



CODEN [USA]: IAJPBB

ISSN: 2349-7750

**INDO AMERICAN JOURNAL OF
PHARMACEUTICAL SCIENCES**<http://doi.org/10.5281/zenodo.1488040>Available online at: <http://www.iajps.com>

Research Article

**ROLE OF INCREASED PERCEIVED STRESS SCORE (PSS)
AND BODY MASS INDEX (BMI) IN CAUSING SECONDARY
SYSTEMIC HYPERTENSION IN PATIENTS OF HEPATITIS C****¹Azhar Hussain, ²Prof. Dr. Muneeza Saeed, ³Dr. Hifsa Noor Lodhi, ¹Uswa Nabi,
¹Hibba Tul Noor**¹MBBS, Ameer Ud Din Medical College, PGMI, Lahore²Head of Physiology Department, Ameer Ud Din Medical College, PGMI, Lahore³Asst Prof. of Physiology Department, Ameer Ud Din Medical College, PGMI, Lahore**Abstract:****Objective**

1. To determine stress level in medical ward patients of Hepatitis C visiting Lahore General Hospital, Lahore, Mayo Hospital Lahore and DHQ Layyah
2. To determine the role of increased stress level and BMI in developing systemic hypertension.

Design: Descriptive type of cross sectional**Place and duration of study:** It took the 8 months starting from August 2, 2017 to April 7, 2018 in Lahore General Hospital, Mayo Hospital Lahore and DHQ Layyah.**Subjects and Methods:** Purposive sample 124 ward patients with sociodemographic questionnaire, Perceived Stress Scale (PSS) and BP recording were filled by research participants.**Results:** Our study showed a significant positive correlation between Perceived Stress Score, Body Mass Index (BMI) and Blood Pressure both SBP as well as DBP. There was a positive correlation in the formal education and developing the perceived stress and it could be designated to the higher work burden and lack of satisfaction with the job ($p < 0.05$). Our study indicated statistically a very strong relationship between perceived stress and developing prehypertension and hypertension stage 1 ($p < 0.001$).**Conclusion:** The height, weight, systolic blood pressure (SBP), and diastolic blood pressure (DBP) were higher among males as compared with females. Prevalence of prehypertension among overweight/obese and tense subjects suggested an early diagnosis of prehypertension and intervention including life style modification, particularly weight management.**Keywords:** Body mass index, Blood pressure (SBP and DBP), Obesity, Prehypertension, Hepatitis C**Corresponding author:****Azhar Hussain,**

MBBS,

Ameer Ud Din Medical College,

PGMI, Lahore

QR code



Please cite this article in press Azhar Hussain et al., *Role of Increased Perceived Stress Score (PSS) and Body Mass Index (BMI) In Causing Secondary Systemic Hypertension in Patients of Hepatitis C., Indo Am. J. P. Sci., 2018; 05(11).*

INTRODUCTION:

High blood pressure is a very important modifiable risk factor for mortality and disability throughout the world. It is a major cause of heart diseases, cerebral vascular accidents (CVA) and renal hyperuricemia. [1] WHO exposed in its report in Geneva, 2013 that elevated blood pressure was found to be a major culprit in causing 7.5 million deaths throughout the world, so rightly considered as a “Silent Killer” [2]. A study on hypertension revealed that the prevalence of hypertension in adults was 40% globally, showing a deepening concern and attention seeking problem of the modern ages.[3].

American Heart Association (AHA) and American College of Cardiology (ACC) defined the new lower readings of hypertension. They considered blood pressure in normal range if Systolic blood pressure/Diastolic blood pressure should be lower than 120/80 mm Hg; for increased blood pressure, SBP between 120-129 mmHg and DBP lower than 80 mmHg ;for hypertension stage-1,SBP should be less than 130-139 mmHg with DBP between 80-89 mmHg; for hypertension stage-2,systolic BP equal to or above 140 mmHg with diastolic BP as 90 mm Hg[4]’.

