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## Variation in Serum Brain-Derived Neurotrophic Factor in Hypertensive Individuals with Depression in Nauth Nnewi, Nigeria

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**Abstract:** Hypertension and depression have synergistically garnered significant attention in the medical community with its growing prevalence in the past decades. These conditions have impacted the individuals and society at large especially low-income countries like Nigeria. Some neurotropic and proteins has been linked with the etiology of both conditions, hence the design of this study. This cross-sectional study was conducted to evaluate the serum level of brain derived neurotrophic factor (BDNF) in hypertensive individuals with and without depression. 90 individuals were recruited, this included forty-five (45) newly diagnosed hypertensive individuals recruited based on their medical history, and forty-five (45) were non-hypertensive individuals. Depressed individuals were recruited with the aid of public health questionnaire 9 (PHQ-9), in total this study comprised of 4 groups; fourteen (14) hypertensive individuals with depression, thirty-one (31) hypertensive individuals without depression (hypertensive), fifteen (15) non-hypertensive individuals with depression (depressive) and thirty (30) non-hypertensive individuals without depression (control). The depressed individuals were determined from screening secondarily using patient health questionnaire-9. Determination of Serum BDNF level was done using ELISA method. Anthropometric measurement was done using standard techniques. The result shows decreased serum BDNF level in hypertensive individuals with depression ( $119.63 \pm 27.66$ ), hypertensive ( $155.76 \pm 53.52$ ) and depressive individuals ( $156.56 \pm 47.77$ ) when compared with control group ( $191.57 \pm 50.96$ ) ( $p < 0.05$  respectively). Reduction in BDNF level was more pronounced in hypertensive with depression in both male and female hypertensive. BDNF was negatively correlated with body mass index among hypertensive individuals with depression ( $r = -0.730$ ,  $p < 0.05$ ). 31.1% prevalence of depression was observed among hypertensive individuals in NAUTH Nnewi. The study reveals significant alteration in serum BDNF level in depressive and hypertensive individuals. This provides valuable insights into the underlying mechanisms connecting these conditions. The understanding opens avenues for diagnostic and novel therapeutic interventions aimed at improving both cardiovascular and mental health outcomes.

**Keywords:** Brain derived neurotrophic factor, Hypertension, Depression, Newly diagnosed, Nigeria

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## Introduction

Hypertension is the most important modifiable risk factor for all-cause morbidity and mortality worldwide and is associated with an increased risk of cardiovascular disease [1]. According to the World Health Organization [2], hypertension affects one in three adults worldwide and causes an estimated 9.4 million deaths per year, or 13% of global mortality from all causes combined. The WHO African Region, mostly Nigeria, has recorded the highest prevalence of hypertension [3, 4], which might be attributed to limited awareness, treatment, and control rates compared to the observed trend in developed countries [5].

Hypertension is an elevation of the normal systemic arterial blood pressure (SABP) [6]. Diagnosis is based on having a systolic and/or diastolic blood pressure above 140 mmHg and 90 mmHg, respectively, in more than two readings and at more than two visits [7]. Several causes of hypertension include obesity, insulin resistance, high salt intake, excessive alcohol intake, having a sedentary lifestyle, smoking, and chronic kidney disease (CKD). These are primary risk factors for cardiovascular disease and may result from the inability of the kidneys to filter out fluid, leading to hypertension and other cardiovascular events [8]. Many people diagnosed with hypertension usually have tough experiences such as somatic symptoms, a lower quality of life, and role impairment. All of these factors may make it easier for them to experience psychological distress, especially clinical depressive disorders, also known as depression [9].

Previous research has ranked depression as the third cause of the burden of disease worldwide in 2008 by the WHO, and may rank first by 2030 [10]. Globally, it is estimated that 3.8% of the population experiences depression, 5% of whom are adults [11] (4% among men and 6% among women), and 5.7% of adults older than 60 years. Approximately 280 million people in the world have depression [12]. Depression is one of the most prevalent mental health disorders currently going undiagnosed in many developing countries, including Nigeria. Stigmatization, inadequate financial resources, poor healthcare facilities for accurate diagnosis, and low research attention are contributing factors to the prevalence of depression among youths in West Africa [13]. Depression is a common serious mental disorder characterized by alterations in thinking, mood, or behaviours associated with distress and/or impaired function. It can also possibly lead to suicide. It remains one of the most prevalent health disorders of the 21st century, placing a considerable economic and social burden on both individuals bearing the disease and society at large [14]. Identification of neuroimmune biomarkers is vital to improving the diagnosis, stratification, and treatment of mental disorders [15]. Many clinical and animal studies have highlighted associations between low levels of BDNF and the development of behavioral symptoms of depression [16].

