are present in the hepatic and biliary cells (Jensen, et al., 2004). These enzymes are usually released from the hepatocytes and leak into circulation causing increase in their serum levels under hepatocellular injury or inflammation of the biliary tract cells. Serum levels of these enzymes are particularly high in acute hepatocellular damage caused by drug toxicity and xenobiotics (Norman, 1998). The extent of the enzymes changes is related to the nature, closes to toxic agent and duration of toxicity (Shi et al., 2003; Song et al., 2003; Brukner et al., 1984).

In an inflammatory condition, there is a leakage of cytoplasmic enzymes into circulation, hence ALT levels increased above that of AST. Thus, when there is gross cellular necrosis, as in STZ-induced diabetes-damaged to the pancreatic cells by STZ, the level of AST may rise higher than that of ALT (Recknagel, 1987). This is because ALT levels is increased in the serum due to conditions where cells of the liver have been inflamed or undergo cell death, and is specific for the liver cells (Jeasen et al., 2004) but the AST levels can be triggered in other conditions such as myocardial infarction apart from hepatocellular damage (Jensen et al., 2004).

In the present study, there was conformity in the levels of the enzymes with available literature (Kim et al., 2006 and Atangwho et al., 2007). The higher levels of AST and ALT observed in DC may be attributed to the fact that the STZ may have caused some injury to other organs, in addition to the liver and pancreatic duct (gland). This now potentiates the release of AST into circulation over the ALT. However, the increase in aminotransferase is generally produced by cellular necrosis (Buckner et al., 1986).

Induction of diabetes by STZ is observed to be associated with increased serum enzyme activities (Atangwo et al., 2008). Hence the elevated levels of the enzymes (AST and ALT), generally was attributed to injury caused to the hepatocytes by STZ, which now affects the normal function of the liver, since these enzymes are indisputably markers of liver injury as stated earlier; they are localized in the cytoplasm under normal conditions and are released into the circulation under abnormal conditions (e.g cellular damage) (Mourelle et al., 1987 and Romeo et al., 1999). The increased level of AST and ALT in rats induced diabetes with STZ was a clear indication of a kind of injury or the other caused by STZ toxicity.

The beneficial or synergistic effect of combination therapy over monotherapy has also been indicated. The seemingly untoward action of G.l extract in both diabetic and non-diabetic rats-decreased AST and ALT activity has effectively been modulated by N.l extract when co-administrated, since results of G.l + N.l group compared well with normal control group. Combined extracts of G.l and N.l may therefore be safer for use as a diabetic management compared to the individual extracts. Considering the result of the lipid profile, antiatherogenic effect is better with combined extracts relative to individual extracts and insulin administration. Evidence from the present study confirms that G.L and N.l were found to be highly effective in reducing TC and LDL thereby exhibiting hypocholesterolaemic effects.

It is evident from the result of this investigation that lower dosages of the two extracts when combined provide higher efficacy in protection against atherosclerosis and hepatotoxicity in diabetes. Hence the need to adopt this strategy in bio-prospecting for antidiabetic natural products.

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24- Hour Chronomics of Ambulatory Blood Pressure Monitoring in Rotating Night Shift Workers and Controls

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Abstract

Background: Concerns about the health of night shift workers has long been debated. Shift work is associated with the disruption of circadian rhythms, where a person's internal body clock is in conflict with the rotating night shift schedule which causes internal desynchronization, sleep disturbances resulting in to increased risk of cardiovascular diseases and diabetes and other physiological disorders.
Objectives: We investigated the circadian pattern of blood pressure and heart rate in night shift workers and day shift controls, and whether the changes in circadian pattern produced by rotating night shift are reversible in due course of time.
Method: 14 healthy nursing professionals, aged 20-40 year, performing day and night shifts and 14 subjects as controls, performing day duty were recruited in the study. Circadian patterns of blood pressure and heart rate were evaluated in night shift workers during the work shift (Night & Day shift) and in controls.
Result: Night shift workers showed a very interesting altered circadian pattern of double amplitude when subject went back to the day shift. An extremely significant different pattern of SBP and DBP double amplitude was found between day shift and controls ($p<0.01$).
Conclusion: Effect of rotating night shift develops later due to rotating shift and desynchronization. Acrophase pattern was clinically significant when studied in individual subjects in different shifts with controls. Alterations in Acrophase were persistent during night as well as day shift due to incomplete recovery and ecphasia was very common among night shift workers.

Keywords: Rotating night shift, ambulatory blood pressure and heart rate monitoring, ecphasia

Introduction

Concerns about the health of night shift workers have been long debated. It was a matter of concern that these subjects, when deprived of night sleep, may have biological parameters that are affected by such

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activity and, whether this deprivation can be and associated parameter change can be compensated for by day time sleep. Researchers have found that there is an increase risk of accidents & human error, an increase in sleepiness and of fatigue due to deprivation of sleep, increased health problems; and disruption to family and social life. Night shift working is associated with a disruption of circadian rhythms, where a person's internal body clock is in conflict with the rotating shift schedule. The circadian rhythm of the human body is characterized with an alternating cycle of sleep and awakening [1]. Among healthy subjects, sleep tends to occur during a particular phase of circadian cycle [2]. Those who work during the night shift may attempt to sleep when their body clock is adjusted for the awakening phase [(3)]. This attempt disturbs the body clock resulting in a contradictory relationship between sleep time and circadian schedule. There is evidence that shift work affects both sleep and awakening by disrupting the circadian regulation which has adverse effects on family and societal life [4]. The night shift work alters both length and quality of sleep. The average sleep cycle for night shift workers is sleeping during the day which may be 2-4 hrs shorter than that of the day worker sleeping at night. Day sleep is light, fragmented, and more likely to be disrupted and hence, the insomnia can be severe in night shift workers [5]. It is possible that the circadian sleep propensity rhythm and hormonal rhythm are under influence of circadian pacemaker as well as sleep habit [6].

Most rhythms are driven by an internal biological clock located in the hypothalamic suprachiasmatic nucleus and can be synchronized by external signals such as light-dark cycles [7]. The rapidly rotating shift system including two consecutive night shifts, do not significantly alter the normal circadian rhythm of the body, particularly performance level, body temperature and hormone release [8]

Majority of the circadian rhythms in our body have both an endogenous component regulated by an internal clock, viz. the suprachiasmatic nuclei (SCN), and an exogenous component composed of a light-dark cycle [1, 5]. The disruption in natural time pattern, under influence of night dark cycle, acts upon the circadian system to bring it into synchronization with the new time pattern.

Normal circadian pattern of blood pressure- Blood pressure is higher during the day time (between 10 a.m. to 6 p.m. and lower at night .There is a characteristic dip in blood pressure between midnight and 3 a.m, however, between 3a.m. and 6 a.m. there is a slow and steady rise in blood pressure but after arousal there is sudden steep elevation of blood pressure. This rapid increase in blood pressure is continuous for 4-6 hour i.e., 6 a.m. to 12 p.m. An interaction between biorhythms, the biological clock and triggers, which may be important in the pathogenesis of altered heart rate variability (HRV) and blood pressure variability (BPV). Circadian rhythms are under the influence of, and physiological variables are mediated by the activation of the adrenals, sympathetic/parasympathetic, hypothalamic and pituitary activity [9, 10]. Circadian rhythms, coordinated in part by the parietal hypothalamic-pituitary and adrenal mechanisms, have been reported in almost all variables examined thus far, including the circulation. It is possible that all metabolic functions undergo circadian rhythms [11].

Previous reports indicate that diurnal blood pressure (BP) variation, in addition to high BP per sec, is related to target organ damage and the incidence of cardiovascular events. Physical activity is one of the determinants of ambulatory BP and diurnal variation. [12]. Day shift workers show typical circadian rhythms with a drop in both systolic and diastolic blood at night. This pattern is reversed in night–shift workers [13].

In the present case-control study, we investigated the circadian pattern of blood pressure and heart rate in night-shift workers and in controls, to determine whether these changes are reversible after change to day-duty schedules.

Methodology

Subjects

Out of 20 volunteers (night shift workers), 6 were excluded due to non-fulfillment of study protocol. The duration and pattern of shift work were the same among all the subjects and 14 healthy nursing professionals, aged 20-40 year, performing day and night shift duties (continuous 9 days night shift with

alternate day shifts) {from last 6 years} and were randomly selected and recruited from the Trauma Center, GM and Associated Hospitals, Chhatrapati Shahuji Maharaj Medical University, Lucknow, UP, India. 14 subjects acting as controls, performing day duty (from 9:00 a.m. to 5:00 p.m.) alone were also recruited. The study was conducted during February to July, 2009 when the average temperature of the city ranged between 34°C and 38°C. At 26.50 N°, Lucknow is located just north of the tropic of cancer. The study was approved by the institutional ethic committee (Ref. code: XXXIV ECM/B-P3) and written, informed consent was obtained from all the subjects to participate in the study. Inclusion criteria (for night shift workers) were healthy nursing professional of both genders, aged between 20-40 years who performed night and day duty and inclusion criteria (for controls) was healthy working professional of both genders, aged between 20-40 years who performed day duty. Exclusion criteria were subjects with any acute/chronic illness, known patients with diabetes mellitus, other endocrinological disorders, hypertension, coronary artery disease, and chronic renal.

24-Housr Ambulatory Blood Pressure and Heart Rate Monitoring in Night Shift Workers and in Controls

Blood pressure and heart rate were recorded by ambulatory blood pressure monitor TM-2430 (A&D, Tokyo, Japan) that measured repeated oscillatory blood pressure and heart rate at selected intervals. Taking serial measurements a few times each day is important to reduce the error associated with a single measurement. The chronobiologic characterization of the circadian amplitude and acrophase in addition to the midline estimating statistics of rhythm (MESOR) further reduces the errors in interpretation. Taking only one or two measurements a day, always at awakening and/or at bed time may fail to reveal abnormalities seen only at other times of the day, or abnormalities that apply only to the variability in blood pressure or heart rate [14].

In this study, the subjects wore an ambulatory blood pressure monitor TM-2430 programmed to automatically measure blood pressure and heart rate at 30 min intervals while awake and sleeping hours during night shift and again when they were shifted to day duties and similarly in controls. The data were downloaded after every monitoring span to a local PC *via* an interface (TM-2421, A&D). Each blood pressure and heart rate profile was analyzed by a sphygmochron, utilizing both a parametric and non-parametric approach. Ambulatory blood pressure monitoring records were sent to the Halberg Chronobiology Center, University of Minnesota, Minneapolis, MN, USA for further interpretations. Original oscillometric data from each blood pressure series was first synchronized according to the activity-rest cycle of each individual by recomputing all the records in hours, from bed time to avoid differences among subjects in actual time of daily activity and to express results in circadian time rather than in less meaningful clock hours. After synchronization, blood pressure and heart rate values were edited according to commonly used criteria for the removal of outliers and measurement errors. The remaining data were analyzed chronobiologically.

The study of human chronomes can serve the derivation of refined reference values to better define health and to identify pre-disease, so that prophylactic interventions can be instituted as early as possible, preferably before the onset of disease [15]. In the current implementation of the chronobiological recommendations, reference values have been specified for clinically healthy peers of a given gender and ethnicity in different age groups [16]. Ambulatory blood pressure monitoring was done during their day and night shifts and in controls. Some essential parameters which are directly under influence of night shift workers such as body temperature, time of arousal, time of going to bed, duration of nocturnal and diurnal sleep, mode of waking up, sleep latency, quality of sleep, feeding habits, menstrual history (for females), and family history were also recorded. Acrophase (hr:min), time of overall high/peak values, and hyperbaric index) were calculated for systolic blood pressure (SBP), diastolic blood pressure (DBP), and heart rate. The circadian amplitude, a measure of the extent of reproducible variability within a day, was obtained by linear curve fitting, which yielded added parameters: in midline-estimating statistics of rhythm, the MESOR (a time structure or chronome-adjusted mean), acrophase (the timing of overall high

values), recurring in each cycles, and the amplitude and acrophase of the 12 hour (and higher order) harmonics of the circadian variation that with the characteristic of the fundamental 24 hours component, describe the circadian wave form. The MESOR is a more precise and more accurate estimate of location than the arithmetic mean [16].

