

## Effect of Hypertension on Executive Functions in Patients with Prediabetes and Diabetes Mellitus Type-II

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**Received:** April 16, 2019; **Published:** April 25, 2019

### Abstract

**Objective:** Hypertension is most commonly found in patients with Diabetes Mellitus. Uncontrolled hypertension in Diabetic patients leads to higher risk of cardiovascular events, including death, atherosclerosis and progression to Neuronal issues like Dementia, Alzheimer's disease. The aim of the present study is to determine the effect of Hypertension on executive functions in patients with Diabetes Mellitus type-2 and prediabetes.

**Method:** Total 60 participants were taken out of 95 participants, looking towards inclusion criteria of age 45-65 years, both males and females and must be having HTN along with DM-2 and prediabetes. Study was conducted in SPS Apollo Hospital, Ludhiana and Home Based. Both the groups were assessed for executive functions. Then scores of executive functions have been compared with Normal participants of same age group. It was an observational study.

**Results:** Participants were divided into 3 groups, group A (HTN + DM-2), group B (HTN + Prediabetes) and group C (Normal) participants. Group A show significant difference in execution scoring (22.43) as compared to group B and group C but group C showed maximum mean in executive functions as compared to group B and group A, It revealed that Normal population have better execution than people suffering from DM-2 along with HTN and prediabetes with HTN.

**Conclusion:** Study concluded that people suffering from DM-2 with HTN have poor executive functions as compared to normal and prediabetes group. Early recognition of execution in such patients is obligatory to not suffer further from problems like Alzheimer's.

**Keywords:** Diabetes Mellitus Type 1; Type-2; Hypertension; Executive Function and Trail Making Test A and B

### Introduction

Diabetes mellitus and hypertension have appeared as chief health and community health issues worldwide [1]. These two ailments habitually coexist than chance alone and often share comorbidities [2]. According to the World Health Organization (WHO), Diabetes Mellitus will be the seventh foremost cause of death by the year 2030 [3]. Diabetes is a collection of metabolic ailments categorised by hyperglycaemic occurring from faults in insulin discharge, insulin activity, or both. The chronic hyperglycaemia of diabetes is related with extended-term injury, dysfunction and failure of diverse organs, especially the eyes, kidneys, nerves, heart and blood vessels [5]. A number of pathogenic steps are concerned

in expansion of diabetes. The development of diabetes mellitus is mainly linked with autoimmune damage of beta cells present in the organ pancreas along with decreased insulin that leads to anomalies which result in conflict to insulin work [8].

### Two wide Classification of diabetes are

- Type 1 diabetes mellitus was formerly called insulin-dependent diabetes mellitus or juvenile-onset diabetes. Although disease arrival can happen at any age, the top-most age for finding is in the mid-teens. Type 1 diabetes mellitus grows when the cells that yield the hormone insulin, recognized as the beta cells, in the pancreas are devastated. This demolition is originated or facilitated by the body's immune system and confines or completely

eliminates the construction and secretion of insulin, the hormone that is mandatory to lower blood glucose levels. To endure, people with type 1 diabetes must have insulin supplied by injection or a pump [6].

- Type 2 diabetes mellitus is a chronic metabolic condition considered by irregularly increased blood sugar levels as a result of inadequate usage of insulin. Presently known as Non-Insulin Dependent Diabetes Mellitus or adult-onset diabetes mellitus, its prevalence expressively rises across adulthood, classically disturbing people over the age of 40 years [7]. Patients suffering from diabetes mellitus may be hypertensive for many years prior to the beginning of overt diabetes. At the time of diagnosis of type 2 Diabetes Mellitus, hypertension is found in around 70-80 percent of patients [8]. Hypertension is an important public well-being problem, with world-wide incidence of 40.5% and a control rate of 32.5% [9].

### Need of the study

Diabetes Mellitus type-2 and Hypertensions are metabolic disorders and in combination both are prone to cause cognitive decline. Deterioration in cognitive profile leads to executive dysfunction. In later stages it might disturbs parenchyma of the brain and lead to diseases like Alzheimer's, Dementia and Parkinsonism. This study seems to highlight relation between Hypertension and Executive functions. People always focused towards control of diabetes and blood pressure but never pay attention that how it can hamper their execution such as working memory, planning, processing speed, emotional control and sustained attention. This study will help such people to look after their mental health and related intervention can be taken further to not suffer from these disorders.