The stress is one of the risk factors in causing hypertension. Stress can be defined as a process in which the adaptive capability of an individual cannot fulfill the environmental demands which results certain biological as well as psychological changes that may lead for increased risk for diseases[6].According to the studies of American Heart Association (AHA), stressful conditions often cause a temporary increase in BP but when the stressor is alleviated, BP returns to the baseline. But if subject is obese and is living a stressful life due to any causative factor for more than a month, he/she is at the verge of developing chronic systemic hypertension. But, the relationship of stress with elevated BP is highly dramatic and colorful as indicated by exercising three to five times a week for 30 minutes can reduce your stress level. [7].

WHO’s Fact Sheet No.311 on Obesity and Overweight, Geneva,2013 reveals that tripled from 1975 to 2016 affecting more than 1.9 billion individuals .39% of patients were aged 18 years, and 13% were falling in the category of obese by 2016. [8]

Similarly, Guyton and Hall in their world’s best textbook in medical physiology cited that overweight, smoking and physical inactivity are strongly correlated to increased disease burden and chronic

diseases’ incidences. [9]Higher prevalence of prehypertension in stouts stressed on early detection and life style modifications and weight management[10].The prevalence of overweight/obesity found in the data for young adults for overweight and obese was 15.4% and 4.0% respectively [5,11,12,].

In present study, comprehensively, relationship between hypertension, stress and BMI was evaluated in a descriptive type of cross-sectional study of medical ward patients of Hepatitis C to overcome the gap in the literature by showing a significant relationship between the psychological stress, BMI and systemic hypertension as the patients of Hepatitis C had presumably higher stress level due to chronicity of disease, lack of money, fear of death and other psychosocial problems.

MATERIALS AND METHOD:

The study was conducted from August 2, 2017 to April 7, 2018 in Lahore General Hospital, Lahore, Mayo Hospital Lahore and DHQ Layyah. All the ethical standards of APA were followed strictly before and during conduction of study. Permission from all the Head of Departments & Senior Registrars of medicine wards of all the three hospitals were taken for the data collection from subjects. There were 124 patients were included in this study of both gender having age above 18 years admitted in medical ward. SBP above 140 and above 90 mmHg was taken to be as hypertension. Similarly, stress level was defined by the Perceived Stress Score with the patients were labelled as mild stress having 0-13 score, moderate stress having 14-23 score and severe stress having 24-40 score as calculated by Perceived Stress Scale.

A standardized questionnaire on sociodemographic status including name, gender, marital status, age, education, blood pressure readings were filled by research participants. Height, weight and Systolic & Diastolic blood pressures were measured by the research participants by using plastic height measuring foot, weight measuring machine provided by ward staff and mercury sphygmomanometer.

Information was collected and data was entered in SPSS version 22. Means and standard deviations were calculated for quantitative variables such as age, BMI, systolic and diastolic pressure. Frequencies and percentages are for qualitative variables gender, marital status, education, and perceived stress scale. Then Chi Square Test was applied to compare two test variables to obtain 2/2 tables to check whether the relationship between the two variables under

investigation is significant or not by looking at Pearson Chi-square coefficient value (p).

INCLUSION CRITERIA AND EXCLUSION CRITERIA:

Questionnaires were filled from those subjects which were diagnosed by the ward physicians as a patient of Hepatitis C at the stage of compensated liver disease (CLD) prior to development of abdominal ascites and peripheral edema excluding all the critically ill patients and patients with severe hypotension. All the patients of suspected or diagnosed dysfunction of Hypothalamic-Pituitary-Adrenal Axis were excluded from the study. In addition, all those patients whom refused to participate in the study for no reason were also excluded.

Perceived Stress Scale:

Sheldon Cohen and his colleagues developed the Perceived Stress Scale. It was published in 1983 and had become one of the most widely used psychological instrument for evaluation of the nonspecific perceived stress [1]. It comprises of 10 items and all the items were measured on 5-point scale (0 = never; 1 = almost never; 2 = sometimes; 3 = fairly often; 4 = very often). In this scale, 10 questions were added about feelings and thoughts. Perceived Stress Scale (PSS) were provided by the Department of Psychiatry, Lahore General Hospital, Lahore after the assurance of no ethical clearance problems by PSS's authors.

