Progress in Chemical and Biochemical Research

Journal homepage: www.pcbiochemres.com

Original Research Article

Serum Gamma-Glutamyl Transferase and Its Level in Hypertension

Mahendra Baduwal[1], Dipendra Bikram Hamal[1], Sankar Pokhrel[1], Saugat Adhikari[1], Shruti Pudasaini[1], Suresh Jaiswal[2], Ashok Kumar Sah[3], Rajesh Kumar Thakur[1]*

[1]*Modern Technical College, Pokhara University, Lalitpur, Nepal*
[2]*School of Health and Allied Sciences, Pokhara University, Kaski, Nepal*
[3]*Amity Medical School, Amity University Haryana, Gurugram, HR, India*

ARTICLE INFO

Article history
Submitted: 2020-07-01
Revised: 2020-08-02
Accepted: 2020-08-16
Available online: 2020-09-04
Manuscript ID: PCBR-2007-1104
DOI: 10.22034/pcbr.2020.113658

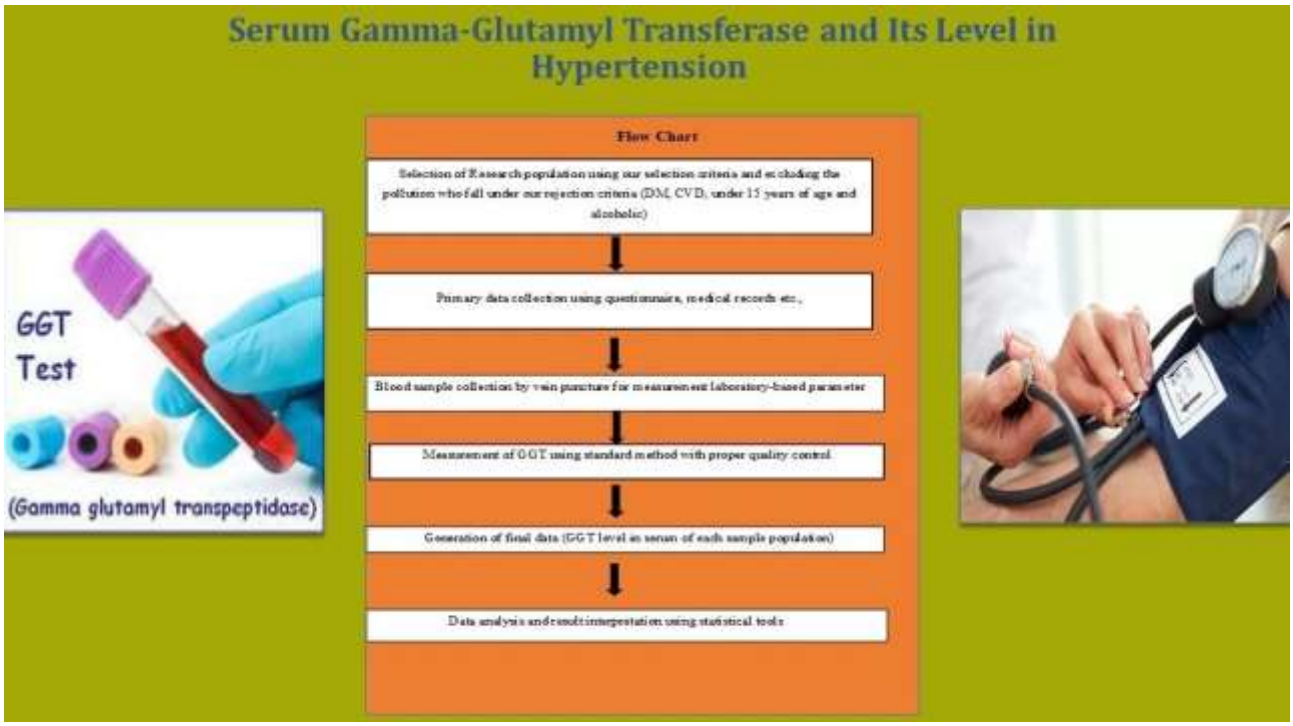
KEYWORDS
Prehypertension
Hypertension
Gamma Glutamyl-transferase

