| Impaired Glucose |

Frequency of Impaired Glucose Tolerance in Patients of Essential Hypertension in Tertiary Care Hospital, Larkana

1. Muhammad Aslam Soomro 2. Ghulam Yasin Abro 3. Imdad Ali Ansari
4. Sayed Aftab Ahmed Shah 5. Sayed Shafiq Rahman Shah

1,2. Sen. Registrars of Medicine 3. Asstt. Prof. of Medicine 4. Prof. of Medicine 5. Sen. Registrar of Medicine, Chandka Medical College & Hospital Larkana

ABSTRACT

Objective: To determine the frequency of impaired glucose tolerance in patients of essential hypertension.

Study Design: Descriptive Cross sectional study.

Place and Duration of Study: This study was conducted at the Medical Outpatient department of Chandka Medical College Hospital Larkana, over one year period from February 2012 to February 2013.

Materials and Methods: Total 171 patients of age 40-70 years having hypertension more than 2 years were purposively selected, while Known cases of DM, secondary hypertension & metabolic syndrome were excluded. Oral glucose tolerance was performed on selected patients of essential hypertension and plasma glucose was measured 2 hours after giving 75 g of glucose to each patient. Patients with (2 hours plasma glucose) level of 140-199 mg/dl were considered impaired glucose tolerance. Frequency was calculated for gender, number & type of medication & impaired glucose tolerance. The mean & SD were calculated for age, height, weight, BMI and duration of HTN. Stratification of age, gender, BMI & duration of hypertension done while applying Chi-Square with p value <0.05 as significant.

Results: One hundred and seventy one (171) patients met the inclusion criteria with mean age of 53.42 $\pm$ 8.059 among those 104 were males (60.81%) while 67 were females (39.19%). Duration of hypertension ranged 3-15 years with a mean duration of 7.47 $\pm$ 3.26 years. Mean Body mass index (BMI) was 25.95 $\pm$ 4.32, minimum BMI 17.88 & maximum BMI was 39.91. Frequency of IGT was 39.2% (n=67). Mean serum glucose level at 2 hours in these patients was 159.33 $\pm$ 27.937 grams/dL. Males were more affected while age has little effect on IGT frequency. More the duration of hypertension more was the prevalence of IGT. BMI was significant effect modifier for IGT; in overweight & obese patients the frequency of IGT was much higher (40.58% in overweight & 69.23% in obese) than normal weight patients (27.78%). (p value <0.003).

Conclusion: IGT is much frequent in essential hypertension. Hypertensive males, elder age, longer duration of hypertension, high BMI & use of more than one antihypertensive medicine are associated with higher rates of IGT. This study suggests that all the patients with essential hypertension should be scrutinized for blood glucose levels.

Key Words: Essential hypertension. Impaired glucose tolerance

INTRODUCTION

Hypertension is one of the most common conditions and is a major risk factor for stroke, myocardial infarction, vascular disease, and chronic kidney disease.[1] Hypertension (HTN) is a trait as opposed to a specific disease and represents a quantitative rather than a qualitative deviation from the normal. HTN is a common health problem worldwide with ongoing global increase in the incidence.[1,2]

Approximately 25% of the adult population are affected with hypertension. Although historically defined as "an elevation of blood pressure" alone, hypertension is characterized by abnormalities of cardiac output, systemic vascular resistance, and arterial compliance.[3] According to the American Heart Association (AHA), approximately 75 million adults in the United States are affected by hypertension.[2]

Despite extensive research over the past several decades, the etiology of most cases of adult hypertension is still unknown, and control of blood pressure is suboptimal in the general population.[4] Due to the associated morbidity and mortality and cost to society, preventing and treating hypertension is an important public health challenge. Fortunately, recent advances and trials in hypertension research are leading to an increased understanding of the pathophysiology of hypertension and the promise for novel pharmacologic and interventional treatments for this widespread disease.[5]

The aim of this study was to investigate and find the frequency of impaired glucose tolerance test in patients with essential hypertension as IGT is much frequent in patients with essential hypertension.