Neurotrophic factors, particularly brain-derived neurotrophic factor (BDNF), has been associated with depression as well as hypertension [17, 18]. Growing

evidence has shown that BDNF plays a significant role in neurobiological modifications [19] and can be of diagnostic and clinical importance for depression as well as hypertension. However, there is a paucity of knowledge on possible link of serum levels of BDNF with hypertension and depression in the sub-Saharan Africa especially in Nigeria where these conditions seems overwhelmingly high.

Exploration of these neuroimmune mechanisms is vital to the understanding of the pathogenesis and pathophysiology of mental disorders like clinical depressive disorders and its association with hypertension hence, the study design.

## **Material and Method**

### **Study site**

The study was conducted on hypertensive individuals with and without depression in the department of Internal Medicine at Nnamdi Azikiwe University Teaching Hospital (NAUTH) Nnewi, Anambra state. Its coordinates are longitude 6.0105° N and latitude 6.9103° E.

### **Study design**

This cross-sectional study was conducted to evaluate the serum level of BDNF in hypertensive individuals with and without depression in Nnamdi Azikiwe University Teaching Hospital (NAUTH) Nnewi, Nigeria. Subjects within the age of 18-65 years were recruited for this study. Written consent was obtained from participants before recruitment. Patients record was used to obtain their bio-data and anthropometric data; height, weight, systolic and diastolic blood pressure. Patients record was used to determine hypertension and depression was diagnosed using public health questionnaire 9 (PHQ-9). A total number of 90 individuals participated in this study; These comprised fourteen (14) hypertensive individuals with depression, thirty-one (31) hypertensive individuals without depression (hypertensive), fifteen (15) non-hypertensive individuals with depression (depressive) and thirty (30) non-hypertensive individuals without depression (control).

### **Inclusion Criteria**

The study included hypertensive individuals with and without clinical depression within the ages of 18-65 years. Apparently healthy individuals who were not hypertensive and without depression were included and served as control participants.

### **Exclusion criteria**

Individuals with cancer or on undergoing chemotherapy were excluded from the study. Individuals outside the age range of 18-65 years were not included.

Individuals with brain injury and mental disorder and those that have stroke were excluded from the study. HIV seropositive individuals were also excluded.

### **Ethical approval and informed consent**

The ethical approval for this study was obtained from the board of ethics committee of Nnamdi Azikiwe University Teaching Hospital Nnewi, Anambra State, Nigeria with Reference number: NAUTH/CS/66/VOL.16/VER.3/412/2023/308. Written consent was sought and obtained from participants before sample collection.

### **Sample collection**

Three (3) mL of venous blood was collected from the participants by venous puncture and the blood was dispensed into a plain container and allowed to clot and retract, then it was centrifuged at 4000 rpm for 10 minutes. The serum was extracted and dispensed into another plain container which was accurately labelled with a code specific to the samples, the samples were stored at four (4°C) until it was analyzed.

### **Screening for depression**

Patient Health Questionnaire (PHQ-9) depressive symptom scale contains 09 items was used. It was a Likert scale with the following response options: Patient health questionnaire (PHQ-9) depressive symptom scale have 09 items. 0 = not at all, 1 = several days, 2 = more than half the days, and 3 = nearly every day. Classification of depression was measured by verbal responses of participants to PHQ-9 scale and expressed in scores. PHQ-9 was categorized as follows: severe depression: respondent with a score between 20 and 27; moderately severe depression: respondent with a score between 15 and 19; moderate depression: respondent with a score between 10 and 14; mild depression: respondent with a score between 5 and 9; minimal depression: respondent with a score between 1 and 4; and non-depressed respondent with score 0 [20]. The internal consistency of this instrument using Cronbach's alpha was 0.883.