ABSTRACT

Hypertension, a chronic medical condition of elevated blood pressure in the arteries which can be classified as prehypertension and hypertension. Serum gamma-glutamyl transferase (GGT), an enzyme that transfers gamma-glutamyl functional group is a diagnostic marker of liver disease, excessive alcohol consumption, but recently its level was found to be elevated in prehypertension or hypertension. A total of 315 people was selected for clinic-based comparative Cross-sectional study. Data was generated using a clinical report, physical examination, review of medical and clinical reports, and interviews using a structured questionnaire. The blood sample was withdrawn after proper consent of the study population for measurement of laboratory-based parameters. Serum GGT was estimated using the method described by Persijn and Van der Slik Kinetic spectrophotometric method as recommended by International Federation for Clinical Chemistry. Data was entered and analyzed using SPSS and Excel. Among 315 study population majority were male and adults. Prevalence of prehypertension and hypertension was relatively high (27.5% and 39.5% respectively). Among the hypertensive population, males (40.2%) and >60 years of age (71.6%) shared a larger percentage. Serum GGT level positively correlates with prehypertension and hypertension with p-value 0.12 and <0.001 respectively. The significance of correlation withstands even after adjustment for age-group and gender. Prevalence of hypertension is increasing with male and older people becoming more prone to hypertension. Serum GGT levels positively correlated with prehypertension and hypertension even after adjustment for age and gender suggesting that GGT level can be used as indicator of prehypertension and hypertension.

* Corresponding author: Rajesh Kumar Thakur
✉ E-mail: npraj01@gmail.com
☏ Tel number: +977-9844104594

GRAPHICAL ABSTRACT



1. INTRODUCTION

Blood pressure (BP) is the pressure applied by circulating blood upon the walls of blood vessels. "Blood pressure" usually refers to the arterial pressure in the systemic circulation. Blood pressure is usually expressed in terms of the systolic (maximum) pressure by diastolic (minimum) pressure and is measured in millimeters of mercury (mm Hg). It is one of the vital signs along with the rate, heart, oxygen saturation, and body temperature. Blood pressure at rest for normal people (Reference blood pressure) is within range of 100-140mmHg systolic and 60-90mmHg diastolic [1].

High blood pressure (Hypertension, HTN or HT) or arterial hypertension is a chronic medical condition in which the blood pressure in the arteries is elevated [1]. Hypertension is present if the blood pressure is persistently at or above 140/90mmHg for most adults; criteria apply differently to children. Initially, hypertension usually does not cause symptoms but sustained hypertension over time is a major risk factor for hypertensive heart disease, coronary heart disease, stroke, aortic aneurysm, peripheral artery disease, and chronic kidney disease [2]. Hypertension is classified as either primary (essential) hypertension, defined as hypertension due to no identifiable cause (90-95%) and secondary hypertension due to an identifiable cause (5-10%). Tobacco, harmful, alcohol, stress, unhealthy diet, and physical inactivity are the risk factors for hypertension [3].

Serum gamma-glutamyl transferase (GGT), an enzyme that transfers the gamma-glutamyl functional group [4]. Other lines of evidence indicate that GGT can also exert a prooxidant

role, with regulatory effects at various levels in cellular signal transduction and cellular pathophysiology [5]. Serum GGT activity is a general clinical marker of excessive alcohol consumption, and GGT reflects changes in oxidative stress and implicated in the progression of hypertension [6,7]. It is found that the GGT level is found to be elevated in hypertensive patients. GGT levels, a marker of oxidative stress, are implicated in the development and progression of hypertension. The aim of the study was to determine the relationship between GGT level and Hypertension.

2. METHODS

2.1. Study design

A Clinic based comparative cross-sectional study was designed and conducted in the Balkrishna clinic (Koteshwor), Deuti Clinic (Sankhamul), and Bio- diagnostic path lab, Kathmandu, Nepal. A total of 315 participants were enrolled in the study visiting these centers were taken as the study population.

A questionnaire was designed for data collection like age, sex, and ethnicity. The patient who had Diabetes Mellitus (DM), Coronary Heart Disease (CHD), who had a recent attack of myocardial infarction and a population under 15 years of age was excluded from the study. Permission was taken from the management of Bio-diagnostic Path lab Nepal, similarly, consent was also taken from the patient before taking the sample.