Results

We measured the effect of rotating night shift by comparisons of night shift workers with actual control group. Night shift workers worked on a different shift (night and day shift) therefore we compared the circadian pattern of blood pressure and heart rate in shift workers during their night shift with controls, again when these night shift workers came back to day shift circadian patterns were compared with controls and we also compared within the shift the circadian pattern of blood pressure and heart rate of night shift with day shift. Data were presented as means and standard deviations (SDs) and statistical significance between the appropriate groups by the *p*-value. The circadian pattern of blood pressure and heart rate as adjudged from the MESOR was not statistically significant in night shift workers during their night as well as day shift and in controls. ($p>0.05$) (Table 2). Therefore changes were not found in MESOR values when we compared night shift to controls, day shift to controls and night shift with day shift (Figure 1). Similarly for hyperbaric index.

Significant difference was found in double amplitude or predictable change during day shift. But these differences were not found between night shift and controls. However, altered circadian patterns of systolic blood pressure, diastolic blood pressure and heart were found between day shift and controls. Controls showed a normal range of systolic and diastolic blood pressure for double amplitude.

Table 1. Baseline characteristics of night shift workers and controls: Means (SDs)

Baseline Characteristics	Night shift workers (n=14)	Controls (n=14)
Age	25.71 (5.28)	30.14 (7.00)
Weight (kg)	51.42 (7.78)	57.00 (5.60)
Height (cm)	159.78 (10.26)	162.00 (6.43)
Body mass index (BMI)	20.08 (1.78)	21.76 (2.20)

n= number of subjects

Data are presented as Means(SDs).

Table 2. Midline statistics of rhythms (MESOR) of Night shift workers and Controls

MESOR of SBP,DBP and HR of Night shift worker (During night shift) and Controls			
	Night Shift (Mean (SD))	Controls (Mean (SD))	*p* Values
SBP	120.16 (8.02)	120.91 (11.74)	0.84
DBP	72.64 (5.22)	76.10 (7.05)	0.15
HR	75.49 (5.47)	77.59 (22.30)	0.733
MESOR of SBP,DBP and HR of Night shift worker (During day shift) and Controls			
	Day Shift (Mean (SD))	Controls (Mean (SD))	*p* Values
SBP	120.66 (6.43)	120.91 (11.74)	0.94
DBP	73.44 (4.72)	76.10 (7.05)	0.25
HR	75.45 (5.68)	77.59 (22.30)	0.73
MESOR of SBP,DBP and HR of Night shift worker (During night shift) and Night shift worker (During day shift)			
	Night Shift (Mean (SD)	Day Shift (Mean (SD))	*p* Values
SBP	120.16 (8.02)	120.66 (6.43)	0.85
DBP	72.64 (5.22)	73.44 (4.72)	0.67
HR	75.49 (5.47)	75.45 (5.68)	0.98

Table 3. Double Amplitude (2A)/Predictable change of Night shift workers and Controls

Double Amplitude of SBP,DBP and HR of Night shift worker (During night shift) and Controls			
	Night Shift (Mean (SD))	Controls (Mean (SD))	*p* Values
SBP	27.36 (18.83)	22.83 (10.99)	0.55
DBP	19.50 (12.78)	17.10 (6.83)	0.54
HR	14.63 (9.28)	18.70 (10.04)	0.27
Double Amplitude of SBP,DBP and HR of Night shift worker (During day shift) and Controls			
	Day Shift (Mean (SD))	Controls (Mean (SD))	*p* Values
SBP	42.98 (20.75)	22.83 (10.99)	0.005**
DBP	29.19 (13.48)	17.10 (6.83)	0.006**
HR	18.87 (8.70)	18.70 (10.04)	0.96
Double Amplitude of SBP,DBP and HR of Night shift worker (During night shift) and Night shift worker (During day shift)			
	Night Shift (Mean (SD))	Day Shift (Mean (SD))	*p* Values
SBP	27.36 (18.83)	42.98 (20.75)	0.04*
DBP	19.50 (12.78)	29.19 (13.48)	0.02*
HR	14.63 (9.28)	18.87 (8.70)	0.22

Abbreviations: MESOR, midline estimating statistics of rhythm; 2A,Double amplitude; SBP, systolic blood pressure; DBP, diastolic blood pressure.

*significant; **extremely significant.

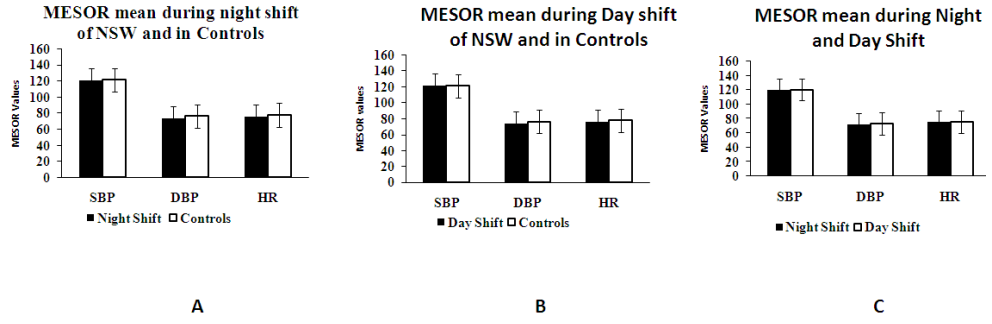

Figure 1. MESOR of SBP, DBP, and Heart rate during night shift, day shift and in controls. (A) MESOR of night shift workers during night shift and in controls. (B) MESOR of night shift workers during day shift and in controls. (C) MESOR of night shift workers during night shift and day shift. Abbreviations: MESOR, Midline statistics of rhythm; SBP, systolic blood pressure; DBP, diastolic blood pressure; HR, heart rate.

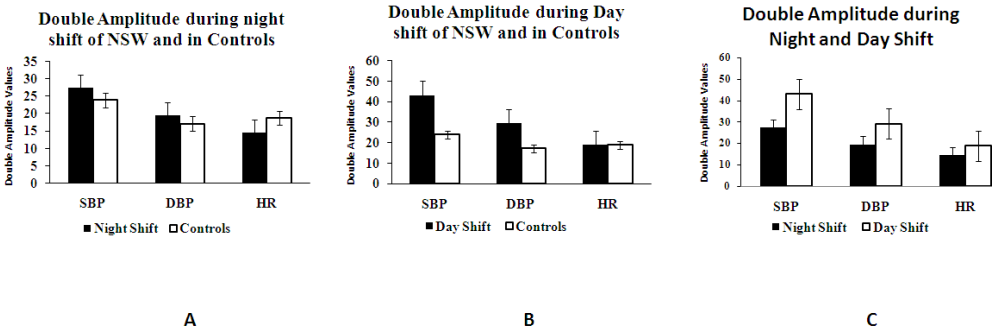

Figure 2. Double Amplitude of SBP, DBP, and Heart rate during night shift, day shift and in controls. (A) Double Amplitude of night shift workers during night shift and in controls. (**B**) Double Amplitude of night shift workers during day shift and in controls. (**C**) Double Amplitude of night shift workers during night shift and day shift. Abbreviations: MESOR, Midline statistics of rhythm; SBP, systolic blood pressure; DBP, diastolic blood pressure; HR, heart rate.

Night shift workers showed a very interesting altered circadian pattern when subject went back to the day shift (Figure 2) that means the effect of rotating night shift develops later due to frequently rotating shifts and associated desynchronization

Extremely significant patterns of SBP and DBP of double amplitude were found between day shift and controls ($p<0.01$) (Table 3). Changes in heart rate during day shift were not found, therefore a significant difference was not found in heart rate between day shift and controls or between night shift with day shift. When we compared night shift with day shift within the group, significant changes were found in the circadian pattern of systolic and diastolic blood pressure due to effects of the rotating night shift developing later during day shift but not in night shift ($p<0.05$).(Table 3).

The acrophase was significant clinically. Chronobiological study needs to evaluate the data individually, not statistically, and this will be interesting when we estimate time patterns i.e. time of overall peak values. The acrophase pattern was clinically significant when we studied individual subjects in different shifts with controls. Very interesting patterns of systolic blood pressure, diastolic blood pressure and heart rate acrophase were found during night shift, however during day shift incomplete recovery was found in a few subjects (Figure 3). Normal patterns of SBP, DBP and HR acrophase (within the range) was found in controls. Hyperbaric index (three hours fractionated time interval/upper limit of tolerance interval) is a parameter by which we can measure the changes above the tolerance limits. Alteration in hyperbaric index of SBP and DBP (ecphasia) was found during night and day shift therefore recovery was not found during day shift. (Figure 4). A change in heart rate of hyperbaric index was not found in different shifts and in controls. Ecphasia (odd timing of circadian pattern of blood pressure not heart) was clearly found during night and day shift.

Significant differences in MESOR were not found for night and day shift. Therefore hypertension was not found in night shift workers. A significant difference was found in double amplitude or predictable change during day shift. We concluded that the effect of rotating night shift was not apparent during the night shift however it develops later when subjects came back to day shift. Very interesting altered circadian patterns was found in night shift workers when subjects came back to the day shift. It indicated that the effect of rotating night shift develops later due to frequently rotating shift and subsequent desynchronization. The present study concluded that alterations in acrophase were persistent during night as well as the day shift due to incomplete recovery and ecphasia was very common among night shift workers.

Discussion

Night shift work has been reported to be associated with altered circadian patterns of blood pressure and desynchronization. The present study determines the effect of night shift on circadian patterns of blood pressure and heart rate and these effects were evaluated by comparison with actual controls who performed day duty. The study determines whether the changes in circadian pattern produced by night shift are reversible in due course of time.

Our results show the changes in the systolic and diastolic blood pressure double amplitude when subjects completed 8-9 days night shift and came back to day shift. The present observation confirmed the previous report of altered and reversed pattern of blood pressure and heart rate (acrophase) in night shift workers. [13, 17] Identical blood pressure and heart rate have been observed among night shift workers. [18] MESOR values were similar in shift workers and controls. On the basis of the findings of the altered circadian pattern of double amplitude we decided that effect of rotating night shift was not present during night shift however it develops later when the subjects came back to day shift. It indicated that the effect of rotating night shift develops later due to frequently rotating shift and desynchronization.

Night shift workers are awake when they are supposed to sleep and they attempt to sleep in day time when they are normally supposed to be awake. Previous findings were similar to our present study which showed that the odd timing of blood pressure (ecphasia) clearly indicates the non dipping pattern of blood pressure at night during night shift.

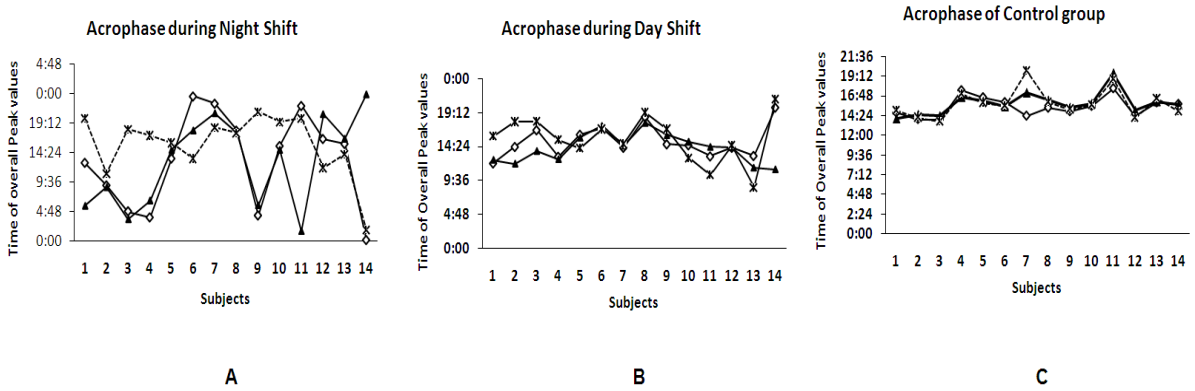

Figure 3. Acrophase (time of overall peak values) of SBP, DBP, and Heart rate. (A) Night shift. (B) Day shift. (**C**) In Controls. , Systolic blood pressure; Diastolic blood pressure; Heart rate.