RESULTS:

124 patients were included in stress and systolic blood pressure study. Frequency analysis showed that male patients were 63{50.8%} and female were 61{49.2%}. Married patients were 113{91.1%} and unmarried were 11{8.9%}. Patients of age below 40 years were 28{22.6%} and equal & above 40 years were 96{77.4%}. Age ranged from 18 to 80 years. The patients with no formal education were 83{66.9%} and with formal education were 41{33.1%}.

For systolic blood pressure minimum value was 90, maximum was 178, mean was 134.2016 and standard deviation was 19.94382. For diastolic blood pressure minimum value was 67, maximum was 109, mean value was 85.0081 and standard deviation was 9.50866. Minimum value of height in meters was 1.52, maximum value was 2.13, mean was 1.7809 and standard deviation was 0.17959. Minimum value of weight in kilograms was 45, maximum was 112, mean value was 73.9113 and standard deviation was

13.49496. Minimum value for perceived stress score was 10.00, maximum value was 156.00, mean value was 27.6048 and standard deviation was 24.97082. (Table 1)

The subjects with low perceived stress (0-13) were 53 (42.7%), with moderate perceived stress score were 15 (12.1%) and with severe perceived stress score were 56 (45.2%). The subjects having BMI in the underweight range were found to be 23 (18.5%), in the normal BMI range were 52 (41.9%) and in the overweight & obese range were 49 (39.5%). (Graph 1). The subjects having normal systolic and diastolic blood pressures were 43 (34.7%), having prehypertension were 16 (12.9%), having hypertension stage 1 were 55 (44.4%) and having hypertension stage 2 were 10 (8.1%). (Graph 2)

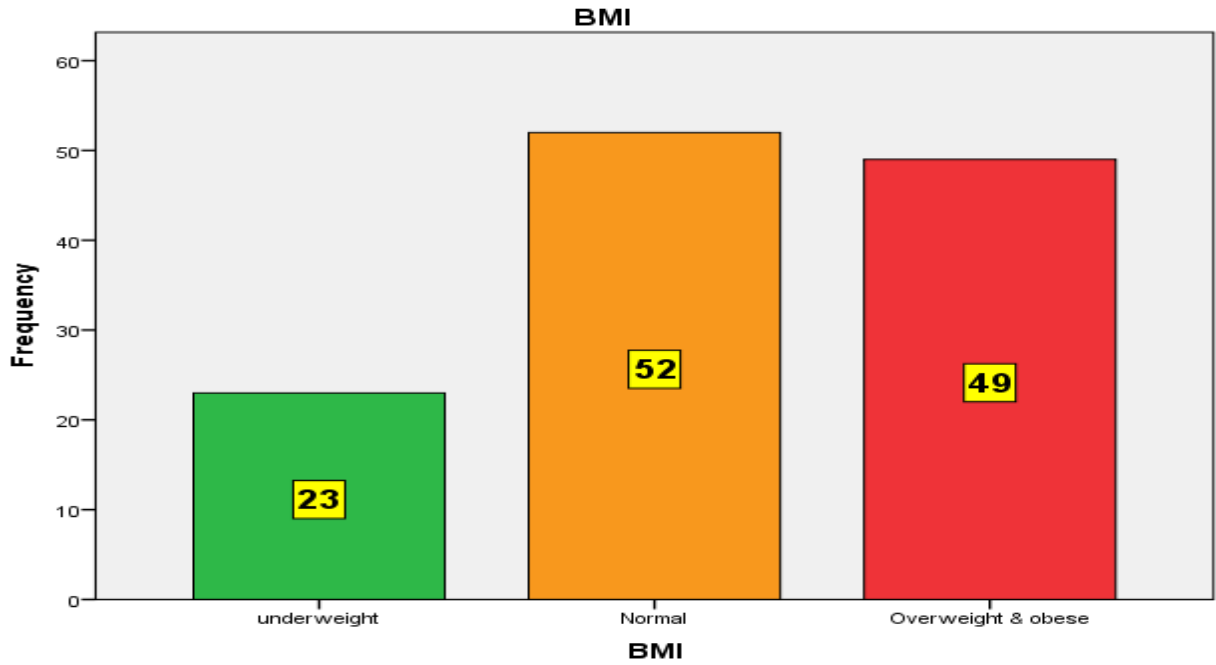
Blood Pressure and Perceived Stress Level:

The subjects having normal BP with low stress level were 34(64.2%), moderate stress level 3(20%) and with severe stress level 6(10.7%) and total number of subjects with normal SBP were 43(34.7%). The subjects with BP in prehypertension range with low stress level were 6(11.3%), with moderate stress level 4(26.7%) and with severe stress level were 6(10.7%) and total number of subjects with prehypertension were 16(12.9%). The subjects with BP within the stage 1 hypertension with low stress level were 6(11.3%), moderate stress level was 8(53.3%) and with severe stress level were 41(73.2%) and total number of subjects were 55(44.4%). The subjects with BP in the Stage 2 hypertension with low stress level were 7(13.2%), moderate stress level was 0(0%) and with severe stress level were 3(5.4%) and total number of subjects were 10(8.1%) and $p < 0.001$. (Table 12)

Body Mass Index and Blood Pressure:

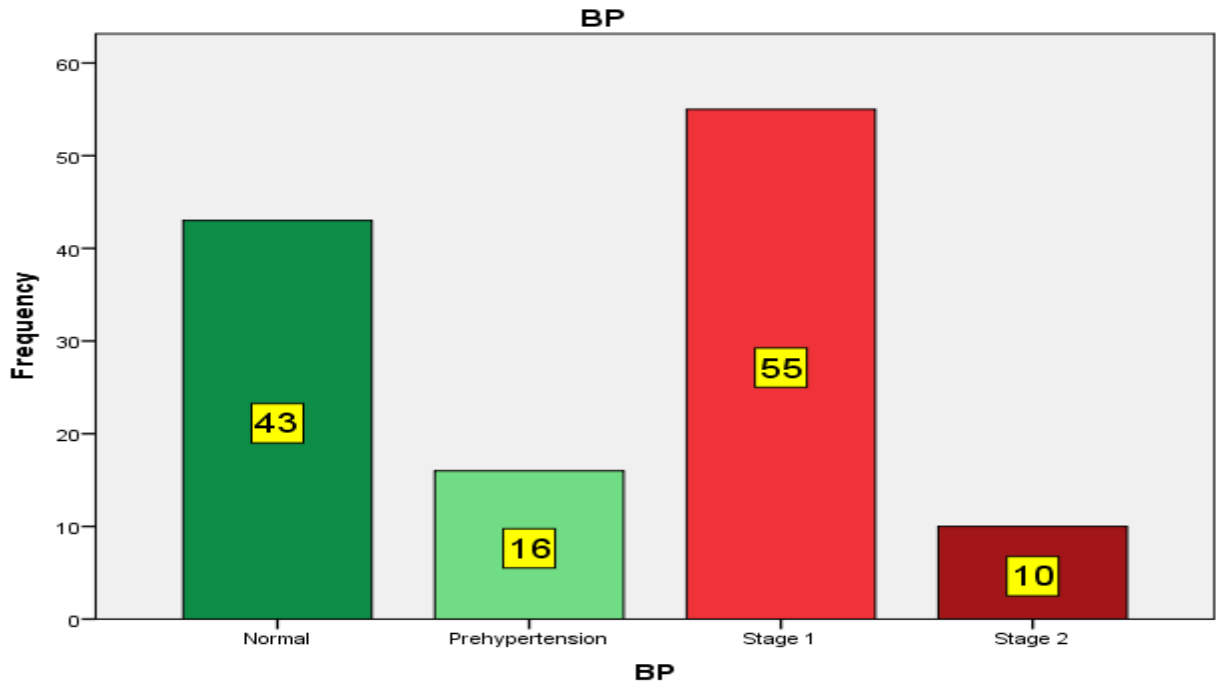
The subjects having normal blood pressure with BMI in the underweight range were 14(60.9%), with normal BMI were 17(32.7%), and with overweight range were 12(24.5%). The subjects having blood pressure in prehypertension category with BMI in the underweight range were 6(26.1%), with normal BMI were 7(13.5%), and with overweight range were 3(6.1%). The subjects having stage 1 hypertension with BMI in the underweight range were 3(13%), with normal BMI were 25 (48.1%), and with overweight range were 27(55.1%). The subjects having stage 2 hypertension with BMI in the underweight range were 0(0%), with normal BMI were 3(5.8%), and with overweight range were 7(14.3%). (Table. 1)