Permission was taken from the management of Bio-diagnostic Path lab Nepal, similarly, consent was also taken from the patient before taking the sample

3. RESULTS

A total of 315 study participants was selected and was used for analysis purposes. These all samples were taken from above mention three clinics. The different results obtained are shown in the following figures and tables in the respective headings.

3.1 Distribution of sample population according to gender

In this study, among the total study population (N=315) male (n=211) and female (n=104) participants as shown in **Table 1**.

3.2. Distribution of study population according to age group

In this study, we have classified age in three different classes for simplification of analysis as shown in **Table 2**.

Table 1: Distribution of sample population according to gender

Characteristics	Number of cases (n)	Percentage %
Male	211	68
Female	104	32
Total	315	100

Table 2: Distribution of study population in different age-group

Characteristics (in years)	Number of cases (n)	Percentage (%)
15-35	44	14
35-60	151	48
60 and above	120	38
Total	315	100

3.3. Distribution of study population according to arterial pressure

Among 315 (N) study population relatively higher percentage were found of hypertensive (n=124) and few populations were pre-hypertensive (n= 87). 33 percentage (n=104) of the total population were on-hypertensive according to their arterial pressure as shown in **Table 3**.

3.4. Comparison of arterial pressure with gender and age group

Among hypertensive population (N=124), male (n=85) a shared large number of hypertensive populations with comparison to female (n=37). While in the Non-hypertensive population (N=104), females (n=64) shared a larger number than males (n=40) as shown in **Table 4** and **Fig. 1.** In the comparison of age group and arterial the pressure, we found that 60 years and above showed a higher prevalence of hypertension (71.6%). While 15-35 years of age group were relatively non-hypertensive (61.3%). In the population of prehypertension (N= 87), many were of male (n=62) and age group of 35-60 years (n=51) of age as shown in **Table 4** and **Fig. 2**.

Table 3. Distribution of sample population according to arterial pressure

Variables	Number of cases (n)	Percentage (%)
Non-hypertension	104	33
Pre-hypertension	87	27.5
Hypertension	124	39.5
Total	**315**	**100**

Table 4. Comparison of arterial blood pressure with gender and age-group.

Variables	Non-Hypertensive case number (%)	Pre-hypertensive case number (%)	Hypertensive cases number (%)	Total
Gender				
Male	64 (30.2)	62 (29.3)	85 (40.2)	211 (100)
Female	40 (38.3)	25 (24.0)	37 (35.5)	104 (100)
Age Distribution				
15-35	27 (61.3)	10 (22.2)	7 (15.9)	44 (100)
35-60	69 (45.6)	51 (33.3)	31 (20.5)	151 (100)
60 and above	08 (6.6)	26 (21.6)	86 (71.6)	120 (100)