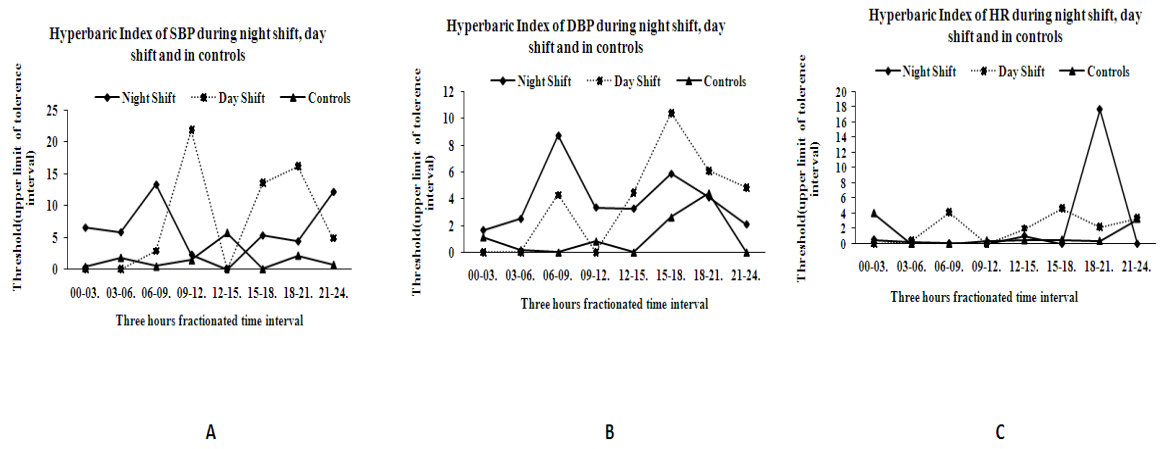

Figure 4 Hyperbaric index of night shift workers during night shift, day shift and in controls. (A) Systolic blood pressure. (B) Diastolic blood pressure. (C) Heart rate. Night Shift, Day Shift, Controls.

In view of these clinical manifestations c by our subjects it is possible that night shift work may be harmful for the health, family and social life. Other studies have also reported higher incidence of poorer sleep and its complications in night shift workers. [19-21] In our study, subjects complained of several sleep related problems viz, difficulty in sleep, sleepiness and other problems related to cognitive function like mental fatigue, difficulty in skilled work, problems remembering, decreased alertness, irritation and depression during night shift which are similar to previous study. [17] The most important physiological mechanisms regarding the shift work, particularly night shift work, is the problem of entrainment (resynchronization) of physiological functions after a phase shift of working and sleeping times. Other similar studies have shown that the shift work is associated with increased cardiovascular morbidity and mortality [22-24].

Singh et al have reported for the first time from India in the years 1988-2001, the results of ambulatory blood pressure monitoring for 4 to 7 days, in several studies among healthy subjects [25-27]. In one study [25], normal systolic and diastolic blood pressures with morning rise and dipping in the night have been reported in 2002. In other studies, subjects doing active prayer had lower heart rate and lower blood pressures compared to those who were not doing regular prayer [26]. It is possible that shift workers may benefit by doing active prayer, although such sub-study could not be done in this subset of shift workers. Singh et al also reported for the first time in the literature, a circadian decline in antioxidant vitamins, nitrite, coenzyme Q10 and magnesium and increase in oxidative stress during

second quarter of the day compared to values in the evening [27,28]. The adverse effects of shift work have been reviewed but no study has reported if shift work would be associated with greater decline in vitamins and greater increase in oxidative stress, because such findings may explain the pathogenesis of increased blood pressure variability, type 2 diabetes mellitus, hypertension insulin resistance and mortality among shift workers [22-24,29].

An Pan et al. contributed substantially to this field of research by examining the association between rotating shift work (≥3 nights/month plus days and evenings) and type 2 diabetes mellitus among 177,000 female nurses aged 25–67 at baseline followed up for up to two decades (the Nurses' Health Study)(30). This large-scale study revealed a graded association between the duration of working life the nurses had been engaged in shift work and risk of developing type 2 diabetes. Compared with women who reported no shift work, participants with 1–2 years of shift work had a 5% excess risk of type 2 diabetes, rising to 20% after 3–9 years, 40% after 10–19 years, and almost 60% for ≥20 years. Further studies showed that shift work can predispose obesity, diabetes and insulin resistance as well as CAD [31-36]. Further studies also reported similar results indicating changes in SBP and DBP seemed to be peak during waking time at the same time on the day off, as they did on the working day.

Whereas HRV profiles usually returned to baseline level after each shift. The SBP and DBP of night shift workers did not completely returned to the baseline levels the following off duty day. 12-h night shift work may elevate BP and HR and decrease HRV which may be associated with delayed blood pressure recovery [37-39]

In brief, it is possible that rotating night shift appears to have adverse effects on workers health, quality of family and social life as well as to patient care. Further studies in a larger number of subjects and long term follow up are necessary to confirm our findings. However, it may be advised that rotating night shift work should be avoided due to the development of the stage of desynchronization. However, we are increasingly residing in a society which wants to work 7 days in a week and 24 hours in a day. Therefore, option to eradicate shift working is not realistic. If the observed association between rotating shift work and noncommunicable diseases is causal, as observed in our study, additional efforts to prevent CVDs and type 2 diabetes among shift workers through promotion of healthy lifestyles, weight control, and early identification and treatment of prediabetic and diabetic employees are needed. Rotating shift work comprises a range of alternative schedule patterns, such as backward- and forward-rotating shift systems, and the proportion of night and early morning shifts varies. Our study, addressed some of these variations and identified a pattern that may minimize the risk. However, large-scale randomized trials are necessary to provide insights into causality.

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Conflicts of Interest

The authors declare there is no conflict of interest.

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Association of Obesity and Abdominal Adiposity with Blood Pressure in Adults

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Abstract

Objective: Obesity is a well known risk factor for cardiovascular diseases (CVD).The present study is aimed to assess the relationship of obesity and abdominal obesity on blood pressure in an adult Indian population.

Subjects and Methods: Cross-sectional survey was conducted among students and staff members of the university. Six hundred and sixty adult subjects (303 males + 357 females) untreated for hypertension in the age range of 21-60 years. Physical assessment included height, weight, circumferences of waist and hip, systolic blood pressure (BP) and diastolic BP besides the information on demographic variables. Body mass index (BMI) was calculated as weight in kg/height in meter^2 (kgm^{-2}), waist-to-hip ratio (WHR) as waist circumference/hip circumference. Logistic regression analysis was carried out apart from one way anova and correlations. Categorical variables are shown in percentages and continuous variables as mean±S.D.

Results: Men are found to have higher abdominal obesity (0.90±0.07) than women (0.84±0.08) ($p<0.05$) while no difference in BMI. The prevalence of hypertension increased with age and BMI quartiles. The indicators of adiposity (BMI, WHR) were positively associated with blood pressure in males, while in females only BMI shown a positive association. Men with higher WHR are 2.988 times, and women with higher WHR are 1.177 times at risk to develop hypertension. The odds of hypertension were more than six fold among the elderly in male sex (OR=6.213: 95%CI 1.815, 21.273), but in females the odds of hypertension in elderly is only two fold (OR= 2.423: 95%CI 0.801, 7.334). The odds of hypertension rose steadily with increase in BMI reaching 7.579 (95CI; 1.510, 38.046) in males and 15.56 (95%CI; 1.883, 128.526) in females with BMI >25 kgm^{-2}. Adjustment for age decreased the odds of hypertension in males and increased in females in the BMI category of >25 kgm^{-2}, while no change in the remaining quartiles.

Conclusion: These findings suggest a linear relation of adiposity with Blood pressure.

Keywords: Body Mass Index. Waist Hip Ratio. Abdominal Adiposity. Blood Pressure

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Introduction

The prevalence of obesity and its associated coronary heart disease (CHD) risk factors are increasing in developing countries [1,2]. Worldwide about 58% of diabetes mellitus and 21% of ischemic heart diseases are attributable to BMI above 21 kg/m^2 [3-5]. Developing countries are increasingly faced with a double burden of hypertension and other cardiovascular diseases, along with infection and malnutrition [1-4]. An increasing number of developing nations are acquiring atherogenic lifestyles which include the adoption of atherogenic dietary habits similar to those seen in industrialized societies. This appears to be consistent with economic development [5]. Major coronary risk factors are smoking, hypertension, dislipidemia, diabetes and obesity.

Obesity and hypertension have been shown to increase in parallel across populations along with their degree of development and Western acculturation [5,6]. Clinical and epidemiological studies indicate that developing countries have a higher susceptibility for developing obesity, central obesity, hypertension and coronary disease.[1-7]. The increased risk of obesity and hypertension may be partly explained by rapid changes in diet and lifestyle factors. The present study is aimed examined the relationship between adiposity (BMI and WHR) and blood pressure in a population where the prevalence of obesity is growing rapidly. It is possible that this information would be relevant for prevention and control of hypertension in developing countries.

Materials and Methods

The present study was conducted at Sri Venkateswara University, Tirupati, India. As a part of our University Silver Jubilee Celebrations, an Obesity Awareness Camp (OAC) was conducted by the Department of Anthropology, with an aim to create awareness about the adiposity among the staff and students of the University.

Formal written requests were sent to the individual faculty and circulars to student community to participate in the OAC. Of total 700 subjects who responded to publicity, 680 subjects volunteered and of these 20 subjects were excluded due to various reasons. Remaining 660 (303 males and 357 females) subjects, aged 21-60 years, volunteered given written informed consent to participate in the programme. Pregnancy (in women), usage of antihypertensive medication and any gross physical abnormality were the exclusion criteria against the physical measurements (n=20). The study protocol was approved by our Institutional Ethics Committee. The present study, focusing on adiposity and blood pressure (BP), has a cross-sectional descriptive design, allowing internal comparisons among the major sociodemographic groups, such as sex, education, occupation etc. The subjects were divided into 10 years age class intervals for internal comparison.

Data were collected using questionnaire and through physical measurements of weight, height, circumferences of waist and hip and Blood pressure. The survey instrument, mainly the questionnaire, has been validated in a small pilot study among our Departmental Staff and Students. The physical assessment included height, weight, circumferences of waist and hip were measured as specified by Reddy et al [8]. Weight and height were measured participants standing without footwear and wearing light clothing. Participants stood upright with the head in Frankfort plane for height measurement. Height was recorded to the nearest 0.5 cm and weight was recorded to the nearest 100g. Body mass index (BMI) was calculated as weight in kg/height in metre^2 (kgm^{-2}). Over weight was defined as BMI >23 and obesity was defined as BMI > 25 [8].

Waist girth was measured at the level of umbilicus with person breathing silently and hip measured as standing inter-trochanteric girth according to the WHO guidelines. Waist hip ratio (WHR) was calculated from the circumferences of waist and hip. Abdominal adiposity was defined as WHR>0.90 for males and >0.85 for females (9). Blood pressure was measured with a random zero muddler sphygmomanometer at the study site in a sitting position after the participant rested for at least 5 min. Three consecutive measurements were taken with an interval of 3 min in between.

Average systolic blood pressure and diastolic blood pressure were determined from the second and third measurements. Hypertension was diagnosed

when the systolic blood pressure was > 140 mmHg or the diastolic blood pressure was > 90 mmHg, as per the guidelines prescribed by the Joint National Committee on detection, evaluation and treatment of high blood pressure [10].

Statistical analysis was carried out via SPSS – 16.0 and alpha levels were set at $p < 0.05$. The prevalence rates were reported as percent. Continuous variables were reported as mean±1SD and differences between genders were tested by students 't' test. Further, logistic regression analysis was carried out to determine the odds of hypertension across the age groups, BMI and WHR categories, education and occupation, while controlling for possible confounding.

Results

Descriptions of the demographic and coronary risk factors are presented in table.1. In both the sexes, around 20 percent of sample is overweight, 15 percent are obese and 13 percent of the males and 18 percent of the females categorized as undernutrition. Forty percent of the males and 36 percent of the females had abdominal adiposity. The prevalence of undiagnosed hypertension in the present sample is 15% in males and 10% in females.