In the several studies, the presence of a family history of diabetes, impaired glucose tolerance, hypertension (HTN), and an increase in BMI were found to be independent risk factors for the development of diabetes.[6-8] It has been reported that changing one's life style (to lessen obesity, increasing physical activities,

changing nutritional habits) causes a serious decrease, or at least a delay in the development of diabetes.[9,10] The morbidity and mortality due to cardiovascular system (CVS) disorders are increased in the Diabetes Mellitus (DM) group. They are also increased in the impaired fasting glucose (IFG) and impaired glucose tolerance (IGT) groups. Thus, the detection of IFG and IGT in patients has more diagnostic value.[11-13]

Obesity, smoking, IGT, hyperlipidemia, and HTN are the risk factors for cardiovascular disease.[14,15] It has been determined that hyper-insulinemia and an impaired glucose uptake in muscle cells are seen in essential HTN.[16]

MATERIALS AND METHODS

This cross sectional study was conducted at medical outpatient department of Chandka Medical College Hospital Larkana from febuary 2012 to febuaru 2013. Due approval was obtained from ethics committee of the hospital to conduct this study. One hundred seventy one patients were enrolled in the study meeting the inclusion criteria of known cases of essential hypertension of either sex with duration of hypertension more than two years and on anti hypertensive treatment. Known cases of diabetes mellitus secondary hypertension and metabolic syndrome were excluded. Informed written consent was taken from all the patients visiting medical outpatient department of Chandka Medical College Hospital Larkana. Brief history was taken for the duration of HTN and medication used (confirmed by Physicians prescription). Height and weight were measured and BMI was calculated by dividing the weight in kg by height in meter square.

The oral glucose tolerance test (OGTT) was performed on selected patients of essential hypertension and plasma glucose was measured 2 hours after giving 75 grams of glucose to each patient. Patients with 2 hour plasma glucose (2h PG) level of 140-199 mg/dL were considered as having impaired glucose tolerance (IGT).

All stastical analysis were conducted with stastical package for social sciences (SPSS) for windows version 19. Descriptive statistics were applied to calculate mean and standard deviation for age of patient, height, weight, BMI and duration of HTN. Frequencies and percentages were calculated for gender, number and type of medication and impaired glucose tolerance. Stratification was done with regards to age of the patients, gender, BMI and duration of hypertension to see the effect of these on outcome. Chi square test was applied to compare the effect of effect modifiers on outcome; P value of less than 0.05 was considered as significant.

RESULTS

One hundred and seventy one (171) patients met the inclusion criteria with mean age 53.42 ± 8.059 were enrolled in the study. Among these 104 were males (60.82%) while 67 were females (39.18%). Duration of hypertension in these patients ranged 3 to 15 years with mean duration 7.47 ± 3.26 years. Mean weight of patients was 73.54 ± 10.13 kg. Minimum weight of patients was 52 Kg while maximum weight was 98 kg. Mean height of patient was 2.85 ± 273 meter squares. Mean body mass index (BMI) on basis of these weight and height measurements was 25.95 ± 4.32 with minimum recorded BMI 17.88 and maximum recorded BMI was 39.91. Table: 1

Number of anti hypertensive medicine used by these patients were range 1 to 4, average patients used 2 anti hypertensive medicines. Table: 1.

The study results show that 39.2% (n=67) patients were having impaired glucose tolerance when tested with OGT. Mean serum glucose level at 2 hours of giving loading dose was 139.17 ± 28.039 grams/dL in all study patients. Table: 1.

When analysed separately for two different categories it was noted that mean serum glucose for those who had impaired IGT was 159.33 ± 27.937 g/dL. While among those who had normal OGTT, the mean glucose level was 126.18 ± 19.048 grams/dL. Table: 1.

Age group categorization showed that 29.8% (n= 51) belonged to 40-50 years of age. Seventy eight patients (45.6%) were in 51-60 years age group. Patients aging 61-70 years were 24.6% (n=42). Table: 2.

Sixty two (36.26%) patients were having hypertension since last upto last 5 years, 73 (42.69%) had hypertension from 6 to 10 years while the patients who had hypertension since 11 to 15 years were 36 (21.05%). Table: 2.

When categorized according to BMI, it was seen that 42.11% were having normal weight (18.5-24.9), 40.35% were overweight (25.0-29.9), 15.20% were obese (30.0 and above) while only 2.34% patients were underweight (BMI < 18.5).