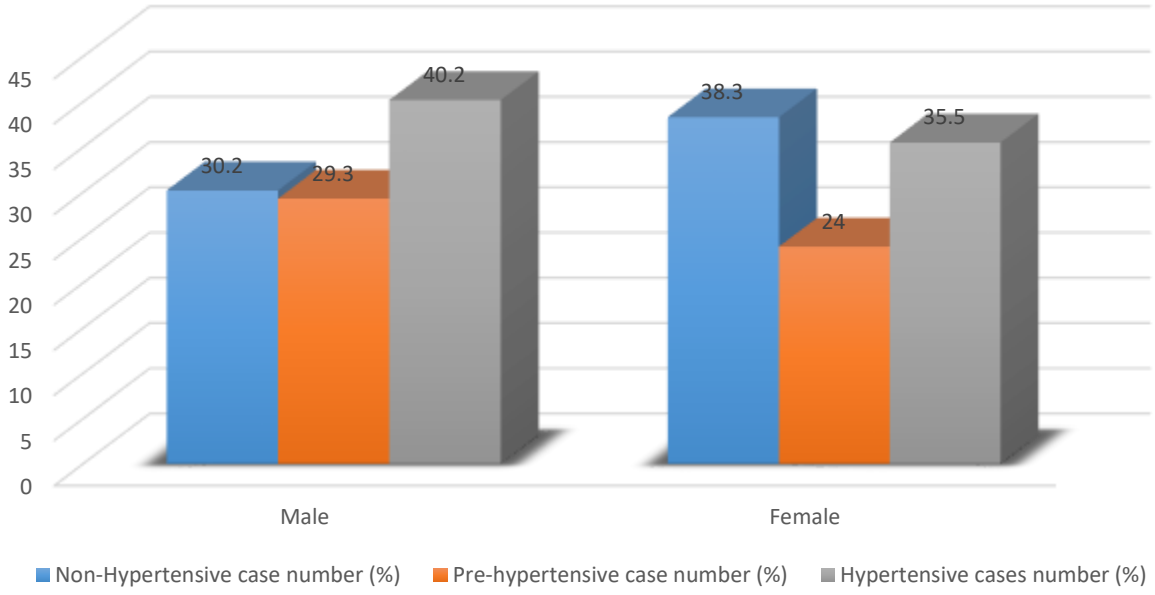


Fig. 1: Comparative graph of arterial pressure and gender.

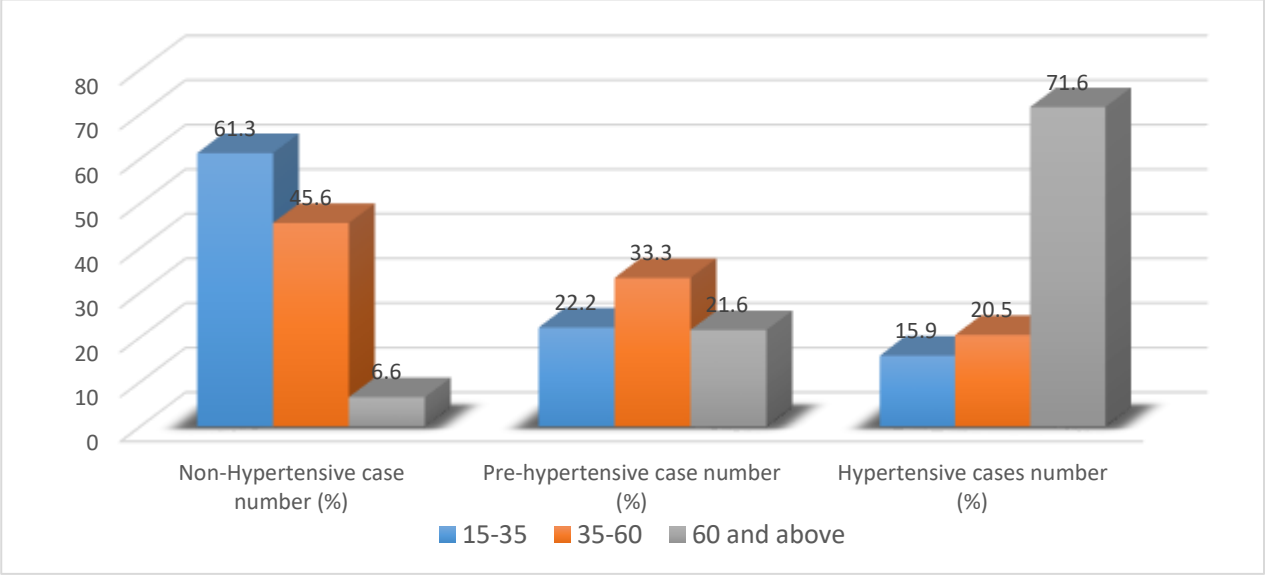


Fig. 2: Comparative graph of blood pressure status and age-group

3.5. Comparison of blood pressure status and serum GTT level

In our study, we found that mean GGT level in hypertension is significantly higher than that of non-hypertension with p-value <0.01 and GTT level in pre-hypertension was slightly higher than non-hypertensive population but was not significant bio-statistically.

For simplification of statistical calculation, we converted our obtained serum GGT level in three tertiles according to Kawamoto et al [20]. We compared blood pressure status with serum GTT we found that a higher percentage of the hypertensive population (50.8%) has Serum GGT level of third tertiles (>53 IU/L) while a greater percentage of non-hypertensive population (62.5%) had serum GTT level of 1st tertile (<29 IU/L) as shown in **Table 5** and **6**.