Physical measurements were available for all the participants, for whom the BMI and WHR could be calculated (table 2). The mean weight and height varied between male and female subjects. Men were taller and heavier than female counterparts. However, the resulting mean BMI in men (22.19±3.09) didn't vary with women (21.65±3.19). Male gender are found to have higher waist circumference than female gender ($p<0.05$), while no significant difference in hip circumference. Men are found to have higher abdominal adiposity (0.90±0.07) than women (0.84±0.08). Although males possess higher systolic and diastolic BP than females, significant difference observed only with systolic blood pressure ($p<0.05$).

Correlation coefficients for age, anthropometry and blood pressure is shown in table 3. The unadjusted pair wise correlations were higher in males than females.

Age has shown a positive association with anthropometry and blood pressure except in height. The correlation coefficients of SBP and DBP for age varied from 0.153- 0.275 ($p<0.05$) in men, from 0.219- 0.171 in women. The indicators of adiposity (BMI, WHR) were positively associated with blood pressure in males, while in females only BMI shown a positive association with blood pressure.

Conventional BMI cutoff points were applied to classify the study populations into underweight (BMI<18.5 kg/m^2), normal (BMI:18.5-22.99 kg/m^2), overweight (BMI:23.0-24.99 kg/m^2) and obese (BMI>25 kg/m^2); abdominal adiposity (Men >0.90; Women>0.85), and the distribution of hypertensives were shown in table 3.

The prevalence of hypertension increased with age and BMI quartiles. However, the extent of this association varied between different age groups and BMI quintiles. The rise in the prevalence of hypertension was more drastic at age group 41-50 years in male sex and 51-60 in female sex.

There is a steep increase in hypertension in second BMI quartile and with no difference to third quartile between sexes and sudden elevation in fourth quartile is noticed in male sex. The prevalence of hypertension is elevated in males and decreased in females with increase in abdominal adiposity.

Selected sociodemographic and adiposity characteristics that are considered as possible determinants of hypertension were subjected to a logistic regression analysis. The analysis was conducted separately for each sex and the resulting OR and 95% CI are presented in table 4. The BMI along with WHR and age were found to be significant determinants of hypertension in the study population. The odds of hypertension were more than six fold among the elderly in male sex (OR=6.213: 95%CI 1.815, 21.273), but in females the same is only two fold (OR= 2.423: 95% CI 0.801, 7.334).

The odds of hypertension rose steadily with increase in BMI reaching 7.579 (95CI; 1.510, 38.046) in males and 15.56 (95%CI; 1.883, 128.526) in females with BMI >25 kgm^{-2}. When age is adjusted in the model, the odds of hypertension sharply declined in male sex (OR=4.339, 95%CI; .698, 26.966) and an increase in female sex (OR=22.019, 95%CI; 2.343, 206.939) in the BMI category of >25 kgm^{-2}, while no change in the remaining categories.

Table 1. Description of the demographic and coronary risk factor characteristics

Variable	Males (n=303)	Females (n=357)
Age in years		
21-30	98 (32.34)	104 (29.13)
31-40	75 (24.75)	106 (29.69)
41-50	73 (24.09)	75 (21.01)
51-60	57 (18.81)	72 (20.17)
BMI Category		
<18.5	39 (12.87)	64 (17.93)
18.5 to 23.0	162(53.46)	162(45.38)
23.0-25	56 (18.48)	75 (21.00)
>25.0	46 (15.18)	56 (15.68)
WHR category		
Men <0.90; Women<0.85	180(59.41)	227(63.58)
Men >0.90; Women>0.85	123(40.59)	130(36.41)
Blood pressure		
Normotensive	258(85.15)	319(89.36)
Hypertensive	45 (14.85)	38 (10.64)

( ) = percentages.

Table 2. Descriptive statistics for the anthropometry and blood pressure in the study population

Variable	Males (Mean±SD)	Females (Mean±SD)	t-value
Height in cm	167.23±6.43 (151-186)	155.23±6.24 (145-176)	19.82*
Weight in Kg	62.18±9.95 (42-86)	52.21±8.50 (35-79)	11.33*
Body mass Index	22.19±3.09 (15.43-29.69)	21.65±3.19 (15.34-28.95)	1.80
Waist circumference in cm	82.11±11.43 (59-116)	75.59±10.39 (51-105)	6.26*
Hip circumference in cm	92.45±8.08 (66-121)	90.56±9.97 (54-121)	2.16*
WHR	0.89±0.07 (0.63-1.09)	0.84±0.08 (0.65-1.01)	6.81*
Systolic BP in mmHg	125.64±12.45 (91-152)	121.58±11.28 (86-153)	3.58*
Diastolic BP in mmHg	82.31±10.21 (50-108)	80.57±8.58 (54-104)	1.94

* $p<0.05$.

On the other hand when WHR and age independently and together adjusted in the model, no significant deviations taken place in the odds of hypertension among BMI categories of males, while in female sex the odds of hypertension increased in BMI >25 kgm-2. Men with higher WHR are 2.988 times at risk to develop hypertension than with lower WHR. Similarly women with higher WHR are 1.177 times at risk to develop hypertension when compared to lower WHR. When age and BMI independently and together adjusted to see the changes in odds of hypertension in WHR categories, a decline in the odds ratio is evident in both males and females. The odds of hypertension among the male employees (OR= 5.025, 95%CI 2.218, 11.383) is grater than female employees (OR= 1.262, 95%CI 0.550, 2.894) in developing hypertension.

Table 3. Distribution of hypertension across the age groups and BMI categories

Variable	Males (n=303)	Females (n=357)
Age in years		
21-30	6 (1.98)	9 (2.52)
31-40	6 (1.98)	12(3.36)
41-50	16(5.28)	3 (0.84)
51-60	17(5.61)	14(3.92)
Total	45 (14.85)	38(10.64)
BMI Category		
<18.5	3 (0.99)	2 (0.56)
18.5 to 23.0	12(3.96)	9 (2.52)
23.0-25	12(3.96)	12(3.36)
>25.0	18(5.94)	16 (4.48)
WHR Category		
Men <0.90; Women<0.85	16 (5.28)	22 (6.16)
Men >0.90; Women>0.85	29 (9.57)	16 (4.48)

( ) = percentages.

Table4. Determinants of high blood pressure in the study population (logistic regression)

	Males		Females	
	OR	95%CI	OR	95%CI
Age in years				
21-30	1.00		1.00	
31-40	1.326	0.315, 5.585	1.333	0.437, 4.065
41-50	4.414	1.313, 14.862	0.437	0.085, 2.264
51-60	6.213	1.815, 21.273	2.423	0.801, 7.334
BMI Category				
<18.5	1.00		1.00	
18.5 to 23.0	0.960	0.191, 4.814	2.471	0.289, 21.152
23.0-25	3.310	0.641, 17.085	8.000	0.968, 66.089
>25.0	7.579	1.510, 38.046	15.56	1.883, 28.526
WHR category				
Men <0.90; Women<0.85	1.00		1.00	
Men >0.90; Women>0.85	2.988	1.336, 6.683	1.177	0.504, 2.748
Education				
Graduation	1.00		1.00	
Post graduation	0.833	0.345, 2.015	0.967	0.422, 2.217
Occupation				
Student	1.00		1.00	
Employee	5.025	2.218, 11.383	1.262	0.550, 2.894

Discussion

In this study, we examined the relationship of hypertension with obesity and abdominal adiposity in a suburban population. The results indicate a unpretentious, but significant linear association of BMI and WHR with blood pressure in males, independent of age. No such association WHR was observed in females. However, BMI greater than 25 kg/m^{-2} was associated with increased risk of

hypertension in presence of higher abdominal obesity. These findings are in agreement with other studies, supporting a comsistent relationship between body mass and abdominal adiposity with Blood Pressure [11]. Logistic regression analysis revealed that obesity, abdominal obesity and age were significant determinants of hypertension in males and females. In presence of insignificant differences in the relationship of BP with adiposity in female gender provides substantial argument against a lower hypertensive effect of obesity than male gender.A few studies from India have also reported the adverse effects of obesity on coronary risk factors and mortality [1-4] A recent cross-sectional survey [1,3], screened 6940 subjects, (3507 men (M), 3433 women (W): 1993-96)aged 235 nyears and above, from cities located in five corners of India (Kolkata, n=900; Nagpur, n=894; Mumbai, n=1542; Thiruanantpuram, n=1602; Moradabad, n=2002). The overall prevalence of obesity was 6.8% (7.8 vs. 6.2%, P<0.05) and overweight 33.5% (35.0 vs. 32.0%,P 0.05) among women and men, respectively.The highest prevalence of obesity (7.8%) and overweight (36.9%) was found among subjects aged 35 to 44years in both sexes. The prevalence of obesity was significantly (P <0.05) greater in Trivandrum (8.5%), Calcutta (7.1%) and Bombay (8.3%) compared to Moradabad (6.2%) among women and in Trivandrum (7.4%) and Bombay (7.2%), compared to Nagpur (5.0%) among men.There was a significant decreasing trend in obesity (P <0.05) and overweight (P<0.05) with increasing age above 35-44 years in both sexes.The overall prevalence of subjects >23kg/m2 was 50.8% and central obesity 52.6%.The overall prevalence of sedentary behaviour was 59.3% among women and 58.5% among men. Both sedentary behavior and mild activity showed a significant increasing trend in women after the age of 35-44years. In men, such a trend was observed above the age of 45years. Sedentary behaviour was significantly (P <0.05) greater in Trivandrum, Calcutta, and Bombay compared to Nagpur. Sedentary behaviour was significantly (P <0.001) associated with obesity in both sexes, compared to non-obese men and women. The overall prevalence of undernutrition was 5.5% (n=380). Diagnosis for prehypertension (BP 130-139/85-89 mm Hg) and hypertension (BP≥140/90 mm Hg) were based on European Society of Cardiology criteria [3]. Prevalence of pre-hypertension and hypertension, respectively, was significantly greater in South India (Trivandrum: W 31.5;31.9%; M 35.1;35.5%) and West India (Mumbai: W 30.0;29.1%; M 34.7;35.6%) compared to North India (Moradabad: W 24.6;24.5%; M 26.7;27.0%) and East India (Kolkata: W 20.9;22.4%; M 23.5;24.0%). Subjects with pre-hypertension and hypertension were older, with higher BMI, central obesity and of sedentary behavior. They had higher salt and alcohol intake, with greater oral contraceptive usage (W). Multivariable logistic regression analysis, revealed strong positive associations of hypertension with age, central obesity, BMI, sedentary lifestyle, salt and alcohol intake and oral contraceptive usage (W). Fruit, vegetable and legume intake showed inverse associations, tobacco intake showed none. In one survey [4] of death records among 2222 subjects, aged 25 to 64 years, majority of the decendents(n=792,35.6%) (men 31.1%,n=431; and women 43.1%,n=361) had normal BMI of 18.5-22.9Kg/m2.The prevalence of underweight victims was 14.2%(n=315), overweight 29.4%(n=654)and obese 20.8%(n=461).There was an overall increase in risk factors; diabetes mellitus, hypertension, and CAD among overweight and obese victims based on BMI criteria, and the trend was significant. However, tobacco intake showed nonsignificant trend, highest in the underweight victims, without significant differences in the other categories of BMI. BMI was positively associated with significant rising trend in the prevalence of circulatory causes of death, both among men and women [4].

The evidence presented above supports a common general physiopathological mechanism linking the excessive fat deposition to elevated BP independently of genetic and environmental background. The mechanism of obesity-associated hypertension appears to be an inadequate vasodilatation in the face of the increased blood volume and cardiac output, which are the natural consequences of an increased body mass. This defect in control of vascular resistance has been attributed to increased activity of the sympathetic nervous system, abnormal renin-angiotensin-aldosterone relations, and insulin resistance [12]. Obesity seems to accentuate the development of a cluster of metabolic disorders (including hypertension and dyslipidemia) in subjects

presenting the syndrome X, referred to as the insulin resistance syndrome [13].