When stratified analysis was performed it was seen that gender has slight effect in frequency of IGT. Though the finding was not significant, it was found that 40.38% males were positive with IGT as compared to 37.31% females (P value = 0.406).Table: 2.

Age affected the frequency of IGT as it was most frequently seen in of 51-60 years age group where almost half (47.4%) had impaired IGT, in patients of 61-70 years it was lower (35.7%) & lowest among 40-50 year patients i-e; 29.4%. (P value = 0.159). Table: 2.

More the duration of hypertension more was the prevalence of IGT. Accordingly IGT raised from 32.26% in those having upto 5 years of hypertension to 39.73% among those who had 6-10 years of hypertension and eventually upto 50% in those who had been hypertensive since 11-15 years (P value = 0.220. Table: 2.

A very significant effect modification was made by body mass index (BMI) of patients upon the impaired

glucose tolerance (IGT). It was seen that in patients who were underweight or had normal weight BMI the IGT was lower and remained upto 25% to 27.78%. as the BMI entered the range of overweight and obesity the frequency of IGT raised (i-e; IGT was 40.58% in overweight & reached upto 69.23% in obese patients with a P value < 0.003. Table: 2.

The cross tabulation of number of antihypertensive medicine used by patient & frequency of IGT was expressed which revealed that with an increase in number of antihypertensive medicine used there was increased frequency of IGT among patients. It increased from 40.74% in 1 medicine users to 50% in those who used 4 antihypertensive medicine (P value = 0.643). Table: 2.

Table No.1 Descriptive Statistics.

n= 171	Minimum	Maximum	Mean	Std. Deviation
Age (Years)	40	70	53.42	8.059
Duration of Hypertension (Years)	3	15	7.47	3.26
Height in meter squares	2.23	3.39	2.85	.273
Weight in Kgs	52	98	73.54	10.13
BMI	17.88	39.91	25.95	4.32
Antihypertensive medicine being used	1	4	2.01	.888
2 hour serum Glucose level in all study patients (mg/dl)	90	199	139.17	28.039
• IGT Positive (mg/dl) (n=67)	140	199	159.33	27.937
• IGT Negative (mg/dl) (n=104)	90	139	126.18	19.048

Table No: 2: Relationship of Frequency of Impaired Glucose Tolerance Test with different variables.(n = 171)

Variables	Impaired Glucose Tolerance Test			P- VALUE
Gender	POSITIVE (%)	NEGATIVE	Total	
Male	42 (40.30)	62 (59.62)	104 (60.81%)	
Female	25 (37.31)	42 (62.69)	67 (39.19%)	0.046
Age in years				
40-50	15 (29.4)	36 (70.6)	51 (29.8%)	0.106
51-60	37 (47.4)	41 (52.6)	78 (45.6%)	
61-70	15 (29.4)	27 (64.3)	42 (24.6%)	
Effect of BMI				
under weight (<18.5)	1 (25%)	3 (75%)	4 (2.34%)	
Normal weight 18.5 – 24.9	20 (27.78)	52 (72.22)	72 (42.11%)	< 0.003
Over weight 25.0 – 29.9	28 (40.58)	41 (61.29)	69 (40.35%)	
Obese > 30.0	18 (69.23)	8 (30.77)	26 (15.20%)	
Duration of hypertension in years				
Upto 5	20 (32.26)	42 (67.74)	62 (36.26%)	
6-10	29 (39.73)	44 (60.27)	73 (42.69%)	0.220
11-15	18 (50)	18 (50)	36 (21.05%)	
Number of anti hypertensive medicine				
1	22 (40.74)	32 (59.26)	54 (31.57%)	0.643
2	25 (34.25)	48 (65.75)	73 (42.70%)	
3	14 (43.57)	18 (56.25)	32 (18.71%)	
4	6 (50)	6 (50)	12 (7.01%)	

DISCUSSION

Essential hypertension is a common comorbid condition in patients with type 1 or type 2 diabetes when compared with the general population and in 75% of patients with the more prevalent form of diabetes type 2.[17] Likewise diabetes in patients of essential hypertension is diagnosed commonly. An estimated 3 million Americans have both diabetes and hypertension.[18,19] Studies have reported that the

prevalence of hypertension in Southern Pakistan is upto19%.[20] while the prevalence of diabetes and IGT is upto 17.5%.[21]

Left ventricular hypertrophy and coronary artery disease are much more common in diabetic hypertensive patients than in patients suffering from hypertension or diabetes alone. The combined presence of hypertension and diabetes concomitantly accelerates the decrease in renal function, the development of diabetic retinopathy and the development of cerebral diseases.[22] Therefore it is of utmost importance that the patients diagnosed with one of these diseases must be scrutinized for other diseases and long term vigilance should be kept to prevent adverse outcome.