Table 5. Comparison of blood pressure status and mean serum GGT

Variables	Number of cases (n)	Mean level of GTT (IU/L)	Standard deviation of level of GTT
Non-hypertension	104	26	4.5
Pre-hypertension	87	56	6.7
Hypertension	124	78	25.4
Total	315		

Table 6. Distribution of three categories of serum GGT in blood pressure status

	Tertile 1 <29 IU/L *N=98*	**Tertile 2 29-53 IU/l *N=105***	**Tertile 3 >53 IU/L *N=112***	**Total**
Non-hypertension	65 (62.5%)	25 (24.0%)	14 (13.4%)	104 (100%)
Prehypertension	18 (20.6%)	34 (39.0%)	35 (40.2%)	87 (100%)
Hypertension	15 (12.1%)	46 (37.1%)	63 (50.8%)	124 (100%)

3.6. Association between GGT categories and risk of pre-hypertension and hypertension

When compared with the lowest tertile of serum GGT, the non-adjusted odds ratio for pre-hypertension was 1.64(95% CI, 1.12-2.38) for the middle tertile and 2.45 (95% CI, 1.47-4.97) for the highest tertile. The multivariate-adjusted odds ratios of 1.53 (95% CI, 0.86-2.71) middle tertile and 2.01 (95% CI, 1.02-4.95) for the highest tertile.

Moreover, the non-adjusted odds ratio for hypertension was 1.70 (95% CI, 1.12-2.83) for the middle and 3.40 (95% CI, 2.12-5.73) for the highest tertile while multivariate-adjusted odds ratios were 1.82 (95% CI, 1.04-3.22) and 3.01 (95% CI, 1.41-6.03) for the middle and highest tertile respectively as shown in **Table 6**.

Table 7. Association between serum GGT levels and blood pressure status

	Tertile 1 <29 IU/L *N=109*	**Tertile 2 29-53 IU/l *N=101***	**Tertile 3 >53 IU/L *N=105***	***P-value***
Pre-HTN vs NHTN				(0.012)
Non –adjusted OR (95% CI)	1.00	1.64(1.12-2.38)	2.45 (1.47-4.97)	
Multivariate-Adjusted OR (95% CI)	1.00	1.53 (0.86-2.71)	2.01 (1.02-4.95)	
HTN vs NHTN				(<0.001)
Non –adjusted OR (95% CI)	1.00	1.70 (1.12-2.83)	3.40 (2.12-5.73)	
Multivariate-Adjusted OR (95% CI)	1.00	1.82 (1.04-3.22)	3.01 (1.41-6.03)	

OR, Odds Ratio; CI, Confidence Interval. Multivariate adjusted for age and sex. p-value: $x2$ test

4. DISCUSSION

In this comparative cross-sectional, population-based study we determined the prevalence of health pre-hypertension and hypertension, as defined by JNC- 7 criteria, and their relationship to serum GGT levels. Hypertension is a common

problem in developing countries and prevalence is currently raising steadily [2,9]. In our study which was predominated by male and adults, prehypertension and hypertension were extremely common with a prevalence rate of 27.5% and 39.5% respectively. The study conducted by Panday *et al.* in 1981 showed that the overall prevalence was only 5.98 % in the rural population in Nepal. But a study conducted by Sharma *et al.,* in the 2005 suburban area of Kathmandu, Nepal revealed that the prevalence of hypertension among people aged 50 years and above was around 42 %. The study in rural Kathmandu conducted by Vaidya et al in 2006 indicated that the prevalence of hypertension in Nepal has been in the increasing trend. The same kinds of trends were also experienced in India. In our study prevalence in male was 40.2% while in female was 35.5. A recent study done by Manandar *et al*. showed the prevalence of hypertension of 44.9 which is like this study. Various studies have shown that hypertension is more prevalent in men compared to women [10-12]. However, some other studies showed female preponderance [13-17]. Our present study revealed that HT and Pre-HT are slightly higher in males, but differences between these two groups were statistically not significant (p=0.216). The variation may be explained by differential distribution in risk factors (e.g. Genetic predisposing, dietary factors, and lack of physical activities). Age is strongly associated with hypertension. In many studies, it was reported that the prevalence of hypertension increases with age [14, 15]. In this study, the prevalence of hypertension in people aged 60 years and more in this study was 70.6% (46.75% in male and 33.73% in females) which is significantly higher than other age groups (p-value 0.020). A higher prevalence of pre-hypertension and hypertension in our study might be due to the target study population were predispose to hypertension and were seeking medical attention or showing some symptoms of high blood pressure.