The relationship of BP to cardiovascular mortality has been found to be similar among different countries, continuous and linear, even at the lower range of BP, ie, below the cut-off points (140/90 or 160/95 mmHg) generally used to define hypertension [14]. Therefore, changes in BP corresponding to defined gains in adiposity can directly be converted into their effect on the relative risk of death from cardiovascular diseases. Measuring the relation of the adiposity parameters (BMI, WC and WHR) to BP by only considering the prevalence of hypertension would underestimate their real impact on mortality. The prevalence of hypertension at different BMI quartiles revealed a steep rise at fourth quartile in both males and females. Significant associations between BMI and BP have also been documented in various populations [15].

Similar findings have been reported in other studies (16). The relationship between adiposity and BP in this study might be potentially confounded by dietary salt intake and physical activity levels, both of which are not available for the present sample. The study demonstrated that adiposity is closely associated with BP in countries at different stages of socioeconomic and epidemiologic transition. Mean BP levels are increasing with categories of BMI and WHR. The risk of hypertension is higher with overall and abdominal obesity. Together with data from other studies [17], there is an overall convergence of evidence towards a steeper rise in BP with the advance of age in developing countries when compared to developed countries. In the present study, this mechanism proved to be independent of body mass and abdominal adiposity while some experts think that body mass is the dominant causal factor [18]. Further research is needed to determine the etiopathology of this mechanism which have been emphasized in other studies (19-25). Oxidative stress, insulin resistance in association with obesity have been reported from India (20,21). In south Asia, only modest increase in BMI above 23Kg/M2 has been associated with insulin resistance and hypertension [21-24]. In view of these findings,it has been proposed that south Asians appear to need modified guidelines regarding diet and lifestyle changes on prevention of CVDs [24,25].

In brief, the findings indicate age-independent linear association between BP and adiposity. A modest increase in BMI appear to be associated with central obesity and hypertension. The present study shares the views about the recommendations of WHO [19] for developing countries by promoting physical activity and healthy dietary habits, including the reduction of alcohol drinking and salt intake and increase in the intake of fruits,vegetables and legumes which are probably important risk factors of high BP with the advance of age.

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Diet and Lifestyle Guidelines and Desirable Levels of Risk Factors for Prevention of Cardiovascular Disease and Diabetes among Elderly Subjects. A Revised Scientific Statement of the International College of Cardiology and International College of Nutrition-2011

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Abstract

Elderly subjects have unique nutrient needs with revised recommended dietary reference intakes based on age, sex, ethnicity and special vulnerability to compromised nutrient status. The food intake tends to decrease with advancing age due to decreased physical activity and metabolic rate. However vitamin; A,E,C, B vitamins and beta-carotine and minerals magnesium, calcium, selenium, chromium, zinc and copper as well as w-3 fatty acids needs either remain constant or increase. Omega-3 fatty acid, calcium, vitamin D and magnesium and antioxidant intakes are inversely associated with ageing and other complications like cardiovascular diseases, diabetes and dementia as well as cancers. It is pertinent to advise to eat 400g/day of fruits, vegetables and nuts and another 400g/day of whole grains in conjunction with 25-40g/day of canola oil or mustered oil, depending upon energy requirement, for prevention of cardiovascular disease and type 2 diabetes mellitus.

Keywords. Ageing, older population, foods, nutrition, chronic diseases

Introduction

Non-communicable diseases such as cardiovascular diseases (CVD), diabetes mellitus, metabolic syndrome and cancer have become a major health problem in the Western world and these are rapidly increasing in the developing world with ageing of the population [1-3]. Elderly populations have unique nutrient needs with revised recommended dietary reference intakes based on age, and special vulnerability to compromised nutrient status. The food intake tends to decrease with

advancing age to compensate for reduced energy requirements, however vitamin; A,E,C, B vitamins and beta carotine and minerals magnesium, calcium, selenium, chromium, zinc and copper as well as w-3 fatty acids needs either remain constant or increase. Omega-3 fatty acid and minerals; magnesium intakes are inversely associated with ageing [1-3]. The overconsumption of energy and nutrients must be avoided. Specific nutritional needs of elderly people were addressed in the Food Guide Pyramid for Older Adults, a modification of the 1990 Food Guide Pyramid for Americans. In 2005, the US Department of Agriculture (USDA) released MyPyramid (Figure 1), which includes an Internet-based program allowing individuals to calculate food-based dietary guidance based on their specific clinical variables. However, older adults tend to be less comfortable with Internet use, so a graphic representation for a Modified MyPyramid for Older Adults is intended for use in this age group as an adjunct to the current Web-based MyPyramid. Such approaches are no good for the developing world where most elderly do not use internet. Singh et al have published several diet and lifestyle guidelines for prevention of cardiovascular diseases and diabetes among adults [4-6].These guidelines may be modified in context of their lower food intake and increased requirement of nutrients in the elderly population. It seems that elderly need more fruits, vegetables, nuts and whole grains as well as more w-3 fatty acid rich oils for prevention of chronic diseases in general and brain degeneration in particular [1-3].

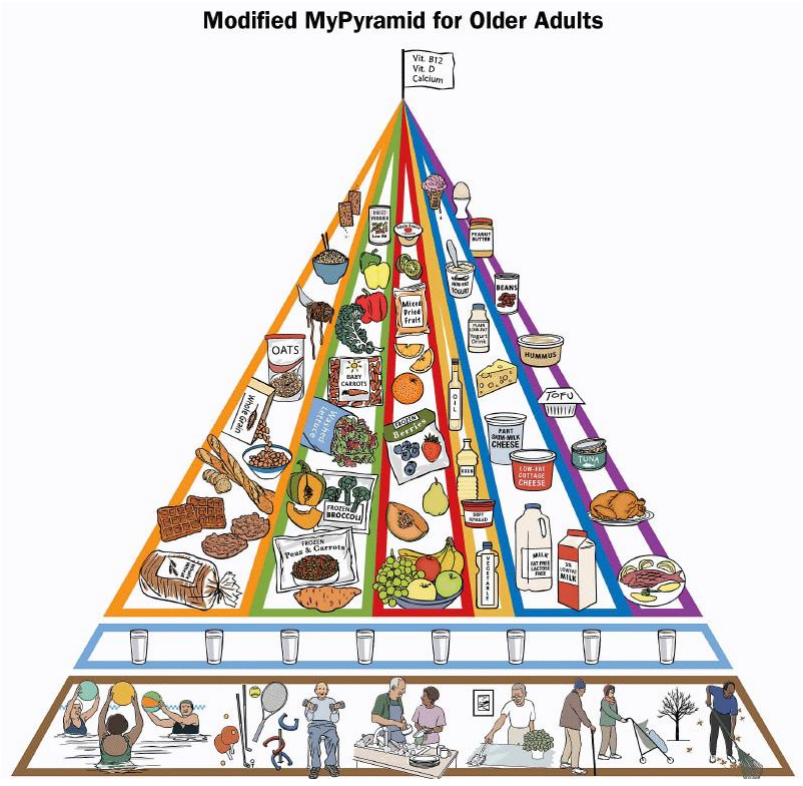

Figure 1. Modified MyPyramid for Older Adults.

How Elderly Differ from Adults

Non-communicable diseases (NCD) are much more common among elderly than among adults. Prevention of NCDs has been shown to be related to specific nutrients, so the key element in planning diets for the elderly should be nutrient based dietary guidelines [1-3]. In order to reduce the burden of chronic diseases by nutritional means, nutrient based guidelines, become, essential to develop. Elderly people have distinctly different metabolic processes

that do not allow for easy extrapolation of nutrient needs from results of experiments performed on younger adults. Because adults over 70 years consume less food than younger people, primarily due to decreases in energy expenditure, which is important to emphasize for old people. Special considerations regarding nutritional needs of the elderly population are that food intake tends to decrease with advancing age, because of reduced energy needs associated with lower energy expenditure in physical activity and basal metabolic rate. However, requirements for vitamins and minerals either remain stable or increase.

United States Food Pyramid

A Modified Food Guide Pyramid was developed for adults aged 70 years and older to address their unique dietary challenges in 1999. Compared with the original USDA Food Guide Pyramid, the modifications included narrowing the base to reflect lower energy needs of older adults because of changes in body composition and metabolic rate. Selected food icons with nutrient-dense examples were replaced to help reconcile decreased food intake with unchanged or increased recommended dietary allowances. Addition of a fiber icon was done in appropriate food categories to facilitate achieving adequate intakes to promote optimal bowel function. A row of glasses at the base of the pyramid were included to remind older adults to maintain adequate fluid intakes; and placement of a flag at the top to alert some older adults that their healthcare provider should consider recommending vitamins B_{12} or D or calcium supplements. Looking upon nutrients as modulators of chronic disease risk represents an important paradigm shift. These nutrients are known to decrease homocysteine (B vitamins and folic acid) for reducing risk of atherosclerotic cardiovascular disease and prevent the bone demineralization and osteoporosis(calcium and vitamin D). The newly evolving Recommended Dietary Intakes in the world would define nutrient intake levels that should decrease an individual's risk of developing chronic diseases and degenerative conditions that are related to specific nutrients and associated with negative functional outcomes [7-9]. There is increased requirement of antioxidant nutrients vitamins C and E and selenium for the prevention of atherosclerotic CVDs and/or certain site-specific cancers and of the carotenoids, zeaxanthin and lutein, and the prevention of age-related macular degeneration as well as cancers [1-10]

The New American Guidelines

The 2010 Dietary Guidelines is available at www.dietaryguidelines.gov . Further details can be seen by visiting; www.health.gov/dietary guidelines and www.healthfinder.gov/prevention. The new guidelines advise that certain basic factors be taken into account when making daily food choices, such as age, ethnicity, and risk factor for diet-related chronic illnesses like diabetes and heart disease. The Dietary Guidelines also call for significant, specific reductions in food components like salt, added sugars, processed flour, solid fats, and saturated fats according to varying factors. The most notable of these specified restrictions is for sodium (salt) intake for persons who are age 51 or older; African American; or have hypertension, diabetes, or chronic kidney disease from the regular 2,300mg to 1,500mg.The Guidelines further change course by not only listing foods that should be encouraged, but also listing foods that should be reduced, such as grain-based deserts, regular cheese, dairy deserts, and even chicken dishes. The USDA supplies multiple pie-charts that show where the average American is going wrong with their diets. Continuous listings of statistics involving diet-related chronic illnesses appears to be the most attention-grabbing element of the Dietary Guidelines for Americans 2010. According to the document, 72 percent of men and 64 percent of women in the United States are overweight or obese, 37 percent of the population has cardiovascular disease, and 35 percent of the adult population suffers from pre-diabetes. In fact, the prevalence is much greater among elderly populations which indicates that the need for nutritional modulators of chronic diseases is greater among elderly subjects compared to adults. There is no advice on adverse effects of w-6 fatty acids and beneficial effects of w-3 fatty acids in the American guidelines.

How to Provide Nutrient Rich Foods to Elderly?

Recent studies indicate that Mediterranean diet, Indo-Mediterranean diet and Japanese diet are rich sources of protective nutrients as well as are known to decrease morbidity and mortality among various population groups [11-28]. Apart from these diets, consumption of nuts, chocolates, Mediterranean soups, fish as well as fish oil have been found to reduce the risk of cardiovascular diseases and diabetes (10-20). Therefore these foods should be preferred among elderly populations in both developing and developed countries for prevention of NCDs.

To evaluate the association of chocolate consumption with the risk of developing cardiometabolic disorders, systematic review and meta-analysis of randomised controlled trials, cohort, case-control, and cross sectional studies carried out in human adults, in which the association between chocolate consumption and the risk of outcomes related to cardiometabolic disorders were reported [10].Data were extracted by two independent investigators, and a consensus was reached with the involvement of a third. The primary outcome was cardiometabolic disorders, including coronary heart disease and stroke, diabetes, and metabolic syndrome. A meta-analysis assessed the risk of developing cardiometabolic disorders by comparing the highest and lowest level of chocolate consumption.