### **Screening for hypertension**

The participants were screened while in a seated position and after 5 minutes of rest using an automated micro life digital sphygmomanometer and the results obtained was compared to the reference which states that if systolic and diastolic blood pressure is consistently above 140 mmHg and 90 mmHg respectively in more than two visits or previous medical history, the patient was diagnosed hypertensive [21]. This was also confirmed from participants' medical history in NAUTH, Nnewi. The body weight and height were measured with a Seca 740 scale and a stadiometer respectively. Body mass index (BMI) was calculated using the formula: weight in kilograms divided by the height in meters squared.

### **Determination of BDNF**

The serum level of brain-derived neurotrophic factor was determined using sandwich ELISA method as was described by Naegelin et al., [22].

### **Principle**

The kit assays Human BDNF level in the sample using purified Human BDNF antibody to coat microtiter plate wells, make solid-phase antibody and then, BDNF was added to the wells. Combined BDNF antibody which with HRP labeled, become antibody - antigen - enzyme - antibody complex, after washing completely, TMB substrate solution was added, TMB substrate becomes blue colour at HRP. Enzyme- catalyzed reaction is terminated by the addition of a sulphuric acid solution and the colour change is measured spectrophotometrically at a wavelength of 450nm. The concentration of Human BDNF in the samples is then determined by comparing the O.D of the samples to the standard curve. The lower detection limit was 5 pg/ml. Concentrations were expressed as nanograms per milliliter (ng/ml). The inter- and intra-assay coefficients of variation were less than 5%.

### **Statistical Analysis**

Data gotten from the questionnaires and laboratory analysis was analyzed using SPSS version 25. Qualitative/categorical variables was analyzed using descriptive statistics and results presented as mean  $\pm$  standard deviation. One-way ANOVA and Post Hoc LSD was used to carry out multiple mean comparison between parameters of the four (4) groups, Independent samples t-test was used to compare the parameters between the male and female participants. Pearson correlation was used to test for correlation between the parameters and anthropometric data obtained and alpha level was set at 0.05.

### **Results**

#### **Mean values of Age, Systolic Blood Pressure (SBP), Diastolic Blood Pressure (DBP) and Body Mass Index (BMI) in Hypertensive Individuals with and without Depression in NAUTH Nnewi**

The result showed that there was no significant difference in the mean age value of the study groups ( $p \geq 0.05$ ). Hypertensive individuals ( $131.11 \pm 10.54$ ) and hypertensive individuals with depression ( $142.86 \pm 18.75$ ) had a significantly higher systolic blood pressure when compared with that of the control individuals ( $113.60 \pm 9.80$ ) ( $p < 0.05$ ). Similarly, hypertensive individuals with depression ( $142.86 \pm 18.75$ ) and Hypertensive individuals ( $131.11 \pm 10.54$ ) had significantly higher systolic blood pressure compared with depressive individuals ( $115.00 \pm 7.07$ ) ( $p < 0.05$  respectively). However, hypertensive individuals with depression ( $142.86 \pm 18.75$ ) had a significantly higher mean systolic blood pressure when compared with hypertensive individuals ( $131.11 \pm 10.54$ ) ( $p < 0.05$ ).

It was also seen that hypertensive individuals ( $88.89 \pm 12.69$ ) and hypertensive individuals with depression ( $90.95 \pm 9.44$ ) had a significantly higher diastolic blood pressure when compared with that of the control individuals ( $75.90 \pm 7.99$ ) ( $p < 0.05$ ). Similarly, hypertensive individuals ( $88.89 \pm 12.69$ ) had a significantly higher diastolic blood pressure compared to that of non-hypertensive individuals without depression ( $76.80 \pm 6.68$ ) ( $p < 0.05$ ).

Lastly, hypertensive individuals ( $30.88 \pm 7.02$ ) and hypertensive individuals with depression ( $30.86 \pm 6.46$ ) had a significantly higher body mass index when compared with the control individuals ( $23.57 \pm 5.51$ ) ( $p < 0.05$ ) (see table 1).

