



The Correlation of Anxiety, Dyslipidemia and Oxidative stress in Prehypertensive and Hypertensive patients

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Received on: 07 Apr 2020
 Revised on: 10 May 2020
 Accepted on: 14 May 2020

Keywords:

Anxiety,
 hypertension,
 oxidative stress,
 prehypertension

ABSTRACT

Studies have evaluated that high blood pressure kills nine million people annually. Psychological factors can be considered as a primary threat to the increase of hypertension. It may lead to cardiovascular disease, stroke and kidney disease. The current work was conducted to analyze the disparity of anxiety, dyslipidemia and oxidative stress in pre-hypertensive and hypertensive subjects. This was a cross-sectional study conducted among 180 subjects. Based on the Joint National Committee 8 Criteria, participants were divided into hypertensive patients (n=60) and pre-hypertensive patients (n=63). Fifty-seven healthy subjects with normal blood pressure were served as the control group. Anthropometric measurements and blood pressure were measured using the standard procedure. The biochemical parameters for measuring oxidative stress, blood glucose levels, and lipid profile were estimated. Anxiety level was assessed with the State-trait anxiety inventory (STAI) questionnaire. It is observed that the serum Malondialdehyde (MDA) levels (nmol/ml) were significantly higher in pre-hypertensive (3.74 ± 0.33) and hypertensive (4.7 ± 0.38) compared to normotensive subjects (3.05 ± 0.38). The Superoxide dismutase (SOD) activity (U/ml) was higher in subjects with normal blood pressure (12.67 ± 2.31) than pre-hypertensive (11.16 ± 2.43) and hypertensive subjects (8.98 ± 2.32). The MDA had a significant positive correlation, and SOD had a negative association with waist-hip ratio, systolic blood pressure, diastolic blood pressure, fasting blood sugar, high-density lipoprotein, and state and trait anxiety. The present study confirmed that pre-hypertensive and hypertensive subjects suffered from more oxidative stress than normotensive subjects.

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ISSN: 0975-7538

DOI: <https://doi.org/10.26452/ijrps.v11i2.2270>

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INTRODUCTION

Cardiovascular disease (CVD) is one of the dominant causes of mortality. The situation is so in developed and developing countries (GBD 2016 Causes of Death Collaborators, 2017). It grounds nearly 17 million deaths per annum worldwide. Hypertension is amenable for a minimum of 45% of demises due to heart disease and 51% of deaths due to stroke (Causes of death, 2008). Hypertension triggered 9.4 million deaths per year (Lim et al., 2010). In 2008, almost 40% of 25-year-old people and above had reported high blood pressure. The situation increased from 600 million in 1980 to 1 billion

in 2008 (WHO, 2011). Estimations in 2015 revealed that the global prevalence of hypertension was 1.3 billion (Mucci *et al.*, 2016).

Based on the Joint National Committee 8 criteria, pre-hypertensives are people with systolic blood pressure 120-139mm Hg and diastolic blood pressure 80-89mm Hg and hypertensive are people with systolic blood pressure ≥ 140 mm Hg and diastolic blood pressure ≥ 90 mm Hg (Manica *et al.*, 2013; Wright and Diamond, 2006; Poulter *et al.*, 2015). Studies have shown that subjects with persistent hypertension have advanced levels of trait anxiety than individuals having normal blood pressure (Sanz *et al.*, 2007). Nevertheless, oxidative stress may be associated with the development of hypertension; it may not be the sole reason for hypertension (Montezano and Touyz, 2012; Montezano *et al.*, 2015). The study reports of (Viridis *et al.*, 2013) and (Vanhoutte *et al.*, 2009) has shown the association of oxidative stress and hypertension.

The imbalance between elevated reactive oxygen species (ROS) and decreased antioxidant status lead to oxidative stress in our body (Higashi *et al.*, 2014). The nonspecific markers of oxidative damage like superoxide and hydrogen peroxide elevated in hypertension (Kumar and Das, 1993). Also, individuals with anxiety were deficient in antioxidants, which indicate elevated oxidative stress (Grases *et al.*, 2014). It has reported the straight connection between oxidative stress and anxiety (Salim *et al.*, 2010). The current study aims to evaluate the association of oxidative stress, dyslipidemia, and anxiety with normal blood pressure, prehypertension, and hypertension.

MATERIALS AND METHODS

This cross-sectional study carried out among employees of Little Flower Hospital and Research Centre, Angamaly. The institutional ethics committee authorization was attained and the informed written consent was obtained from the entire participants. A total of 180 subjects were included in the study. They were aged between 25 and 65 years and the group comprised of both male and female. Subjects with coronary artery disease, myocardial infarction, stroke, hepatic disorder, renal disorders, mental disorders, chronic alcoholism, and smoking were excluded from the study.