From 4576 references seven studies met the inclusion criteria (including 114 009 participants). None of the studies was a randomised trial, six were cohort studies, and one a cross sectional study. Large variation was observed between these seven studies for measurement of chocolate consumption, methods, and outcomes evaluated. Five of the seven studies reported a beneficial association between higher levels of chocolate consumption and the risk of cardiometabolic disorders. The highest levels of chocolate consumption were associated with a 37% reduction in cardiovascular disease (relative risk 0.63 (95% confidence interval 0.44 to 0.90)) and a 29% reduction in stroke compared with the lowest levels.Based on observational evidence, levels of chocolate consumption seem to be associated with a substantial reduction in the risk of cardiometabolic disorders. Further experimental studies are required to confirm a potentially beneficial effect of chocolate consumption.

Pathogenesis of Diet and Risk of Diseases

There is evidence that Western diet may be important in the pathogenesis of non-communicable diseases and all cause mortality [21-28]. The beneficial or adverse effects of certain foods may be due to their effects on inflammation, free fatty acids, hyperglycemia, hyperinsulinemia, oxidative stress, hypertriglyceridemia, hypercholesterolemia and high oxidized low density lipoprotein cholesterol (LDL) as well as on oxidized high density lipoprotein cholesterol(HDL), which are considered to be highly atherogenic [21-24]. These risk factors and other biological factors cause an adverse impact on vascular biology resulting in to endothelial dysfunction and inflammation which may be independently athero-thrombotic [29-33]. Hormone replacement therapy (HRT), oral contraceptive intake in women, anti-inflammatory effects of statins [29] and postprandial endothelial dysfunction and inflammation are indicator of vascular index responsible for atherosclerosis. In women, oestrogen therapy has been used to lower their cardiovascular risk in post-menopausal women, prior to HRT trials, showing no beneficial effects. Oestrogens are known to decrease LDL and increase HDL but they also increase proinflammatory C-reactive protein, coagulation and lipotrotein(a), which are known for their adverse effects on atherothrombosis [29-33]. It seems that vascular biological states appear to be most important determinant of atherothrombosis compared to circulating LDL, although most expert give greater importance to circulating LDL. Infact C-reactive protein has been found to be as predictive of subsequent coronary events as LDL on treatment with statins [29]. The concentration of oxidized LDL particularly in the vascular cells, depends on the internal antioxidant environment which is determined by dietary patterns. Dietary patterns consisting of high intakes of vegetables, fruits, legumes, fish, poultry, and whole grains, have been found to be protective against risk from cardiovascular disease (CVD) and malignant diseases.[21-26]. Dietary patterns closer to

a Western diet have adverse effects on these biomarkers and risk of CVD, diabetes and cancer. Other primary risk factors such as sedentary behaviour, tobacco intake, alcoholism and stress are also known to increase the risk of chronic diseases of affluence.

The Concept of Paleolithic Diet and the Ying Yang Tsim Tsoum Concept

About 40,000 years ago, our genes appear to be similar to the genes of our ancestors during the Paleolithic period, the time when our genetic profile was established. Man appears to live in an nutritional environment which completely differs from that for which our genetic constitution was selected. However, it was only during the last 100-160 years that dietary intakes have changed significantly, causing increased intake of saturated fatty acids (SFA) and linoleic acid, and decrease in w-3 fatty acids, from grain fed cattle, tamed at farm houses, rather than meat from running animals. The food and nutrient intake among hunter-gatherers and during Paleolithic period are given in Tables 1, 2. There is marked reduction in consumption of w-3 fatty acids, vitamins and minerals and proteins and significant increase in the intakes of carbohydrates, (mainly refined,), fat (saturated, trans fat, linoleic acid) and salt compared to Paleolithic period.

The Columbus concept of diet means that humans evolved on a diet that was low in saturated fat and the amount of w-3 and w-6 fatty acids was quite equal.[23,40]. Nature recommends to ingest fatty acids in a balanced ratio (polyunsaturated: saturated=w-6:w-3=1:1)as part of dietary lipid pattern in monounsaturated fatty acids(P:M:S=1:6:1).These ratios represent the overall distribution of fats in a natural untamed environment. (www.columbus-concept.com). The Columbus foods include egg, milk, meat, oil , and bread, all rich in w-3 fatty acids, similar to wild foods, consumed about 160 years ago from now. Blood lipid composition does reflect one's health status: (a) circulating serum lipoproteins and their ratio provide information on their atherogenicity to blood vessels and (b) circulating plasma fatty acids, such as w-6/w-3 fatty acid ratio, give indication on pro-inflammatory status of blood vessels.; (a) and (b) are phenotype-related and depend on genetic, environmental and developmental factors. As such, they appear as universal markers for holistic health. Blood cholesterol is central to this approach. Its 3D-representation shows how circulating lipoproteins affect blood vessels integrity upon their circulating throughout the body. Of major importance appear the essential dietary nutrients (essential amino acids, fatty acids, antioxidant vitamins and minerals) and the functional component of the regimen (diet, sport, spiritualism, etc).The Ying Yang Tsim Tsoum (YYTT) Concept is an extension of the Columbus Concept (YYCC). While YYCC is a 1-D approach that establishes the basis for the "essential" components of the diet, YYTT is a 2-D approach that focuses on the "functional" components of the lifestyle; stress, sedentary behaviour, meditation. YYCC and YYTT are complementary and do not compete against each other. Chronobiology is an important aspect of YYTT because it is based on mind- brain- body interactions.(http://www.tsimtsoum.net/introduction_07.php). It seems that the YYTT approach favors the analysis of memes and genes as well as of (hu)man's influence on nature and also possibly the influence of nurture and environment on human health and behaviour. In several studies, breathing exercises, meditation and yoga have been found to influence brain function, cardiovascular function as well as biomarkers [32-34]. Experimental studies [35-37] indicate that ω3 PUFAs play an important role in neuronal structure and function. The brain is quite rich in ω3 PUFAs and several studies suggest a role for ω3 PUFAs in neurotransmitter synthesis, degradation, release, reuptake and binding [35-37]**.**

Fatty acids belong to the phospholipid group and, consequently, are part of all biological membranes. The membrane's fluidity, which is of crucial importance for its functioning, depends on its lipid components. Phospholipids built up of chains of polyunsatured fatty acids increase the membrane fluidity because, by binding some chains, double bonds prevent them from compacting themselves perfectly.

In addition, membrane fluidity is determined by the phospholipids/free cholesterol ratio, as cholesterol increases membrane viscosity.

Table 1. Food and nutrient intake among hunter-gatherer and western population

Food and nutrient	Huntergatherer	Western population
Energy density	Low	High
Protein	High	Low-moderate
Animal	High	Low –moderate
Vegetable	Very low	Low –moderate
Carbohydrate	Low-moderate(slowly absorbed)	Moderate-rapidly absorbed
Fiber	High	Low
Fat	Low	High
Animal	Low	High
Vegatable	Very low	High
Total w-3	High(2.3g/day)	Low (0.2g/day)
Ratio w-6:w-3	Low 2.4	High 15-20
Vitamins and minerals	high	low

Modified from ref [19,20].

Table 2. Estimated fatty acid consumption in the late Paleolithic period

Sources	Fatty acids(g/day) en 35.65/day
Plants	
Linoleic acid	4.28
Alpha-linoleic acid	11.40
Animal	
Linoleic acids	4.56
Alpha-linolenic acid	1.21
Total	
Linoleic acid	8.84
Alpha linolenic acid	12.60
Animal	
Arachidonic acid(w-6) (AA)	1.81
Eicosapentaenoic acid(w-3)(EPA)	0.39
Docosatetraenoic acid(w-6) (DTA)	0.12
Docosapentaenoic acid(w-3)(DPA)	0.42
Docosahexaenoic acid(w-3)(DHA)	0.27
Ratios of w-6/w-3	
Linoleic acid/alpha linolenic acid	0.70
AA+DTA/EPA+DPA+DHA	1.79
Total w-6/w-3	0.79

Modified from Eaton et al in ref [19,20].

DHA deficit is associated with dysfunctions of neuronal membrane stability and transmission of serotonin, norepinephrine and dopamine, which might be related to the aetiology of the mood and cognitive dysfunction of depression [38,39]. On the other hand, EPA is essential to balance the immune function and physical health by reducing the proportion of arachidonic acid (AA, C20:4ω6) in cell membrane and prostaglandin E2 (PGE2) synthesis. A diet based on a high proportion of essential polyunsatured fatty acids allows a higher incorporation of cholesterol in the membranes to balance their fluidity, which, in turn, would contribute to lower blood cholesterol levels and inflammation and lower risk of CVD and psychological disorders [37-39]. These interactions of

diet, neurotransmitters, neuronal function and other body functions and dysfunctions provide a basis for YYTT concept and the mind-body connection.

New Biomarkers for CVD and Dietary Patterns

Several epidemiological studies, have reported an inverse relationship between consumption of fruits and vegetables and the incidence of coronary artery disease (CAD) [21-24]. Only a few randomized, controlled trials, using fruits, vegetables, legumes, fatty acids, and nuts are available, showing significant reduction in mortality and cardiovascular events [25-27]. There is further evidence that inflammation could be an independent mechanism for pathogenesis of atherothrombosis, resulting into heart attack or acute coronary syndrome (ACS)(28-30). Therefore, statins are being used for primary prevention of cardiovascular events in patients with increased high sensitive C-reactive proteins (hsCRP), without much consideration of serum cholesterol levels (29). Moreover, LDL cholesterol becomes atherogenic only, when it is modified into oxidized LDL cholesterol, which is most attractive to macrophages in the pathogenesis of atherosclerosis. It seems that statins not only reduce LDL but also decrease oxidized LDL which may be more important for prevention of CVD. The results of the JUPITER (Justification for the Use of statins in Primary prevention: an Intervention Trial Evaluating Rosuvastatin) trial add up to a formidable amount of information about the beneficial effects of statins in healthy subjects with high hsCRP [29]. High levels of CRP as well as other proinflammatory cytokines; interleukin-6 (IL-6), IL-1,IL-18 and tumor necrosis factor-alpha are also risk factors of CVD, diabetes, brain degeneration, psychological disorders and cancer[30-39]. The JUPITER study screened almost 90, 000 healthy volunteers aged 50 years or more for participation in this trial among healthy subjects. One in five [17, 802] of those screened were included in the trial. Treatment with statin is not indicated in such individuals because they had no history of CAD, and their LDL-cholesterol levels were below the usual threshold for treatment of 130 mg/dL (3.33 mmol/L). Those who achieved a dual treatment target of LDL cholesterol lower than 1.8 mmol/l (70 mg/dl) and hsCRP lower than 2 mg/l had a 65% reduction in CVD events, compared with a 33% reduction in patients who achieved one or neither target. The authors reported that participants who achieved an LDL cholesterol level of below 1.8 mmol/l (70 mg/dl) had a 55% reduction in CVD events and those who achieved a hsCRP reduction of below 2 mg/l a 62% reduction, which is slightly greater benefit compared to LDL reduction. However, patients who achieved the more stringent target of a LDL cholesterol level of below 1.8 m mol/l (70 mg/dl) and a hsCRP reduction of below 1 mg/l had a 79% reduction in CVD events. This shows that decrease in inflammation in conjunction with LDL reduction has greater benefit at the same level of LDL reduction, which appears to be due to a further decrease in oxidized LDL. There is a need to measure oxidized LDL as well as total LDL to find out the mechanism of this interaction.