### Significance of the study

Earlier many studies have been done on diabetes mellitus-2 along with hypertension but only few on its effects along with prediabetes. This study will further focus on control of these disorders as well as for better executive functioning in patients. Rather than only focusing the metabolism, a new line of concentration will be towards brain functions so people will be aware and will be towards the prevention of disorders which occurs because of disturbance in their cognition and execution such as Alzheimer's. The work done in this research will give a new protocol for diabetes, prediabetes and hypertensive patients for the prevention of their brain functions and not to suffer in later stages of life.

### Aims and objectives

- To determine effect of Hypertension on executive functions in prediabetics.

- To determine effect of Hypertension on executive functions in diabetes mellitus type- 2.
- To see comparison of readings in normal subjects, Pre diabetics and Type 2 Diabetes Mellitus.

### Study design

Observational Study

### Study setting

SPS Hospital Ludhiana and Home Based Setting in Ludhiana

### Sampling

Convenient Sampling

### Inclusion criteria

Subjects will be chosen according to following criteria:

- Subjects with Hypertension and Diabetes mellitus for group A
- Subjects with Hypertension and Pre diabetes for group B
- Subjects without Hypertension and Diabetes for group C
- Age 45-65 years
- Both Males and Females
- Able to read and write

### Exclusion criteria:

Subjects will not be taken according to following criteria

- Any serious Medical or Psychiatric conditions
- Any cognitive behavioral therapy should not be taken
- Deaf people
- Uncooperative patients
- Neoplasms of spine or brain
- Neurological conditions like epilepsy.

### Parameters

Executive functions

Tools

- Sphygmomanometer
- Trail making test
- Stop Watch

### Procedure

Total 90 participants were taken for research purpose. An Endocrinologist from SPS Apollo Hospital Ludhiana, Dr. Ramanbir Singh has referred 85 diagnosed cases on various different OPD days. Before starting up with assessment criteria, all the patients been asked to show their reports and other prescription. All the partici-

pants were asked to show their reports for Hb1Ac Test. Total 30 out of 85 were taken in group A (HTN+DM-2) and other 30 were taken in group B (HTN+ Prediabetes). 25 participants have been eliminated because few of them were not matching the inclusion criteria and few have refused to be part of research. After this participants were asked to read and sign informed consent. Informed consents were asked to sign, to make participant aware about protocols and norms of research. All the participants met the inclusion criteria of age group 45-65years and educated more than 10 classes, were both males and females and were having normal vision either with spectacles or with lenses. Out of all the participants, none of the participant was deaf and no one was having any psychological and neurological sufferings.

Initially Demographic Data was taken via informed consent and then complete history related to disease and family history has been taken. Patient has been asked about years on disease and what medications he is taking and from when and whether patient is having any Diabetes related Neuropathy, Nephropathy or Retinopathy. Complete observation and examination has been done for all the participants.

Blood Pressure was measured by trained assistant in the Endo OPD for all the participants by Gold standard traditional Sphygmomanometer after 5 minutes of quite sitting two times, with 2 minutes between each measure. Average systolic BP and diastolic BP were obtained. Participants were assigned into 2 different groups. In group A, all the participants with HTN and DM-2 and in group B all the participants with HTN and prediabetes. Average BP measured was 140/95 mmHg. Least number of participants were having 160/100mmHg.

Executive function assessment: After complete demographic profile, history taking and physical examination, patients were asked to go through Neuropsychological assessment for executive functions. Neuropsychological test used to assess executive functions was Trail Making Test (TMT) A and B. TMT-A assess abilities like processing speed, visual scanning and sustained attention. TMT-B considers visuospatial ability, working memory and processing speed. Trail Making Test A has a series of numbers 1-24 bounded in circles, which participant have to connect in particular time period without lifting hand. In part B, participants were asked to connect a series of numbers 1-12 and alphabets A-M simultaneously. Therapist observed and sits along the participant and will notify if any error participant makes. Therapist recorded the time taken to perform trail A and trail B. Stop watch has been used to re-

cord the time taken for both the trails. After time have been recorded therapist will reduce time taken in part A from time taken in part B to have average time taken to complete both the trails. There should not be much time difference in completing two trails. The average time to complete trail A was 45seconds and for Trail B it was 75 seconds. Deficient ranges for Trail making A was more than 78 seconds and for trail making B it was more than 273 seconds.