Graph No.1: Frequencies and number of underweight, normal, overweight and obese patients.



Footnotes:
BMI: Body Mass Index

Graph No.2: Frequencies and number of patients showing normal, prehypertension, hypertension stage 1 & 2



Footnotes:
BP: Blood Pressure

Table 1: Descriptive statistics of systolic blood pressure, diastolic blood pressure, height, weight and perceived stress score.

	N	Minimum	Maximum	Mean	Std. Deviation
Systolic Blood Pressure (mmHg)	124	90.00	178.00	134.2016	19.94382
Diastolic Blood Pressure (mmHg)	124	67.00	109.00	85.0081	9.50866
Height (feet)	124	5.00	7.00	5.8427	.58922
Weight (kg)	124	45.00	112.00	73.9113	13.49496
Perceived Stress Score	124	10.00	37.00	27.6048	24.97082
Valid N (listwise)	124				

Table 2: Relationship of blood pressures and perceived stress score.

			Stress			Total
			Low	Moderate	Severe	
Blood Pressure	Normal	Count	34	3	6	43
		% within Stress	64.2%	20.0%	10.7%	34.7%
	Prehypertension	Count	6	4	6	16
		% within Stress	11.3%	26.7%	10.7%	12.9%
	Stage 1	Count	6	8	41	55
		% within Stress	11.3%	53.3%	73.2%	44.4%
	Stage 2	Count	7	0	3	10
		% within Stress	13.2%	0.0%	5.4%	8.1%
	Total	Count	53	15	56	124
		% within Stress	100.0%	100.0%	100.0%	100.0%

	Value	df	Asymp. Sig. (2-sided)
Pearson Chi-Square	53.279 ^a	6	.000
Likelihood Ratio	58.551	6	.000
Linear-by-Linear Association	25.592	1	.000
N of Valid Cases	124		

Table 3: Relationship of blood pressure and body mass index.

			Blood Pressure				Total
			Normal	Prehypertension	Stage 1	Stage 2	
Body Mass Index	underweight	Count	14	6	3	0	23
		% within BMI	60.9%	26.1%	13.0%	0.0%	100.0%
	Normal	Count	17	7	25	3	52
		% within BMI	32.7%	13.5%	48.1%	5.8%	100.0%
	Overweight & obese	Count	12	3	27	7	49
		% within BMI	24.5%	6.1%	55.1%	14.3%	100.0%
Total	Count	43	16	55	10	124	
	% within BMI	34.7%	12.9%	44.4%	8.1%	100.0%	

	Value	df	Asymp. Sig. (2-sided)
Pearson Chi-Square	22.001 ^a	6	.001
Likelihood Ratio	24.366	6	.000
Linear-by-Linear Association	15.788	1	.000
N of Valid Cases	124		

DISCUSSION:

In this study, results depicted a higher number of subjects (57.3%) having perceived stress score in moderate & severe stress scale ranges. It was also indicated in other studies showing a significantly raised stress level in the patients of chronic diseases i.e. AIDS, Diabetes Mellitus, T.B, Thalassemia's and chronic Hepatitis C. Latest APA survey showed a relationship between chronic diseases and stress publicized by American Psychological Association (APA) at Jan,2012[13]. Similarly, prevalence of obesity in the subjects considerably high (39.5%) which was also indicated in the WHO's Obesity Chart No.311[7]. The present study indicated a much higher prevalence in the subjects of prehypertension and stage 1 hypertension. Allim Ud Din Aziz and Muhammad Ishtaq's studies had evaluated the same prevalence in our community. [14,15]

Current study showed that men were having greater odds of developing moderate & severe stress as compared to male which could be attributed the inequality of gender and increased occupational stress in men as compared to that of women. Study also indicated that married population had a greater risk of developing perceived stress. Older people were more stressed than younger (80.4%). Hu B also observed the same relationship in the gender, marital status, age and stress [16].

There was a positive correlation in the formal education and developing the perceived stress and it

could be designated to the higher work burden and lack satisfaction with the job. ($p < 0.05$). The subject that were formally educated were found to be more tense than uneducated subjects. These findings were the same that were concluded by the Chow CK and his coworkers in his study. [17] Although, the frequency of obese & overweight subjects was considerably higher than those subjects having BMI in the underweight and normal ranges but that relationship between BMI and stress was not statistically significant.

The present study indicated a very strong positive relationship between BMI and SBP & DBP which could be attributed the increased body mass cause a mark increase in the blood volume and cardiac output [8]. Also, current study indicated statistically a very strong relationship between perceived stress and developing prehypertension and hypertension stage 1 ($p < .001$). Present study documented the and statistically significant relationship between BMI and blood pressure ($p < 0.001$) in the obese & overweight subjects and similar results had been documented by Baniyas, Jamaican population and industrialized economies. [19,20,21].

POSSIBLE MECHANISM:

Stress is a compromised state of homeostasis which may be elicited by intrinsic or extrinsic stressors and stress response contributed by highly interconnected cellular and molecular infrastructure and neuroendocrine interactions. Following are the key

mechanisms through which stress causes the increased BP:

1. Major components of stress system are the CRH and AVP secretory neurons with catecholaminergic neurons. Stress causes sympathetic ANS to release different catecholamines which stimulate CRH and vasopressin secretion. CRH is secreted into the hypophyseal portal system and holds a key role in the stress response, representing the most important modulator of pituitary ACTH secretion. CRH directly and angiotensin II synergistically stimulate ACTH secretion. CRH binds G-protein-coupled class II seven-transmembrane receptors. CRH-R1 (Anterior Pituitary, Adrenal Cortex, Lateral Hypothalamic Nucleus, Locus Coeruleus & Neocortex) and CRH-R2 (VM hypothalamic Nuclei, Cerebellum & Brain stem) causing the activation of stress response. [23] During stressful conditions, CRH and AVP secretory pulses increase to maximum. In addition to it, cytokines of inflammation and angiotensin II are acted on HPA axis to mainly stimulate its activity. [25]

2. The adrenal cortex is a major target organ of ACTH. ACTH stimulates glucocorticoid and androgens secretion by the ZF and ZR Zones, ACTH released into blood binds with G α and GR β receptors and receptor-hormone complex enters the nucleus, interacting with glucocorticoid response elements (GREs) of the DNA to hormone-responsive genes and translation and transcription of anti-inflammatory effects giving proteins such as AP-1, Necrotic Factor- κ B and released glucocorticoids have the ability to regulate mitochondrial functions and energy metabolism. [24]

3. Stress causes activation of sympathetic NS releases NE from the postganglionic neurons which innervate many viscera (skeletal muscles, heart, kidneys, gut, the smooth muscle cells of the vasculature, adipose tissue) responding to stressor. [26]

4. Stress System also interacts with other systems including arcuate nucleus POMC neuronal system, amygdala/hippocampus, thermoregulatory center - temperature regulation, appetite/satiety centers - appetite regulation, mesocorticolimbic dopaminergic system, CLOCK system to respond to the stressor to maintain homeostasis. [23]