A metaanalysis, quantitatively assessed the relation between fruit and vegetable intake and incidence of CAD in all cohort studies which reported relative risks (RRs) and corresponding 95% confidence interval (CI) of CAD with respect to frequency of fruit and vegetable intake [22]. These studies, included a total of 278 459 individuals (9143 CAD events) with a median follow-up of 11 years. The individuals who had less than 3 servings/day of fruit and vegetables, the pooled RR of CAD was 0.93 (95% CI: 0.86–1.00, P¼0.06) while those with more than 5 servings/ day , the RR was 0.83 (0.77–0.89, P<0.0001).This meta-analysis of prospective cohort studies demonstrated that increased consumption of fruit and vegetables, less than 3 to more than 5 servings/day is related to a 17% reduction, whereas increased intake to 3–5 servings/day is associated with a smaller and borderline significant reduction in CAD risk. These results provide evidence supporting that 5 or more servings per day of fruit and vegetables, are needed to protect from CVD. In a large, prospective, observational study (24) involving 72,113 female nurses who were free of CAD, stroke, diabetes, and cancer, factor analysis identified 2 dietary patterns from data collected on serial food frequency questionnaires. One pattern, called prudent, was characterized by a high consumption of vegetables, fruit, legumes, fish, poultry, and whole grains. The other pattern, called Western,

corresponded to a high consumption of red meat, processed meat, refined grains, french fries, sweets, and desserts. Individuals were classified by their level of adherence to both the prudent diet and the Western diet. After baseline data collection in 1984, follow-up lasted 18 years, during which time 6011 deaths occurred (3319 [52%] as a result of cancer; 1154 [19%] resulting from CVD; and 1718 (29%) resulting from other causes. In multivariable analyses, there was a 17% lower risk of total mortality among those who were most adherent to the prudent diet (highest versus lowest quintile of adherence), a 28% lower risk of CVD mortality, and 30% lower mortality from non-CVD, non-cancer causes. Interestingly, there was no significant relationship between the prudent dietary pattern and cancer. A comparison of the highest and lowest quintiles of adherence showed that consumption of the Western diet was associated with increased total mortality (21%), CVD mortality (22%), cancer mortality (16%), and mortality from non-CVD, non-cancer causes (31%). Hence, except for cancer, risk relationships for the prudent and Western dietary patterns appear to be the inverse of each other: Mortality thus was increased as adherence to the prudent diet decreased and adherence to the Western diet increased.

The relationship between dietary patterns and risk of acute coronary syndrome (ACS) was examined in a standardized case-control study INTERHEART, involving participants from 52 countries.[41] Using the principle-component analysis technique, the authors identified 3 major dietary patterns; Oriental (high intake of tofu and soy and other sauces), Western (high in fried foods, salty snacks, eggs, and meat), and prudent (high in fruit and vegetables). Consistent with previous studies in single within-population cohort studies, the authors found an inverse association between the prudent pattern score and risk of ACS and a significant positive association between the Western pattern score and increased risk of ACS. The Oriental pattern was not significantly associated with risk. The investigators constructed a dietary risk score based on 7 food items on the food-frequency questionnaire (meat, salty snacks, fried foods, fruits, green leafy vegetables, cooked vegetables, and other raw vegetables) and found that a higher score (indicating a poor diet) was strongly associated with ACS risk: Those in the highest quartile of the score had nearly 2-fold increased risk, even after adjustment for established coronary risk factors. In sensitivity analyses, the investigators found a consistent association for the composite diet score between men and women and across different regions of the world (North America, western Europe, Australia, central Europe, Middle East, Africa, south Asia, southeast Asia, China, and South America). On the basis of an arbitrary cut point of the score (top 3 quartiles versus the bottom quartile), the investigators estimated that 30% of MI could be explained by unhealthy diets worldwide.

Although Western-style changes in food patterns are widely believed to adversely influence risk of chronic diseases, few epidemiological studies have directly linked dietary patterns and mortality from coronary heart disease. The INTERHEART study is the first large study to quantify eating patterns in all geographic regions of the world. It provides evidence that despite different food habits in various populations, reproducible patterns can be found in diverse regions of the world. These findings are important because there has been a concern that dietary patterns derived through a data-driven approach such as principle-component analysis may be highly unstable and nonreproducible because of very different eating habits in different populations.

In recent years, dietary-patterning analysis has been increasingly used as an alternative method to traditional single-nutrient analysis because it can assess cumulative effects of the overall nutrients in the diet. Habitual intake patterns are typically quantified by statistical methods such as factor or cluster analysis or diet-quality indexes based on prevailing dietary recommendations or healthful traditional diets eg, the Mediterranean diet, and Indo-Mediterranean diet. Principle-component analysis is commonly used to define dietary patterns using food consumption information to identify common underlying dimensions (factors or patterns) of food intake. The method aggregates specific food items based on the degree to which these food items are correlated with each other. A summary score for each pattern is then derived and can be used to examine relationships between various eating patterns and outcomes of interest such as coronary heart disease and other chronic diseases. Previous validation studies found that 2 major patterns (the prudent and Western

patterns) identified through principle-component analysis of food consumption data assessed by food frequency questionnaires were reproducible over time and correlated reasonably well with the patterns identified from diet records.

In a more recent study [42], 74 886 women 38 to 63 years of age in the Nurses' Health Study, a cohort study of female nurses, without a history of cardiovascular disease and diabetes were followed up from 1984 to 2004. The authors computed an Alternate Mediterranean Diet Score from self-reported dietary data collected through validated food frequency questionnaires administered 6 times between 1984 and 2002. Relative risks for incident CAD, stroke, and combined fatal cardiovascular disease were estimated with Cox proportional-hazards models adjusted for cardiovascular risk factors. During 20 years of follow-up, 2391 incident cases of CAD, 1763 incident cases of stroke, and 1077 cardiovascular disease deaths (fatal CAD and strokes combined) were ascertained. Women in the top Alternate Mediterranean Diet Score quintile were at lower risk for both CAD and stroke compared with those in the bottom quintile (relative risk [RR], 0.71; 95% CI, 0.62 to 0.82; *P* for trend<0.0001 for CHD; RR, 0.87; 95% CI, 0.73 to 1.02; *P* for trend=0.03 for stroke). Cardiovascular disease mortality was significantly lower among women in the top quintile of the Alternate Mediterranean Diet Score (RR, 0.61; 95% CI, 0.49 to 0.76; *P* for trend<0.0001) indicating that Mediterranean diet may be protective against CVD. The consistent association observed between the Western or unhealthy dietary pattern (high in animal products, salty snacks, refined starches and sugar and fried foods and low in fruits and vegetables) and ACS risk in different regions of the world from the INTERHEART study and other studies,[21,24,41,42] provides reliable evidence of the adverse effects of globalization on human nutrition and chronic disease risk, but the evidence is indirect because these studies did not specifically assess the impact of global trade and marketing on food consumption patterns, and their effects on inflammation, endothelial dusfunction, across different countries.[21,24,41,42] Despite this weakness, most recent studies suggest that the current trend of dietary convergence toward a typical Western diet is likely to play a role in the globalization of obesity, CVD, diabetes and cancer(38-44). These studies further emphasize the role of anti-inflammatory, hypocholesterolemic and hypoglycemic agents in the pathogenesis and prevention of heart attack (21-29).

The endothelium plays a major role in regulating vascular tone, mainly by secreting the potent vasodilator nitric oxide (NO), which is antiatherogenic.NO is synthesized from its precursor, L-arginine (Arg), by endothelial NO Synthase (NOS)[24].It is possible that L-arginine levels are under influence of dietary aminoacid arginine which is rich in nuts. NOS is competitively inhibited by asymmetric dimethylarginine (ADMA), an endogenous compound that is elevated in renal failure, cardiovascular disease (CVD), and diabetes mellitus. A low ratio of Arg to ADMA (Arg/ADMA ratio) is also a marker of endothelial dysfunction. Prospective investigations of ADMA have highlighted its role as a predictor of CVD events or death in patients with established coronary artery disease, advanced renal failure, or other high-risk conditions. There is evidence that NO levels are under influence of dietary w-3 fatty acids, physical activity and meditation and may be mediated by inflammation [43-46].

Chronobiology and the YYTT Concept

Study of biological functions according to time structure that are usually under influence of environmental factors, are included in chronobiology [47-50]. Chronobiology establishes a strong relation of mind with brain and their effects on body functions and dysfunctions. The YYTT concept is based on such interactions of mind, brain and various organs of our body. We detect blood pressure overswinging and other vascular variability disorders, (VVDs), including a high blood pressure, that is an elevation of the MESOR, for midline estimating statistic of rhythm, i.e., MESOR-hypertension, that is also a VVD [47] Moreover this is a principal point, other VVDs can complicate a high blood pressure or may be induced by treating a high blood pressure. Most of the conventionally unrecognized VVDs change a risk of stroke or of a myocardial infarction within the next

6 years from ~5% to near 100% and can be eliminated, sometimes by changing only the time of taking the medication. A recent international consensus, guided by leaders in cardiovascular physiology, recognizes that 7-day/24-hour blood pressure and heart rate monitoring interpreted chronobiologically can detect new risks associated with a very high likelihood of stroke [47]. It also recognizes that over one-third of 72 million Americans said to be treated for hypertension can have a great, conventionally unrecognized risk increase that can often be removed by adjusting the timing of antihypertensive drugs. If and only if analyzed chronobiologically, computer-implemented self-surveillance of blood pressure and heart rate by 7-day/24-h monitoring detects conditions to which conventional treatment is now blind [47-50].

Availability of Foods

Availability of prudent wild foods at reasonable cost, time taken in preparation, taste and aggressive publicity of western foods by the food industry are major problems that need attention. Food industry in general is not very interested in preparing health foods, that are known to decrease mortality and morbidity, because their primary goal is to sell the product at competitive price, to gain profit and prevent losses. Wild foods as the amount of wild fish, animal foods is rapidly getting impossible to get, because the oceans are overfished. Therefore the goal is to have sufficient cultivated wild type of foods with characteristics of wild type ones, as there is a limited and decreasing supply of real wild foods. We are now in a situation where the public health policies are clear for recommending prudent dietary patterns and providing health foods to community. However, the food policies of the government and of the farming and food industries are geared to completely different goals. The growing demands on the farmers and the food industry for a healthier diet are now being recognized, as marketing opportunity for developing healthy foodstuffs, with balanced amount of fatty acids, low glycemic foods and other nutrients in the diet.

World Health Organization and Food and Agriculture Organization should join hands with international scientific societies like the World Heart Federation, International College of Cardiology, American Heart Association, European Society of Cardiology, International College Of Nutrition and International Union of Nutritional Sciences, and collaborate with World Mind-Body Council, and YYTT Institute http://www.tsimtsoum.net/introduction_07.php).), to formulate guidelines for manufacturing of health foods. This non-profit organization has expertised, how to develop wild type of foods for prevention of diseases and enhance high quality of productive life. These foods are rich in micronutrients, antioxidants, vitamins and minerals, while providing high w-3 fatty acids, monounsaturated fatty acids, proteins and slowly absorbed carbohydrates. Longterm, randomized, controlled clinical trials are necessary to provide a scientific proof regarding the safety and efficacy of these foods in the prevention of diseases. These trials should be supported by the government agencies and international organizations such as European Union grants, because private companies are not capable in providing large amount funds, necessary for such trials.

In one such trial, [23], it has been demonstrated that whole grain- enriched hypocaloric diet is superior to refined grain group in decreasing risk of CVD in patients with metabolic syndrome. However, no study has referred to w-6/w-3 fatty acid ratio of the two diets, which could have been a more important factor for decreasing inflammation due to increased content of w-3 fat and low w-6 fat[24]. Wild - whole grains rich in w-3 fatty acids, antioxidants and magnesium may provide even better results compared to whole grain grown by modern farming. The western diet is rich in w-6 fatty acids and low in w-3 fatty acids, fiber, phytoestrogens, minerals and antioxidants. CVD, diabetes mellitus, cancer, autoimmune diseases, rheumatoid arthritis, asthma and depression are associated with increased production of thromboxane A2, leucotrienes, interleukins-1 and 6, tumor necrosis factor-alpha and C-reactive proteins. Increased dietary intake of w-6 fatty acids is known to enhance all these risk factors as well as atherogenicity of cholesterol which have adverse proinflammatry effects resulting into thrombosis and CAD [23-28].