Anthropometric measurements encompassed of height, weight, waist circumference, and hip circumferences. The waist and hip circumference measured by WHO STEPS protocol (WHO, 2008). The auscultatory method of blood pressure estimation was done with a mercury sphygmomanometer

(Elko mercurial sphygmomanometer 300 manufactured by Anita Industries New Delhi) according to standard methods (Smith, 2005). The total cholesterol, triglycerides, and high-density lipoprotein were analyzed by a diagnostic kit method with a fully automated clinical chemistry analyzer. Friedwalds equation was used to calculate low-density lipoprotein and very-low-density lipoprotein.

For the measurement of superoxide dismutase (SOD) and malondialdehyde (MDA), samples were kept cooled and centrifuged at 4000 rpm at 4°C for 10 minutes. The spectrophotometric method used to determine the concentration of SOD by using Marklund and Marklund protocol (Marklund and Marklund, 1974) and MDA by Beuge and Aust method (Buege and Aust, 1978).

Spielberger State-Trait Anxiety Inventory (STAI) in Malayalam by Vinod Kumar and Das was used for the state and trait anxiety assessment (Alice, 2003). STAI comprises of two subscales with state anxiety (STAI-S) and trait anxiety (STAI-T). Both subscales cover 18 statements, and the subject chooses the appropriate answer from the 4-point rating scale (not at all, somewhat, moderately so, very much so). The STAI ratings on both scales range from 18-72.

Statistical analysis

Statistical package for social sciences (SPSS) version 20 was used for data analysis. Baseline parameters assessed using descriptive statistics. The quantitative variables expressed as mean \pm SD. The statistical significance of the difference among the values was calculated by one way ANOVA. The Karl Pearson correlation coefficient used to calculate the correlation among the parameters. A p-value of < 0.05 was considered statistically significant.

RESULTS AND DISCUSSION

The study consisted of 180 subjects aged between 25 and 65 years with normal BP, prehypertension, and hypertension. Table 1 shows the clinical characteristics. The results show that both BMI and WHR elevated in pre-hypertensive and hypertensive subjects than normotensive subjects.

Values expressed as Mean \pm SD. BMI- Body Mass Index, WHR-Waist Hip Ratio, SBP- Systolic Blood Pressure, DBP- Diastolic Blood Pressure.

Comparison of parameters among groups

The biochemical characteristics, oxidative stress parameters, and anxiety levels among the groups are as shown in Table 2. The pre-hypertensive and hypertensive group had significantly higher HDL, and MDA and the serum SOD had substan-

Table 1: Baseline parameters and anthropometric measurements of studied subjects

Variables	Normotensive (n=57)	Prehypertensive(n=63)	Hypertensive (n=60)
Age (years)	55.56±11.12	51.58±6.87	53.38±7.64
BMI (Kg/m ²)	24.71±3.60	25.95±4.39	25.02±2.60
WHR	0.95±0.01	0.97±0.02	0.97±0.01
SBP (mm Hg)	111.92±8.33	131.77±6.47	148.36±13.63
DBP (mm Hg)	76.10±4.96	82.44±4.59	89.23±9.15

Table 2: Comparison of biochemical parameters, oxidative stress parameters, and anxiety levels among groups.

Variable	Normotensive (n= 57)	Prehypertensive (n=63)	Hypertensive (n=60)	P-value
TC(mg/dl)	191.98±44.40	201.69±35.97	194.80±44.49	.41
HDL(mg/dl)	45.17±6.63	47.61±7.88	42.71±7.09	.001
LDL(mg/dl)	120.21±33.11	125±36.70	124.36±39.19	.72
VLDL(mg/dl)	27.12±13.84	28.84±18.24	27.71±13.59	.82
TG(mg/dl)	135.05±69.35	144.52±91.16	138.31±67.89	.79
TC/HDL	4.28±0.95	4.33±0.59	4.64±1.12	.07
MDA(nmol/ml)	3.05±0.38	3.74±0.33	4.7±0.38	.000
SOD(U/ml)	12.67±2.31	11.16±2.43	8.98±2.32	.000
State Anxiety	40.68±1.41	43.84±2.61	49.81±3.73	.000
Trait Anxiety	40.64±1.32	44.33±3.44	50.83±4.60	.000

Table 3: The correlations between oxidative stress markers and clinical and biochemical parameters in the total subjects.