The current study was undertaken to investigate and findout the frequency of impaired glucose tolerance (IGT) in patients of essential hypertension. Mean ± SD age of patients was 53.42± 8.059 years. The youngest patient in the study was 40 and the oldest was of 70 years. Two third of patients (75.40%) were in the age group of 40-60 years. Although the frequency of IGT was higher in 51-60 years aged patients but the finding was not significant. These findings were in relevance with finding of local study by Ram K, et al [23] , who found that mean age ± SD was 55.72 ± 13.36 years. Tugrul A et al [24] found that mean age ± SD of the essential hypertension patients who had IGT was 51.1 ± 6.4 years.

Korhonen P et al [25] found that the mean age ± SD of IGT positive hypertensive patients was 60.37 ± 6.62 years.

Male to female ratio in this study was 1.5-5:1. Which is slightly higher than other studies (Korhonen P et al [25] 1:1; & 1.35:1 in Ram K et al [23]). It was proved when the stratified analysis was done which significantly revealed that in males IGT was more prevalent (40.38%) than females (37.31%; p value = 0.046). Similarly Tugrul A et al [24] using logistic regression found that male were four times more prone to IGT (p = 0.004, odd ratio = 4.194). This corresponds to the unsolved male preponderance of diabetes mellitus worldwide.[26]

The current study found that among 171 selected patients of essential hypertension, 39.2% patients were having IGT. Which is slightly higher than Tugrul A et al [24] who found that 33% patients of essential hypertension had IGT, on the other hand recent study in Finland; found lower prevalence of impaired glucose tolerance (25%).[25] while higher rate was described by a Ram K et al [23] who found frequency of IGT in 46.2% of patients with essential hypertension. The lower rate described y Tugrul A et al [24] & Korhonen P et al [25] included more of rural subjects, like the current study which was conducted in a tertiary care hospital at a major city of Sindh but its draining population is mostly rural. On the other hand the Ram K et al [23] who found a

higher rate conducted the study in Karachi which is the largest urban dwelling of Pakistan.

Other study which found a higher frequency of IGT in hypertensive patients were; Misra A et al [27] who found that in New Dehli, India (again a very thickly populated urban city) the frequency of IGT 70% overall hypertensive patients while Johson KC et al detected 43.2% prevalence of IGT among hypertensive patients.[28] In a recent study the Ramachandran A and coworkers did not agree with difference of urbanization regarding IGT and reported that town and city had similar prevalence of IGT and diabetes in southern India.[29]

Mean ± SD serum glucose level in all hypertensive patients of current study was 139.17 ± 28.039 grams/dL. Mean ± SD serum glucose level among IGT positive was 159.33 ± 27.937. Ram K et al [23] found that in patients of IGT the blood sugar values of 2 hrs with mean ± SD was 156.70 + 14.03 mg/dL. Further it was observed that although the mean serum glucose level among non IGT was lower (i-e 126.18 grams/dL) still it was on higher side and it is possible that some of these normoglycemic declared patients develop IGT or turn out to be IGT positive on very next OGTT screening or even at fasting glucose test.

In several studies it has been observed that raised BMI was a strong risk factor for IGT in hypertensive patients. In our study about 56% patients were either overweight (BMI 25-29.9 Kg/m^2) or obese (BMI $\geq$30Kg/m^2) and among these patients the frequency of IGT was much higher (40.58% in overweight & 69.23% in obese) than normal weight and underweight patients (27.78% & 25% respectively) (p value <0.003). It is evident from studies that there is a linear relationship between BMI and blood pressure.[30] In middle-aged hypertensive individuals body weight frequently shows a progressive increase, which definitely hampers the glucose metabolism and thus causes IGT. In such patients weight stabilization is a most effective tool to treat hypertension and to prevent diabetes. Several studies have found an association between higher BMI and glucose intolerance in hypertensive patients. [25,24,27,31-33]