**Table 1. Mean values of Age, Systolic Blood Pressure (SBP), Diastolic Blood Pressure (DBP) and Body Mass Index (BMI) in Hypertensive Individuals with and without Depression in NAUTH Nnewi**

Group	Age (years)	SBP (mmHg)	DBP (mmHg)	BMI (Kg/m <sup>2</sup> )
A (n=14)	51.21 $\pm$ 9.82	142.86 $\pm$ 18.75	90.95 $\pm$ 9.44	30.86 $\pm$ 6.46
B (n=31)	47.33 $\pm$ 7.32	131.11 $\pm$ 10.54	88.89 $\pm$ 12.69	30.88 $\pm$ 7.02
C (n=15)	50.48 $\pm$ 9.38	115.00 $\pm$ 7.07	76.80 $\pm$ 6.68	26.74 $\pm$ 6.12
D (n=30)	47.00 $\pm$ 10.82	112.60 $\pm$ 9.80	75.90 $\pm$ 7.99	23.57 $\pm$ 5.51
F-value	1.099	20.138	12.071	5.461
p-value	0.354	0.000*	0.000*	0.002*
A vs B	0.147	0.033*	0.573	0.994
A vs C	0.841	0.012*	0.006*	0.161
A vs D	0.200	0.001*	0.001*	0.006*
B vs C	0.219	0.000*	0.000*	0.093
B vs D	0.884	0.000*	0.000*	0.000*
C vs D	0.270	0.648	0.800	0.200

A- Hypertensive individuals with depression, B- Hypertensive individuals without depression, C- Non-hypertensive individuals with depression, D- Control. \* Significant mean difference at  $p < 0.05$ .

### **Serum level of Brain-derived Neurotrophic Factor (BDNF) in hypertensive individuals with and without depression in NAUTH Nnewi**

It was also observed that hypertensive individuals with depression ( $119.63 \pm 27.66$ ) had a significantly lower serum BDNF level when compared with hypertensive ( $155.76 \pm 53.52$ ), depressive individuals ( $156.56 \pm 47.77$ ) and control group ( $191.57 \pm 10.96$ ) ( $p < 0.05$  respectively). Similarly, hypertensive individuals ( $155.76 \pm 53.52$ ) and depressive ( $156.56 \pm 47.77$ ) individuals had significantly lower serum BDNF level when compared with control participants ( $191.57 \pm 10.96$ ) ( $p < 0.05$ ) (see table 2).



**Table 2. Serum level of Brain-derived Neurotrophic Factor (BDNF) in hypertensive individuals with and without depression in NAUTH Nnewi**

Group	BDNF (ng/L)
Hypertensive individuals with depression (n=14)	119.63±27.66
Hypertensive individuals without depression (B)(n=31)	155.76±53.52
Non-hypertensive individuals with depression (C) (n=15)	156.56±47.77
Control (D) (n=30)	191.57±10.96
F- value	4.368
P- value	0.008*
A vs B	0.040*
A vs C	0.047*
A vs D	0.001*
B vs C	0.971
B vs D	0.016*
C vs D	0.018*

Key: \* Significant mean difference at  $p < 0.05$ .

### **Serum level of Brain-derived Neurotrophic Factor (BDNF) between Male and Female Hypertensive Individuals with and without Depression in NAUTH Nnewi**

Serum BDNF level was significantly lower in female and male hypertensive individuals with depression ( $122.44 \pm 30.23$ ,  $117.52 \pm 27.04$ ) when compared with their counterparts without depression ( $153.08 \pm 38.10$ ,  $165.14 \pm 60.85$ ) ( $p < 0.05$  respectively). Similarly, BDNF level was significantly lower in female and male hypertensive individuals with depression ( $122.44 \pm 30.23$ ,  $117.52 \pm 27.04$ ) when compared with their corresponding depressive individuals ( $157.27 \pm 37.58$ ,  $151.85 \pm 55.84$ ) ( $p < 0.05$  respectively). Furthermore, BDNF level was significantly lower in female and male hypertensive individuals with depression ( $122.44 \pm 30.23$ ,  $117.52 \pm 27.04$ ), hypertensive without depression ( $153.08 \pm 38.10$ ,  $165.14 \pm 60.85$ ) and depressive individuals ( $157.27 \pm 37.58$ ,  $151.85 \pm 55.84$ ) when compared with their control counterparts ( $180.56 \pm 48.85$ ,  $188.77 \pm 93.85$ ) ( $p < 0.05$  respectively).