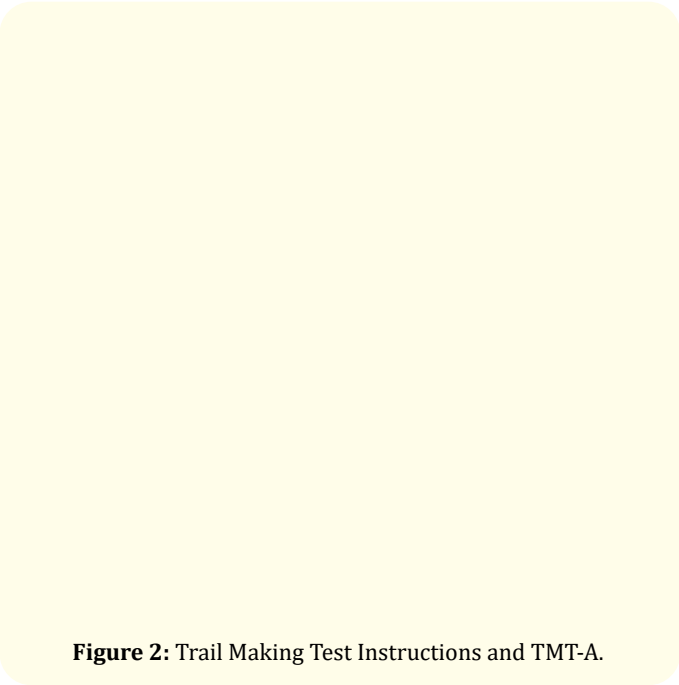
For group C, Normal individuals were taken as per home based. All the 30 Normal individuals were not having hypertension, diabetes 2 and prediabetes. All the Participants were meeting inclusion criteria. Both males and females were taken with age group 45-65. All the participants were gone through BP measurements and Hb1Ac test. These tests were done to exclude participants who have high BP ranges and who was prediabetes or diabetic. Participants were not told about what ability we are measuring in them. After complete demographic profile, history taking and another physical examination, participants were asked to perform Trail making Test A and B to rule their executive functions.



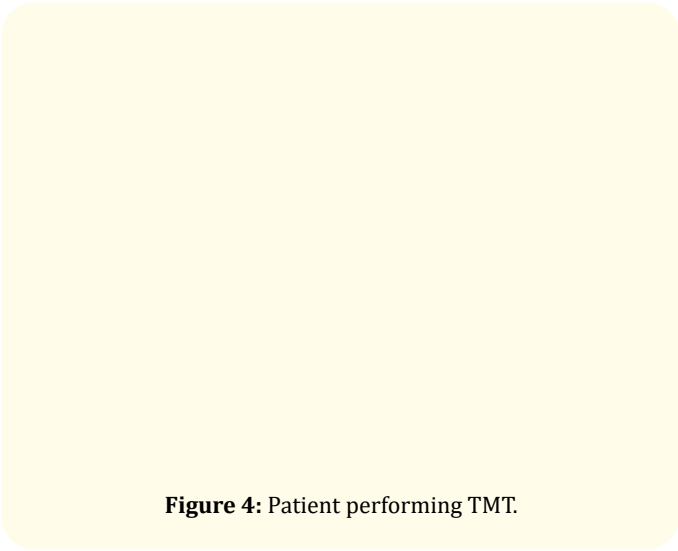
**Figure 1:** Trail Making Test Instructions TMT A and B.



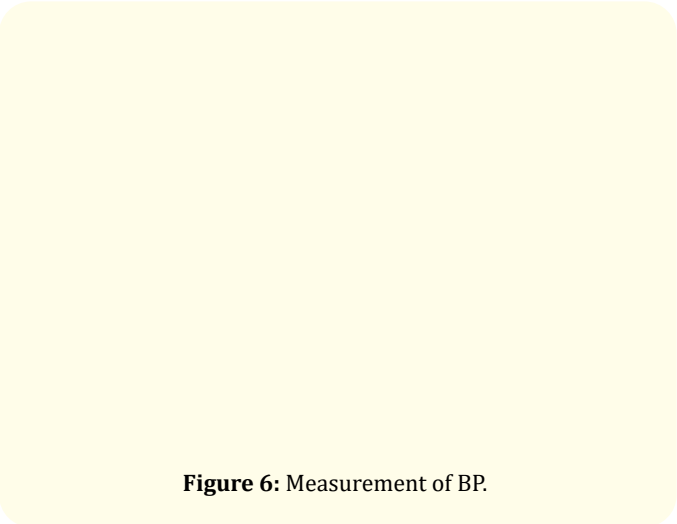
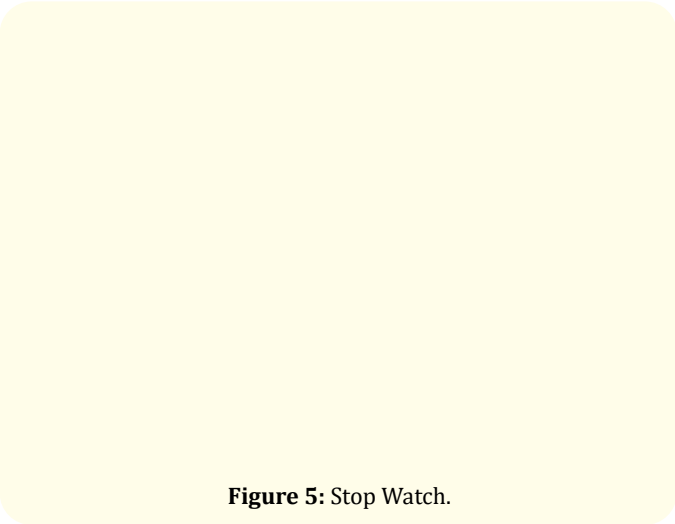
**Figure 3:** Trail Making Test Part B.