Mean duration of hypertension was 7.47 ± 3.26 years and the current study also found that duration of hypertension was also associated with IGT. Frequency of IGT increased with increasing duration of hypertension from 32.26% in patients of upto 5 Years history of hypertension to 39.73% among those with 6-10 Years of hypertension and finally this rate increased upto 50% in patients who were hypertensive for 11- 15 Years. In a study from Turki, Tugrul A et al [24] found that mean duration of hypertension was 8.9 ± 6 years in the IGT patients but it did not modify the frequency of IGT in cases and control group. Use of more than one antihypertensive medicine was associated with increased but fluctuating frequency of IGT than with

single drug but this finding was not significant in current study.

CONCLUSION

Pakistan has a high prevalence of hypertension and diabetes mellitus therefore this study suggests that all the patients with essential hypertension must be scrutinized for blood glucose levels both fasting and random in order to diagnose hyperglycemia / IGT at an earliest possible time to minimize the burden of this disease which is caused by dual effects of hypertension and diabetes mellitus.

REFERENCES

1. Giles TD, Berk BC, Black HR, Cohn JN, Kostis JB, Izzo JL, et al. Expanding the Definition and Classification of Hypertension. J Clin Hypertension 2005;7:505-12.
2. Roger VL, Go AS, Lloyd-Jones DM. Heart disease and stroke statistics--2012 update: a report from the American Heart Association. Circulation 2012; 125(1):e2-e220
3. Carmeliet P. Angiogenesis in life, disease and medicine. Nature 2005;438:932.
4. Semenza G. Vasculogenesis, angiogenesis, and arteriogenesis: mechanisms of blood vessel formation and remodeling. J Cell Biochem 2007;102:840.
5. Garcia-Cardena G, Gimbrone M: Biomechanical modulation of endothelial phenotype: implications for health and disease. Handb Exp Pharmacol 2006;176:79.
6. American Diabetes Association. Screening for type 2 diabetes. Diabetes Care 2002;25:21-4.
7. von Eckardstein A, Schulte H, Assmann G. Risk for diabetes mellitus in middle-aged Caucasian male participants of the PROCAM study: implications for the definition of impaired fasting glucose by the American Diabetes Association. Prospective cardiovascular Münster. J Clin Endocrinol Metab 2000;85:3101-8.
8. Dunstan DW, Zimmet PZ, Welborn TA, De Courten MP, Cameron AJ, Sicree RA, et al. The rising prevalence of diabetes and impaired glucose tolerance: the Australian Diabetes, Obesity and Lifestyle Study. Diabetes Care 2002;25:829-34.
9. Knowler WC, Barrett-Connor E, Fowler SE, Hamman RF, Lachin JM, Walker EA, et al. Reduction in the incidence of type 2 diabetes with lifestyle intervention or metformin. N Engl J Med 2002;346:393-403.
10. Tuomilehto J, Lindström J, Eriksson JG, Valle TT, Hämäläinen H, Ilanne-Parikka P, et al. Prevention of type 2 diabetes mellitus by changes in lifestyle among subjects with impaired glucose tolerance. N Engl J Med 2001;344:1343-50.
11. Barzilay JI, Spiekerman CF, Kuller LH, Burke GL, Bittner V, Gottdiener JS, et al. Prevalence of clinical and isolated subclinical cardiovascular disease in older adults with glucose disorders: the Cardiovascular Health Study. Diabetes Care 2001;24:1233-9.
12. Rodriguez BL, Abbott RD, Fujimoto W, Waitzfelder B, Chen R, Masaki K, et al. The American Diabetes Association and World Health Organization classifications for diabetes: their impact on diabetes prevalence and total and cardiovascular disease mortality in elderly Japanese-American men. Diabetes Care 2002;25:951-5.
13. Lim SC, Tai ES, Tan BY, Chew SK, Tan CE. Cardiovascular risk profile in individuals with borderline glycemia: the effect of the 1997 American Diabetes Association diagnostic criteria and the 1998 World Health Organization Provisional Report. Diabetes Care 2000;23:278-82.
14. Borde-Perry WC, Campbell KL, Murtaugh KH, Gidding S, Falkner B. The association between hypertension and other cardiovascular risk factors in young adult African Americans. J Clin Hypertens 2002;4:17-22.
15. Simon NR, Frishman WH. Diabetes mellitus in the aging: epidemiologic and therapeutic considerations. Am J Geriatr Cardiol 1992;1:22-36.
16. Gouveia LM, Paccola GM, Torquato MT, Menezes FO, Piccinato CE, Foss MC. Peripheral glucose metabolism in patients with essential hypertension. Horm Metab Res 2000;32:35-9.
17. Schutta MH. J Diabetes and hypertension: epidemiology of the relationship and pathophysiology of factors associated with these comorbid conditions. Cardiometab Syndr 2007 Spring;2(2):124-30.
18. Epstein M, Sowers JR. Diabetes mellitus and hypertension. Hypertension1992;19:403-18.
19. The National High Blood Pressure Education Program Working Group. National High Blood Pressure Education Program Working Group report on hypertension in diabetes. Hypertension 1994;23:145-58.
20. Shera AS, Rafique G, Khawaja IA, Ara J, Baqai S, King H. Pakistan national diabetic survey: Prevalence of glucose intolerance and associated factors in Shikarpur, Sindh Province. Diabetic Med 1995;12:1116-21.
21. Shera AS, Rafique G, Khawaja IA, Ara J, Baqai S, King H. Pakistan national diabetic survey: Prevalence of glucose intolerance and associated factors in Baluchistan province. Diabetes Res Clin Pract 1999;49-58.
22. Grossman E, Messerli FH. Hypertension and diabetes. Adv Cardiol 2008;45:82-106. doi: 10.1159/0000115189.