However, there was no significant difference in the serum BDNF and tyrosine kinase level between male and female hypertensive individuals with and without depression in NAUTH Nnewi ( $p \geq 0.05$ ) (see table 3).



**Table 3. Serum level of Brain-derived Neurotrophic Factor (BDNF) between Male and Female Hypertensive Individuals with and without Depression in NAUTH Nnewi**

Group	Parameter	Female	Male	t-value	p-value
<b>A(f=8, m=6)</b>	BDNF (ng/L)	122.44±30.23	117.52±27.04	-0.264	0.534
<b>B (f=15, m=16)</b>	BDNF (ng/L)	153.08±38.10	165.14±60.85	0.214	0.833
<b>C(f=7, m=8)</b>	BDNF (ng/L)	157.27±37.58	151.85±55.84	0.935	0.620
<b>D(f=14, m=16)</b>	BDNF (ng/L)	180.56±48.85	188.77±93.85	-1.898	0.074
<b>F-value</b>		4.242	5.099		
<b>P-value</b>		0.003*	0.001*		
<b>A vs B</b>		0.030*	0.001*		
<b>A vs C</b>		0.022*	0.024*		
<b>A vs D</b>		0.009*	0.000*		
<b>B vs C</b>		0.883	0.828		
<b>B vs D</b>		0.037*	0.594		
<b>C vs D</b>		0.044*	0.044*		

*A- Hypertensive individuals with depression, B- Hypertensive individuals without depression, C- Non-hypertensive individuals with depression, D- Control. \* Significant mean difference at  $p<0.05$ .*

### **Correlation of serum Brain-derived Neurotrophic Factor (BDNF) with Diastolic Blood Pressure (SBP), Diastolic Blood Pressure (DBP) and Body mass Index (BMI) in Hypertensive Individuals with and without Depression in NAUTH Nnewi**

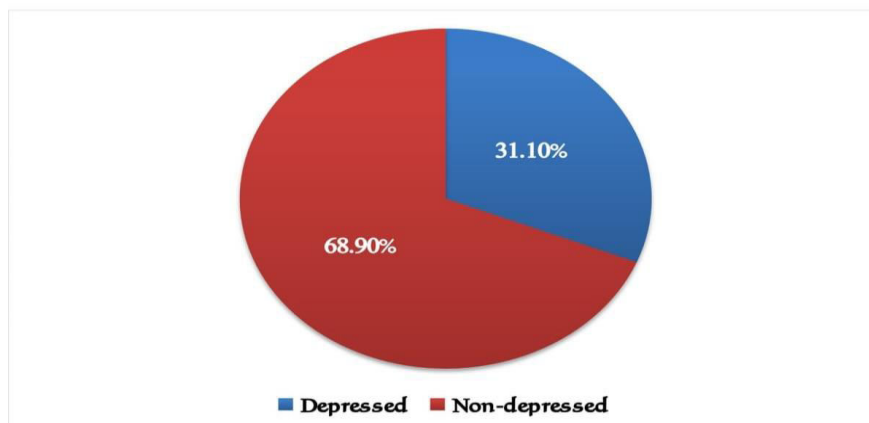
Among the hypertensive individuals with depression there was strong negative correlation between the serum BDNF level and body mass index ( $r=-0.730$ ,  $p<0.05$ ). (See table 4)

**Table 4. Correlation of serum Brain-derived Neurotrophic Factor (BDNF) with Diastolic Blood Pressure (SBP), Diastolic Blood Pressure (DBP) and Body mass Index (BMI) in Hypertensive Individuals with and without Depression in NAUTH Nnewi**

Correlation	A (n=14)		B (n=31)		C (n=15)		D (n=30)	
	R	P	R	P	R	P	R	P
BDNF vs Age	-0.308	0.419	-0.155	0.501	0.475	0.165	0.320	0.169
BDNF vs SBP	0.079	0.840	0.167	0.469	0.337	0.341	0.231	0.328
BDNF vs DBP	0.113	0.773	-0.015	0.950	0.557	0.095	0.091	0.702
BDNF vs BMI	-0.730*	0.025	0.012	0.960	0.347	0.326	0.003	0.989

*A- Hypertensive individuals with depression, B- Hypertensive individuals without depression, C- Non-hypertensive individuals with depression, D- Control. \* Significant correlation at  $p<0.05$ .*

Figure 1. Prevalence of Depression among Hypertensive Individuals in NAUTH Nnewi



Pie chart showing 31.1% prevalence of depression among hypertensive individuals in NAUTH Nnewi.