5. Finally, the renin-angiotensin system is intimately involved with the stress response with angiotensin II is a major stress hormone with increased plasma renin activity (PRA) and plasma aldosterone

concentration [27]

Dysfunction and Dysregulation of this system can lead to a state of eustasis or allostasis, with a broad spectrum of clinical manifestations and disorders like hypertension. [22]

CONCLUSION:

Psychological stress and increased BMI were associated with an increased risk for prehypertension and stage 1 hypertension in patients of CLD stage of Hepatitis C. In addition, psychological stress affected men more than women in developing hypertension. Obese population when classified as "Prehypertensive" should cause these subjects to take notice and have regular BP charting. Therefore, weight management and life style modifications programs must be started.

REFERENCES:

1. Mancia G, Fagard R, Narkiewicz K, et al. 2013 ESH/ESC guidelines for the management of arterial Arterial Hypertension of the European Society of Hypertension (ESH) and of the European Society of Cardiology (ESC). *Eur Heart J* 2013; 34(28): 2159-219.
2. World Health Organization. A global brief on hypertension. Silent killer, global public health crisis. Geneva 2013. Available from: http://apps.who.int/iris/bitstream/10665/79059/1/WHO_DCO_WH_D_2013.2_eng.pdf?ua=. Accessed at 1st April, 2018.
3. Chow CK, Teo KK, Rangarajan S, et al. Prevalence, awareness, treatment, and control of hypertension in rural and urban communities in high-, middle-, and low-income countries. *JAMA* 2013; 310(9): 959-68
4. Lower Definition of Hypertension; New ACC/AHA High Blood Pressure Guidelines, Nov 13, 2017. Available at: <http://www.acc.org/latest-in-cardiology/articles/2017/11/08/11/47/mon-5pm-bp-guideline-aha-2017>. Accessed at 1st April, 2018.
5. Hu B, Liu X, Yin S, Fan H, Feng F, Yuan J (2015) Effects of Psychological Stress on Hypertension in Middle-Aged Chinese: A Cross-Sectional Study. *PLoS ONE* 10(6): e0129163. <https://doi.org/10.1371/journal.pone.0129163>. Accessed at 1st April, 2018.
6. Does stress increase my blood pressure? American Heart Association. http://www.heart.org/HEARTORG/Conditions/HighBloodPressure/Prevention/Treatment/HighBloodPressure/Stress-and-Blood-Pressure_UCM_301883_Article.jsp. Accessed at 1st April, 2018.
7. World Health Organization. Fact Sheet No 311. Obesity and overweight. Geneva 2013. Available from: <http://www.who.int/mediacentre/factsheets/fs311/e>