We found that higher GGT levels were positively associated with prehypertension or hypertension, independent of other confounders. Similar results have found by many researchers around the globe. In a community based cross-sectional study in US adults (Shankar *et al.,* 2007), with a multivariate-OR (95% CI) of 1.84 (1.37-2.46) comparing quartile 4 of GGT (>29 IU/L) to quartile 1 (<13 IU/L) [18]. This association persisted in separate analyses in men and women. Moreover, results were consistent in age and gender-adjusted analyses. Another study was done in city-dwelling men in the US by Kawamoto *et al.,* (2009) showed similar kind of results with serum GGT correlated with the relative change in BP in an individual with normal GGT concentration, these results were consistent to other research done by Miura *et al.,* 1994; lee *et al.,* 2003. These all study suggested that serum GGT levels may predict the future development of hypertension among drinkers after adjustment for baseline BP level and the amount of alcohol consumption. While a recent study was done by Yamada *et al.,* (1995) and Kawamoto et al (2009) suggested that association between serum GGT and hypertension appears to be quite similar in both drinkers and non-drinker [19,20]. In this study, we excluded alcoholic patients to eliminate the effect of alcohol consumption in serum GGT level. Results are similar to previous studies, so it is evident that serum GGT levels increase in hypertensive or pre-hypertensive population without much effect of alcohol consumption [15].

The mechanism that leads to increased BP with increased GGT is not completely understood. Serum GGT is associated with hypertension, dyslipidemia, and abnormal glucose tolerance, suggesting that it is related to hepatic insulin resistance rather than non-alcoholic fatty liver

disease [14]. GGT plays a direct role in the generation of reactive oxygen species in the presence of iron or other transition metal, including lipid peroxidation in a human biological membrane, and is an indirect marker of antioxidant systems, with the primary function of maintaining the intracellular concentration of glutathione in response to oxidative stress. These findings suggest that GGT could be an early marker of oxidative stress to the pathology of increased BP as an oxidative stressor. (13)

Many studies had been done to evaluate the correlation between serum GGT levels and blood pressure and many had shown a positive correlation of GGT to pre-hypertension and hypertension along with this study. So it is safe to say that GGT can be used as an indicator of prehypertension or hypertension but our study did not take in account of many confounders and there are many other possible confounding factors like drugs, alcoholism, obesity, lifestyle, and other conditions few of them had been studied by lee *et al.,* 2003 and found that the correlation between GTT and hypertension was significant after adjusting for these factors. But many other factors might be involved in the high GGT level. These factors should be identified and adjusted before suggesting the GGT as a true indicator of hypertension syndrome [16].

CONCLUSION and RECOMMENDATION

The Prevalence of Pre-Hypertension and Hypertension is slightly higher in males than in females. The prevalence of hypertension increases with increasing age and the highest prevalence of hypertension was found in the above 60 age group. Serum GTT levels increase inpatient with pre-hypertension and hypertension without much variance in gender and age group.

The male and older population seems to be more prone to hypertension so these populations should be more careful about their health should be educated about possible causes of hypertension and its preventive measures. Studied should be performed in much larger scale in wide range of population with identification of all possible confounding factors for determination of the more accurate significance of GGT as an indicator of pre-hypertension and hypertension

Conflict of Interest

The authors declare no conflict of interest.

REFERENCES

[1] Association AH. Understanding blood pressure readings. 2014.

[2] CA Emdin, SG Anderson, T Callender, N Conrad, G Salimi-Khorshidi, H Mohseni, M Woodward, K Rahimi, Usual blood pressure, peripheral arterial disease, and vascular risk: cohort study of 4.2 million adults*, Bmj*. (2015 Sep 29) 351.

[3] N Henningsen, O Ohlsson, I Mattiasson, E Trell, H Kristensson, B Hood, Hypertension, Levels of Serum Gamma Glutamyl Transpeptidase and Degree of Blood Pressure Control in Middle-Aged Males, *Acta medica scandinavica*, 207 (1980) 245-251.

[4] D-H Lee, R Blomhoff, DR Jacobs, Review is serum gamma glutamyltransferase a marker of oxidative stress? *Free radical research*, 38(6)(2004) 535-53.