## Discussion

Hypertension is among the leading cause of cardiovascular disease and premature death worldwide and individuals diagnosed often experience significant challenges including somatic symptoms, reduced quality of life and role impairment.

Our study recorded 31.1% prevalence of depression. This is consistent with previous report by Yeboah et al., [23] which noted 31.5% prevalent rate of depression with decreased levels of serum BDNF in their study with T2DM individuals in Ghana. A higher prevalence of depression was rather reported by Mahmood et al., [24] in Pakistan (40.1%) and Theresa et al., [25] in Tamil Nadu (53.1%). Racial variations in circulating BDNF levels have been previously reported among HIV seropositive individuals as well as pregnant women in sub Saharan African when compared with their Caucasians counterparts [26, 27].

This study unveiled that hypertensive individuals with depression had significantly lower serum BDNF level when compared with hypertensive individuals and depressive individuals. This finding aligns with a study conducted by Harlyjoy et al., [18] that also indicated a decreased serum level of BDNF in hypertensive individuals. But contrary to a study by Erdos et al., [28] that associated a higher serum level of BDNF with hypertension. The diminished serum level of BDNF in our study may be attributed to the accompanying conditions following hypertension, such as inflammation and oxidative stress, both of which are known to induce endothelial dysfunction and consequently impact the serum level of BDNF. Other potential factors contributing to the decrease in serum BDNF levels include genetic factors, lifestyle choices, stress management, and the methodologies employed to measure BDNF levels. Previous researches have shown that dysregulation of circulating BDNF levels can

affect cognitive functions through its capacity to modulate neurite outgrowth, neuronal differentiation among others [29, 30]. BDNF can control tissue metabolism through its central and peripheral influence on various enzymes that modulate intermediary metabolism, leading to adverse cardiovascular complications including hypertension, dysglycemia and dyslipidaemia [31]. Variation in circulating BDNF levels in individuals with inflammatory conditions such as hypertension, diabetes, affective disorders etc have also been markedly reported, indicating the psychophysiological importance of BDNF as a good diagnostic indices for cardiovascular and mental disorders [32, 33].

Our study also noted a significant reduction in BDNF level in hypertensive and depressed individuals when compared with control participants. This indicates BDNF deficiency in the study participants and can subsequently lead to neuronal loss and cortical atrophy with cardiovascular damage

Occurrence of depression generally, have been attributed to several neuronal processes including catecholamine and serotonin deficiency [34, 35]. Mitochondrial dysfunction, oxidative stress, and neuroinflammation are also involved in the pathogenesis of depression as well as hypertension [36]. The renin-angiotensin system (RAS) involved in the pathogenesis of depression has been shown to have a protective role in hypertension [37]. However, the interplay of uncontrolled brain RAS-induced depression still remains unclear. Serotonin however, plays a very significant role in BDNF signaling in the central nervous system, therefore its uncontrolled variation can result to different mental disorders [38, 39]. Previous research noted that BDNF promotes the survival and morphological differentiation of 5-HT neurons and improves the functioning, sprouting, and growth of 5-HT neurons in various brain regions [40]. However, increased inflammatory conditions such as in hypertension due to oxidative stress and ROS may adversely lead to destruction of neurons and affecting the production of BDNF thereby causing significant neuronal impairments [41]. Increased cell membrane and cell receptors damage with modification of the enzymes and genes functions are adverse inflammatory processes which can disrupt the functions of cells and contribute to their death thereby, impacting adequate release of BDNF. This therefore, shows that oxidative stress causes neuroprogression by interfering with neurotransmission, especially with regard to 5-HT signals [42]. A decreased sensitivity of 5-HT receptors has also been observed as a result of impaired neurogenesis of these neurons in depressive individuals [41].