- n/accessed at 1st April, 2018.
8. Excess fat- Obesity. John E. Hall. Guyton and Hall Textbook of Medical Physiology. 13th ed. Philadelphia PA: Saunders-Elsevier 2015.69:870
 9. Savva SC, Kourides YA, Hadjigeorgioua C, Tornaritis MJ. Overweight and obesity prevalence and trends in children and adolescents in Cyprus 2000-2010. *Obesity Res Clin Pract* 2013; ORCP-348, article in press.
 10. 13. Dua S, Bhuker M, Sharma P, Dhall M, Kapoor S. Body Mass Index Relates to Blood Pressure Among Adults. *North American Journal of Medical Sciences*. 2014;6(2):89-95. doi:10.4103/1947-2714.127751
 11. 14. Dua, Suman et al. "Body Mass Index Relates to Blood Pressure Among Adults." *North American Journal of Medical Sciences* 6.2 (2014): 89–95. PMC. Web. 1 Apr. 2018.
 12. 15. Dua, S., Bhuker, M., Sharma, P., Dhall, M., & Kapoor, S. (2014). Body Mass Index Relates to Blood Pressure Among Adults. *North American Journal of Medical Sciences*, 6(2), 89–95. Available at: <http://doi.org/10.4103/1947-2714.127751>. accessed at 1st April, 2018
 13. Latest APA Survey Reveals Deepening Concerns About Connection Between Chronic Disease and Stress. American Psychological Association. Jan 02, 2012. Available at: <http://www.apa.org/news/press/releases/2012/01/chronic-disease.aspx>. Accessed at 2nd April, 2018.
 14. Aalim Uddin Aziz. Evolution of Systemic Hypertension in Pakistani Population. *Journal of the College of Physicians and Surgeons Pakistan* 2015, Vol. 25(4): 286-291
 15. Gul S, Atif Hussain, Muhammad Ishtiaq, Zarka Ahmad, Imranullah, Muhammad Kamran Khalil ASSESSMENT OF RISK FACTORS FOR HYPERTENSION AMONG ADULT POPULATION OF HAYATABAD, PESHAWAR *J. Med. Sci. (Peshawar, Print)* July 2015, Vol. 23, No. 3: 158-162.
 16. Hu B, Liu X, Yin S, Fan H, Feng F, Yuan J (2015) Effects of Psychological Stress on Hypertension in Middle-Aged Chinese: A Cross-Sectional Study. *PLoS ONE* 10(6): e0129163. <https://doi.org/10.1371/journal.pone.0129163>. Accessed at 1st April, 2018.
 17. WHO expert consultation. Appropriate body mass index for Asian population and its implication for policy and intervention strategies. *Lancet*. 2004; 363:157–63.
 18. Kusuma YS, Babu BV, Naidu JM. Blood pressure levels among cross cultural/populations of Visakhapatnam district, Andhra Pradesh, India. *Ann Hum Biol*. 2002; 29:502–12
 19. Ferguson TS, Younger NO, Tulloch-Reid MK, Wright MB, Ward EM, Ashley DE, et al. Prevalence of prehypertension and its relationship to risk factors for cardiovascular disease in Jamaica: Analysis from a cross-sectional survey. *BMC Cardiovasc Disord*. 2008; 8:20
 20. Doll S, Paccaud F, Bovet P, Burnier M, Wietlisbach V. Body mass index, abdominal adiposity and blood pressure: Consistency of their association across developing and developed countries. *Int J Obes Relat Metab Disord*. 2002; 26:48–57.
 21. Gupta S, Kapoor S. Sex differences in blood pressure levels and its association with obesity indices: Who is at greater risk. *Ethn Dis*. 2010; 20:370–4
 22. Tsigos C, Chrousos GP. Physiology of the hypothalamic-pituitary-adrenal axis in health and dysregulation in psychiatric and autoimmune disorders. *Endocrinol Metab Clin North Am* 1994; 23:451-466.
 23. Abou-Samra AB, Harwood JP, Catt KJ, Aguilera G. Mechanisms of action of CRF and other regulators of ACTH release in pituitary corticotrophs. *Ann N Y Acad Sci* 1987; 512:67-84
 24. Adrenocortical Hormones. John E. Hall. Guyton and Hall Textbook of Medical Physiology. 13th ed. Philadelphia PA: Saunders-Elsevier 2015. 78:965-981.
 25. Burnstock G, Miller P. Structural and chemical organization of the autonomic nervous system with special reference to noradrenergic non-cholinergic transmission, in *Autonomic Failure. A Textbook of Clinical Disorders of the Autonomic Nervous System*. Bannister R, Mathias CJ (eds), Oxford Medical Press, Oxford, 1989, pp107
 26. The Autonomic Nervous System and the Adrenal Medulla. John E. Hall. Guyton and Hall Textbook of Medical Physiology. 13th ed. Philadelphia PA: Saunders-Elsevier 2015.61:773-785
 27. The Renin-Angiotensin System: Its Role in Arterial Pressure Control and Role of the Kidneys in Long-Term Control of Arterial Pressure and in Hypertension. John E. Hall. Guyton and Hall Textbook of Medical Physiology. 13th ed. Philadelphia PA: Saunders-Elsevier 2015. 213-228.