Variables	MDA		SOD	
	R value	P value	R value	P value
BMI	-.098	.191	-.120	.108
WHR	.444	.000**	-.082	.274
SBP	.795	.000**	-.450	.000**
DBP	.652	.000**	-.306	.000**
TC	-.073	.328	-.126	.091
HDL	-.182	.015*	-.199	.007**
LDL	-.080	.284	-.139	.062
VLDL	.057	.445	-.102	.173
TG	.057	.445	-.102	.175
TC/HDL	.096	.201	-.327	.000**
State Anxiety	.740	.000**	-.475	.000**
Trait Anxiety	.735	.000**	-.476	.000**

*- statistically significant

tially higher values in healthy controls. In the pre-hypertensive and hypertensive groups anxiety had significantly higher scores.

Values expressed as Mean \pm SD. One way ANOVA. TC- total cholesterol, HDL- high-density lipoprotein, LDL- low-density lipoprotein, VLDL- very-low-density lipoprotein, TG- triglycerides, TC/HDL- total cholesterol/high-density lipoprotein, MDA- malondialdehyde, SOD- superoxide dismutase. A p-value <0.05 was considered as statistically significant.

Pearson correlation coefficient analysis

Results of Pearson correlation coefficient analysis among MDA, SOD, and other parameters in total study subjects showed in Table 3. MDA has a significant positive correlation with WHR, SBP, DBP, HDL, and state and trait anxiety. It also observed that SOD has a significant negative correlation with SBP, DBP, HDL, TC/HDL, and state and trait anxiety.

BMI- Body Mass Index, WHR-Waist Hip Ratio, SBP-Systolic Blood Pressure, DBP- Diastolic Blood Pressure, TC- total cholesterol, HDL-high density lipoprotein, LDL- low-density lipoprotein, VLDL-very-low-density lipoprotein, TG- triglycerides, TC/HDL- total cholesterol/high-density lipoprotein, MDA- malondialdehyde, SOD - superoxide dismutase.

The increased blood pressure, pulmonary embolus, blood vessel occlusion, venous inefficiency, and other cardiovascular diseases were caused by vasoconstriction, and increased vascular resistance resulted from oxidative stress (Jiang *et al.*, 2016). Ahmad *et al.* confirmed a decrease in antioxidant enzymes in hypertension and its negative correlation with blood pressure. It indicates that oxidative stress had a positive relationship with SBP and DBP (Ahmad *et al.*, 2013). The present study demonstrated higher levels of SOD and decreased MDA in healthy controls. Nwanjo *et al.* reported an increase in MDA level due to oxidative stress (Nwanjo *et al.*, 2007). Lipid peroxidation augmented in severe hypertension than the early stages of hypertension (Cracowski *et al.*, 2003).

Trait anxiety and anger trait were higher in hypertensive patients than in individuals with normotension (Suls *et al.*, 1995; Francés *et al.*, 2001; Lázaro *et al.*, 1993). Patients with persistent hypertension exhibited higher ranks of trait anxiety (García-Vera *et al.*, 2010; Sanz *et al.*, 2007), which is consistent through our results. A study in the monocytes of individuals with hypertension had shown a significant correlation among trait anxiety and reactive oxygen species formation (Yasunari *et al.*, 2006). In the present work, MDA had a significant posi-

tive correlation, and SOD had a negative correlation with state and trait anxiety. It confirms the relation between anxiety and oxidative stress.

MDA produced in our body from polyunsaturated fatty acids (Ho *et al.*, 2013). A human study has demonstrated increased MDA with progressive hyperlipidemia and a positive correlation of MDA along with atherogenic index (Yang *et al.*, 2008). Lopes reported that the induction of acute hyperlipidemia increases the oxidative stress marker (Lopes, 2003). It has described that augmented oxidative stress and altered lipid profile predisposes to atherosclerosis (Rao and Kiran, 2011).

Al-Benna *et al.* demonstrated that, in CAD patients, the endothelial malfunction could be due to LDL cholesterol and oxidative stress. They also confirmed the significant negative correlation among LDL, markers of endothelial function, and oxidative stress (Al-Benna *et al.*, 2006). We estimated the correlation of oxidative stress with lipid profile and found that MDA and HDL have a significant association. Also, SOD has a meaningful negative relationship through HDL as well as with TC/HDL. We could not demonstrate the correlation of oxidative stress markers with LDL and other parameters of lipid profile.

CONCLUSIONS

Hypertension is a quiet, obscure assassin that seldom grounds indications and is a severe threatening sign that the substantial daily life modifications are instantly required. The findings strongly confirmed that oxidative stress in hypertensive and pre-hypertensive patients influenced by both blood pressure and state and trait anxiety. Hence the therapies targeting oxidative stress and anxiety levels can avoid or suspend the commencement of hypertension as well as its complications.

ACKNOWLEDGEMENT

Authors are thankful to the Management, Little Flower Hospital, and Research Centre, Angamaly, for giving the needed facility for the research work.

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