The present study observed that serum BDNF level was significantly lower in female and male hypertensive individuals with depression when compared with their counterparts without depression and their corresponding male and female control participants. This indicates BDNF deficiency, establishing that combined

impact of depression and hypertension on BDNF levels may be more pronounced when both conditions are present leading to disease severity. This is consistent with previous findings [23, 43], showing the role of BDNF in depression and hypertension. However, there was no significant difference in serum BDNF level based on the gender of the participants within the groups. This is consistent with a similar study by Lommatzsch et al., [44]. This finding may be attributed to the essential roles BDNF plays in fundamental neurobiological processes that are common to both males and females [45]. However, this finding contrasts with a study by Piancatelli et al., [46] that identified a significant gender-related decrease in serum BDNF and suggested that this difference could be influenced differently in males and females by various mechanisms, such as stress, gonadal hormones, and epigenetic modulation.

The findings from this study also indicated that hypertensive individuals, including those with and without depression, had significantly higher systolic and diastolic blood pressure and body mass index compared with control group which characterized the presence of hypertension and obesity in the study. This observation is supported by a study done by Aydin et al., [47]. The combined effect of hypertension and increased BMI can lead to more oxidative stress and may have exposed the individuals to observed depression and subsequently increase the affective disorder. This is supported by the previous work done by [48]. Decreased levels of Brain-Derived Neurotrophic Factor (BDNF) have been associated with both hypertension and depression. In depressed patients, lower BDNF secretion is believed to contribute to the pathological mechanisms of depression. Similarly, hypertension has been linked with reduced serum levels of BDNF, suggesting that this neurotrophic factor plays a role in both conditions, potentially influencing mood and vascular health [49]. A strong positive correlation has been indicated between body mass index and arterial blood pressure [48, 50, 51]. The mechanism of interconnectivity between hypertension and depression still remain unknown. However, Hypertension has been linked to an increased risk of mood disorders such as anxiety and depression. The relationship may be bidirectional, where hypertension contributes to mood disorders, and vice versa [52, 53]. Chronic stress can contribute to elevated blood pressure. Stress activates the body's "fight or flight" response, releasing hormones that increase heart rate and constrict blood vessels. High blood pressure can affect cognitive function over time, leading to challenges such as memory problems or decreased cognitive flexibility. Growing evidence has shown that untreated hypertension may increase the risk of dementia later in life [54]. Furthermore, Individuals with hypertension may experience limitations in their activities due to health concerns, potentially leading to social isolation. This can exacerbate feelings of anxiety and depression. Most of the antihypertensive formulations can also have side effects that impact mood or cognitive function, which might influence an individual's mental health [55]. Chronic hypertension has also been linked with increased inflammatory processes that can affect

neurotransmitter systems, these may impact significantly on mood regulation and cognitive health [56].

The negative correlation observed between the serum level of BDNF and body mass index among subjects who were both hypertensive and depressed individuals is consistent with the studies by Taha et al., [57] and Mruczyk et al., [58]. This relationship may be attributed to genetic variations affecting both BDNF levels and BMI. Specific gene polymorphisms associated with BDNF can also influence susceptibility to obesity by impacting food intake behaviors and metabolic processes [59]. Obesity and hypertension can lead to depression [60]. Serum BDNF has been shown to be negatively associated with high blood pressure [23]. The mechanism associating circulating BDNF with blood pressure and obesity is yet to be fully elucidated. However, it has been documented in hypertensive rats that oxidative stress influences BDNF synthesis before an elevation of in blood pressure is observed [61]. Similarly, in other studies, BDNF has been linked with hypertrophic remodeling of the carotid artery, indicating that BDNF affects the atherogenic process in humans [23, 62].

### Conclusion

The significantly decreased serum BDNF level in hypertensive and depressed individuals strongly indicates BDNF deficiency which may have resulted from increased stress and arterial hypertension. This may subsequently lead to neurodegenerative disorders and neuronal loss and may further predispose the affected individuals to congestive heart failure and other cardiovascular complications establishing the association between hypertension and depression. Managing hypertension effectively may therefore, have positive implications for an individual's mental well-being. More longitudinal studies may be needed to investigate the in depth role of BDNF in modulation of obesity, hypertension and depression to ameliorate the development of neuropsychiatric complications.

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