The second quarter of the day, particularly 8.00-11.00 AM may be associated with activation of

neurohormones and proinflammatory cytokines; interleukin- 6, and 18, resulting into neuroendocrine dysfunction, which worsens the internal environment of our body predisposing greater prevalence of cardiovascular events due to mind-brain and body interactions(24-28). There may be oxidative stress, hyperglycemia, hyperinsulinemia, hypertrigly ceridemia, increased levels of catecholamines, free fatty acids and cortisol which may cause endothelial dysfunction and rupture of plaque resulting in to recurrent cardiovascular events and VVDs [47-50]

Recent studies [24-28, 40-43]), indicate that eating high fat, refined carbohydrate rich fast foods (western diet), can produce a similar proinflammatory state in our body, with increase in oxidative stress, free fatty acids and triglycerides; resulting into endothelial dysfunction. It is therefore, logical to avoid western diet in patients with CVD, and to administer Indo-Mediterranean foods which may be beneficial to vascular endothelium and myocardium.[22-28]. There is no precise and proven, guideline for dietary advice, in patients with CAD, which may be protective against recurrent cardiac events. A Mediterranean soup (tomatoes, grapes/raisins, vegetables; carrot, spinach, walnuts, almonds+lin/chia seeds and olive oil) or yogurt containing, walnuts, almonds, raisins, could be prepared for ready use, for nonpharmacological intervention, among patients of CVD. These foods appear to be protective against metabolic syndrome.[23]. Such recepies have been commonly used in the Indo-Mediterranean diet heart study and Indian experiment of infarct survival [26-28]. .Therefore for prevention of metabolic syndrome, or CAD, or cardiovascular and all cause mortality ,eating 400g/day of fruits and vegetables along with 400g/day of legumes and other whole grains, and 50g/day of almonds and walnuts,in conjunction with 25-50g/day of Columbus oil(olive oil 88 %+ flax seed oil 12.0%) P:S= w-6:w-3:=1:1 Patent Application WO2005 020698 may be protective against all cause mortality and morbidity. Since egg intake upto one daily, has no adverse effects on coronary risk factors and proinflammatory factors, including egg in the breakfast along with Mediterranean soup, in place of refined starches and meat, may be a prudent choice in the primary prevention of CVD. Designer eggs with modified fatty acid composition and increased content of w-3 fatty acids appear to be good for prevention of metabolic syndrome [24] Designer bread and chicken rich in w-3 fatty acids may be another prudent substitute for whole grains and meat, due to their most beneficial chemical composition causing slow absorption without glycemia.

Although, Most workers working on dietary patterns do not mention the nutrient content of their prudent diet, [21,22,33-35,40] but one single difference is the w-3 fatty acids, apart from other micronutrients, which is rich in fruits, leafy vegetables, nuts and whole grains. It would be very interesting to know the role of refined starches and sugar, large meals, decreased intake of fruits, vegetables, whole grains and nuts and serum nitrite levels as risk predictors of CVD in these cohorts [21,22,35]. Fruits, vegetables, nuts, whole grains, animal foods rich in w-3 fatty acids are slowly absorbed and may prevent the increase in free fatty acids, and inflammation, which is a characteristic of Columbus foods (www.columbus-concept.com) and therefore such foods may decrease the risk in CVD as well as metabolic syndrome [23-28, 33-35,39-44]. Omega-3 fatty acids can regulate leptin gene expression and the concentrations of anandamides in the brain, which in turn binds to endogenous cannabinoid receptors and regulate food intake and satiety and weight gain [24]. It seems that suboptimal nutrition is an important factor in the global burden of CAD. Cohort studies [21,22,38-40] add to this evidence by identifying the association between an unhealthy dietary pattern and risk of ACS in 52 countries around the world and among women in the United States [21,22,38]. By defining a common feature of nutrition transitions with their accompanying risks to public health, the authors underscore the importance of developing an effective and comprehensive set of health policies that address globalization and its impact on obesity and diet-related chronic diseases. Indeed, the findings from recent studies indicate [23-28,38-40] that a common set of dietary recommendations based on availability of wild type of foods can be made to prevent chronic diseases on a worldwide basis. These foods are known to have anti-inflammatory effects and can modulate about 125 genes, most of them proinflammatory, which express due to increased consumption of western meals [43, 44]. Such a public health strategy

should emphasize replacing saturated, *trans* fats and w-6 fats with unsaturated fats from natural vegetable oils rich in w-3 fatty acids (canola oil, rapeseed oil), and replacing refined grain products, starches and sugar with whole grain products, legumes, fruits, and vegetables, fish and nuts.[23-28] International College of Cardiology and International College of Nutrition in association with Columbus Paradigm Institute have emphasized to develop guidelines[40] to include wild type of foods in the dietary patterns as well as moderate physical activity and yogasan, which may be highly protective in the prevention of morbidity and mortality due to CVD, diabetes and Cancer (Table 3).

Table 3. Dietary guidelines and desirable level of risk factors for populations

Factors	Desirable Values
Energy (k calories/day)	1900-2300
Total Carbohydrate (k calories/day)	65.0
Complex Carbohydrate ((k calories/day)	55.0
Total Fat (k calories/day)	21.0
Saturated Fatty Acids (k calories/day)	7.0
Polyunsaturated Fatty Acids (k calories/day)	7.0
Polyunsaturated/Saturated Fat Ratio	1.0
n 6/n-3 Fatty Acid Ratio	1:1
Dietary Cholesterol (mg/day)	100
Whole Grains (wheat, rice, corn, legumes) (g/day)	400-500
Fruit, vegetables and nuts (g/day)	400-500
Salt (g/day)	<6.0
Brisk Walking (km/day)	>9.0
Meditation/pranayam (minutes/day)	30.0
Body Mass Index (kg/m^2)	
Range	19.0-23.0
Average	21.0
Waist-Hip Girth Ratio	
Male	<0.88
Female	<0.85
Serum Total Cholesterol (mg/dl) (4.42 mmol/L)	<170
Mild Hypercholesterolemia (mg/dl) (4.42-5.20 mmol/L)	170-200
Hypercholesterolemia (mg/dl) (>5.20 mmol/L)	>200
Low Density Lipoprotein Cholesterol (mg/dl) (2.32 mmol/L)	<90
Borderline High (mg/dl) (2.32-2.84 mmol/L)	90-110
High (mg/dl) (2.84 mmol/L)	>110
Triglycerides (mg/dl) (1.7 mmol/L)	<150
High Density Lipoprotein Cholesterol (mg/dl) (0.9 mmol/L)	>40 men, >50women
Blood Pressure (mmHg)	<130/85
Drug therapy in view of high risk of diabetes and CAD.	Amblodipine,ACE-I , receptor blockers.
Moderate physical activity and	Fish oil,aspirin, statins
Meditation and yogasan, pranayam.	30 min daily
	30 min daily

Modified from Indian Consensus Group, J Nutr Environ Med, 1996, Singh et al 2009(Ref [4-6]).

Key Points, USFD

- Older adults have no or less access and familiarity with computers vs younger adults and are less adept at obtaining Web-based information.
- The Modified Food Guide Pyramid for adults aged 70 years and older has a narrower base to reflect lower energy needs of older adults because of changes in body composition and metabolic rate.
- Selected food icons are replaced with nutrient-dense examples so that decreased food intake can accommodate unchanged or increased recommended dietary allowances for vitamins, minerals, and other crucial nutrients.
- Fiber icons in appropriate food categories emphasize adequate fiber intake to promote optimal bowel function.
- Older adults may be prone to overconsumption of energy and nutrients, which is addressed by a new category of recommendations: tolerable upper intake levels, or the highest average daily nutrient intake that is likely to pose no risk for adverse health effects to almost all individuals in the general population.
- Folate and sodium tend to be overconsumed in the older population.
- The proposed Modified MyPyramid for Older Adults is in a format consistent with the MyPyramid graphic, but it is not intended to substitute for MyPyramid (a multifunctional, Web-based program providing individualized, food-based dietary guidance and supplemental information regarding food choices and preparation, based on sex, body weight, height, and level of physical activity).
- The new graphic version of MyPyramid specifically targets relatively healthy individuals aged 70 years and older who are reasonably active and live independently. Consistent with current guidelines, it portrays a diet rich in fruits, vegetables, whole grains, low-fat and nonfat dairy products, legumes, fish, and lean meats.
- The Modified MyPyramid for Older Adults specifically emphasizes whole grains; variety within the grains group; variety and nutrient density; vegetables and fruits that are easy to prepare (eg, frozen foods); low-fat and nonfat dairy products including reduced lactose alternatives in the milk group; low saturated fat and trans fat choices in the oils group; and low saturated fat and vegetable options in the meat and beans group. There is a need to avoid w-6 rich oils and substitute with w-3 rich foods.
- Because of risks associated with alcohol consumption in elderly people, alcohol is not included as an integral component of the Modified MyPyramid for Older Adults.
- The focus is on nutrient-rich and fiber-rich foods within each group, recommending food sources of nutrients rather than supplements, and use of fluid and physical activity icons.
- The base of the pyramid has a row of glasses to remind older adults that it is crucial to remain well hydrated.
- In the second row, pictures of various physical activities emphasize the need for regular exercise.
- A flag on top of the pyramid highlights the possible need for supplemental forms of calcium and vitamins D and B_{12} because of increased requirements for these nutrients associated with aging.
- The Modified MyPyramid for Older Adults is a graphic intended to improve understanding and use of MyPyramid by the elderly population, who may be less comfortable with obtaining Web-based information.

In brief, eat 400g/day of fruits, vegetables and nuts and another 200-400 g/day of whole grains in conjunction with 25-40g/day of w-3 fatty acid rich oils for prevention of NCDs [4-15]. Reduce daily sodium intake to less than 2,300 milligrams (mg) and further reduce intake to 1,500 mg among persons who are 51 and older and those of any age who are African American, Asians or have hypertension, diabetes, or chronic kidney disease. The 1,500 mg recommendation applies to about half of the World population, including children, and the majority of

adults. Consume less than 7 percent of calories from saturated fatty acids by replacing them with monounsaturated and polyunsaturated fatty acids. Consume less than 300 mg per day of dietary cholesterol. Keep trans fatty acid and w-6 fatty acid consumption as low as possible, especially by limiting foods that contain synthetic sources of trans fats, such as partially hydrogenated oils, and by limiting other solid fats and w-6 rich oils. Reduce the intake of calories from solid fats and added sugars. Avoid the consumption of foods that contain refined grains, especially refined grain foods that contain solid fats, added sugars, and sodium. A Mediterranean soup containing carrot(100g), tomatoes(150g), walnuts (50g), almonds(50g), raisins(50g) and coriander leaves and salt for taste and flavor, appears to be the best functional food dish, for health and prevention of diseases among elderly [51].

If alcohol is consumed, it should be consumed in moderation—up to one drink per day for women and two drinks per day for men—and only by adults of legal drinking age. One drink is defined as 12 fluid ounces of regular beer (5% alcohol), 5 fluid ounces of wine (12% alcohol), or 1.5 fluid ounces of 80 proof (40% alcohol) distilled spirits. One drink contains 0.6 fluid ounces of alcohol. Strong evidence from observational studies has shown that moderate alcohol consumption is associated with a lower risk of cardiovascular disease. Moderate alcohol consumption also is associated with reduced risk of all-cause mortality among middle-aged and older adults and may help to keep cognitive function intact with age. However, it is not recommended that anyone begin drinking or drink more frequently on the basis of potential health benefits because moderate alcohol intake also is associated with increased risk of breast cancer, violence, suicides,drowning, and injuries from falls and motor vehicle crashes.

Older adults should follow the adult guidelines [4,5]. When older adults cannot meet the adult guide-lines, they should be as physically active as their abilities and conditions will allow.Older adults should do exercises that maintain or improve balance if they are at risk of falling. Older adults should determine their level of effort for physical activity relative to their level of fitness.Older adults with chronic conditions should understand whether and how their conditions affect their ability to do regular physical activity safely.Moderate-intensity physical activity: Aerobic activity that increases a person's heart rate and breathing to some extent. On a scale relative to a person's capacity, moderate-intensity activity is usually a 5 or 6 on a 0 to 10 scale. Brisk walking, dancing, swimming, or bicycling on a level terrain are examples.Vigorous-intensity physical activity: Aerobic activity that greatly increases a person's heart rate and breathing. On a scale relative to a person's capacity, vigorous-intensity activity is usually a 7 or 8 on a 0 to 10 scale. Jogging, singles tennis, swimming continuous laps, or bicycling uphill are examples. Muscle-strengthening activity: Physical activity, including exercise that increases skeletal muscle strength, power, endurance, and mass. It includes strength training, resistance training, and muscular strength and endurance exercises. Bone-strengthening activity: Physical activity that produces an impact or tension force on bones, which promotes bone growth and strength. Running, jumping rope, and lifting weights are examples. Regular physical activity, yogasan, meditation and pranayam [16] each for 30 minutes, may be protective against NCDs and may provide better spiritual, mental, social and physical wellbeing of the elderly population.

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