23. Ram K, Masroor M, Qamar R, Ahmed I, Sattar A, Imran K, Khan MS. Frequency of impaired glucose tolerance in hypertensive patients. Pak Heart J 2005;38(3-4):46-51.

24. Tugrul A, Guldiken S, Ugur-Altun B, Arikan E. An Evaluation of Glucose Tolerance in Essential Hypertension. Yonsei Med J 2009 30;50(2):195-9.

25. Korhonen P, Aarnio P, Saaresranta T, Jaatinen P, Kantola I. Glucose Homeostasis in Hypertensive Subjects. Hypertension. 2008;51:945-949.

26. The World Health Report 2002-Reducing Risks, Promoting Healthy Life. Geneva, Switzerland: World Health Organization; 2002:

27. Misra A, Kathpalia R, Lall SB, Peshin S. Hyperinsulinemia in non-obese, non-diabetic subjects with isolated systolic hypertension. Indian Heart J 1998;50(1):49-54.

28. Johson KC, Graney MJ, Applegate WB, Titabchi AE, Runyon JW, Shorr RI. Prevalence of undiagnosed non-insulin dependent diabetes mellitus and impaired glucose tolerance in a cohort of older persons with hypertension. J Am Gesiatr Soc 1997; 44(6)695-700.

29. Ramachandran A, Mary S, Yamuna A, Murugesan N, Snehalatha C. High prevalence of diabetes and cardiovascular risk factors associated with urbanization in India. Diabetes Care 2008; 31(5):893-8.

30. The trials of hypertension prevention collaborative research group. Effects of weight loss and sodium reduction intervention on blood pressure and hypertension incidence in overweight people with high-normal blood pressure.Arch Intern Med 2001;134:1–11.

31. Mutebi E, Nakwagala F N, Nambuya A, Otim M. Undiagnosed diabetes mellitus and impaired glucose tolerance among hypertensive patients in mulago hospital, Kampala, Uganda. Afr J Diabet Med 2012;20(1):20-3.

32. Govindarajan G, Sowers JR, Stump CJ. Hypertension and Diabetes Mellitus. Euro Cardiol 2006;2(1):1-7.

33. Bombelli M, Facchetti R, Sega R, Carugo S, Fodri D, Brambilla G, et al. Impact of body mass index and waist circumference on the long-term risk of diabetes mellitus, hypertension, and cardiac organ damage. Hypertension 2011;58(6):1029-35.

Address for Corresponding Author:
Dr. Muhammad Aslam Soomro
Senior Registrar Department of Medicine
Chandka Medical College & Hospital Larkana
E-mail: dr_soomro_aslam@outlook.com
Cell # 0333-7543724