[5] C Courtay, T Oster, F Michelet, A Visvikis, M Diederich, M Wellman, et al., γ-Glutamyltransferase: nucleotide sequence of the human pancreatic cDNA: evidence for a ubiquitous γ-glutamyltransferase polypeptide in human tissues, *Biochemical pharmacology*, 43(12) (1992) 2527-33.

[6] G Lum, SR Gambino. Serum gamma-glutamyl transpeptidase activity as an indicator of disease of liver, pancreas, or bone, *Clinical Chemistry*, 18(4) (1972) 358-362.

[7] D Giugliano, A Ceriello, G Paolisso, Diabetes mellitus, hypertension, and cardiovascular disease: which role for oxidative stress? *Metabolism*, 44(3) (1995) 363-368.

[8] JP Persijn, W Slik. A new method for the determination of γ-glutamyltransferase in serum 1976.

[9] WHO. Global Health Observatory (GHO) data, Data repository Reports, Country statistics, Map gallery, Standards Raised blood pressure, Situation and trends.

[10] Organization WH. A global brief on hypertension: Silent killer, global public health crisis. 2013. URL: http://apps who int/iris/bitstream/10665/79059/ 1/WHO_DCO_WHD_2013 2_eng pdf [accessed 2013-07-17][WebCite Cache ID 6IBqAI2eN]. 2015.

[11] KK Aryal, Non communicable diseases risk factors: *STEPS Survey Nepal* 2013-2014.

[12] S Laurent, P Boutouyrie, R Asmar, I Gautier, B Laloux, L Guize, et al., Aortic stiffness is an independent predictor of all-cause and cardiovascular mortality in hypertensive patients, *Hypertension,* 37(5) (2001) 1236-1241.

[13] M Lida, K Ueda, A Okayama, K Kodama, K Sawai, S Shibata, et al., Impact of elevated blood pressure on mortality from all causes, cardiovascular diseases, heart disease and stroke among Japanese: 14 year follow-up of randomly selected population from Japanese--Nippon data 80, *Journal of human hypertension*, 17(12) (2003) 851-857.

[14] K Miura, ML Daviglus, AR Dyer, K Liu, DB Garside, J Stamler, et al., Relationship of blood pressure to 25-year mortality due to coronary heart disease, cardiovascular diseases, and all causes in young adult men: the Chicago Heart Association Detection Project in Industry, *Archives of Internal Medicine*, 161(12) (2001) 1501-1508.

[15] K Karki, B Dahal, A Regmi, A Poudel, Y Gurung, WHO STEPS Surveillance: Non Communicable Diseases Risk Factors Survey, 2008. Kathmandu: *Ministry of Health and Population, GoN, Society for Local Integrated Development Nepal (SOLID Nepal) and WHO.* (2008).

[16] STEP I. Non Communicable Diseases Risk Factors: STEPS Survey Nepal 2013. 2012.

[17] CF Liu, YT Gu, HY Wang, NY Fang, Gamma-Glutamyltransferase Level and Risk of Hypertension: A Systematic Review and Meta-Analysis, *PLoS ONE*, 7(11) (2012).

[18] A Shankar, J Li, Association between serum gamma-glutamyltransferase level and prehypertension among US adults, *Circulation Journal*, 71(10) (2007) 1567-1572.

[19] Y Yamada, E Ikai, I Tsuritani, M Ishizaki, R Honda, M Ishida, The relationship between serum gamma-glutamyl transpeptidase levels and hypertension: common in drinkers and nondrinkers, *Hypertension Research*, 18(4) (1995) 295-301.

[20] R Kawamoto, K Kohara, Y Tabara, T Kusunoki, N Otsuka, T Miki, Association between serum gamma-glutamyl transferase level and prehypertension among community-dwelling men, The Tohoku journal of experimental medicine, 216(3) (2008) 213-221.

HOW TO CITE THIS ARTICLE
Mahendra Baduwal, Dipendra Bikram Hamal, Sankar Pokhrel, Saugat Adhikari, Shruti Pudasaini, Suresh Jaiswal, Ashok Kumar Sah, Rajesh Kumar Thakur, Serum Gamma-Glutamyl Transferase and Its Level in Hypertension, Prog. Chem. Biochem. Res. 2020, 3(4), 319 -328
DOI: 10.22034/pcbr.2020.113658
URL: http://www.pcbiochemres.com/article_113658.html