**Figure 2:** Trail Making Test Instructions and TMT-A.



**Figure 4:** Patient performing TMT.



Descriptive Age										
					95% Confidence					
	N	Mean	Std. Deviation	Std. Error	Interval for Mean		Minimum	Maximum	F	Sig.
					Lower Bound	Upper Bound				
Group A	30	56.9667	4.96528	.90653	55.1126	58.8207	47.00	65.00		
Group B	30	51.8000	5.89213	1.07575	49.5998	54.0002	41.00	65.00	6.50	.002
Group C	30	53.7667	5.89379	1.07605	51.5659	55.9674	45.00	66.00	4	
Total	90	54.1778	5.93708	.62582	52.9343	55.4213	41.00	66.00		

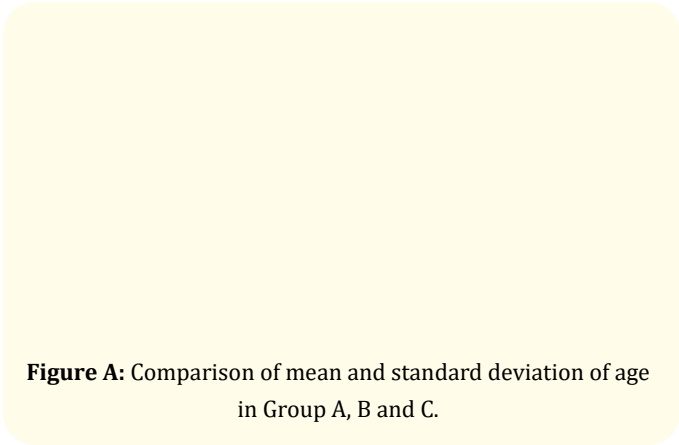
Table 1: Mean and standard deviation of age in Group A, B and C.

Comparison of mean and standard deviation of subjects age (18-40) years between Group A (HTN + DM-2) Group B (HTN + Pre diabetes), Group C ( Normal) respectively.

The Mean age of group A was (56.96 ± 4.96), Group B was (51.80 ± 5.89), Group C (53.76 ± 5.89) respectively. The F value was 6.504. P Value was .002 (P<0.05) which shows the significant difference in the age group.

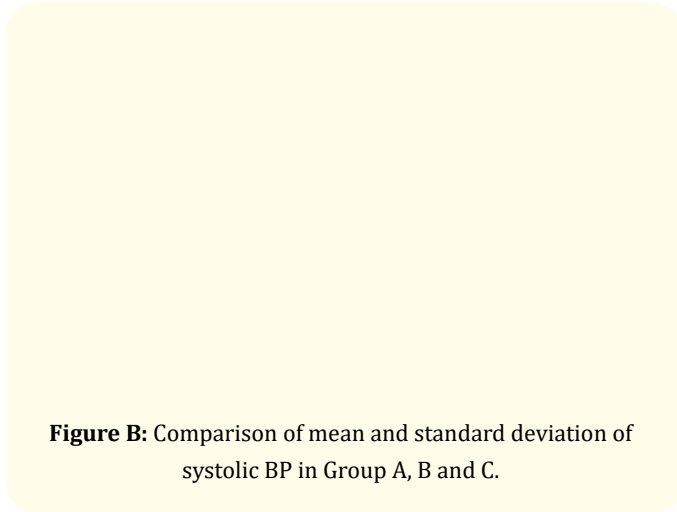
Descriptives										
Systolic BP										
					95% Confidence					
	N	Mean	Std. deviation	Std. error	Interval for Mean		Minimum	Maximum	F	Sig
					Lower bound	Upper bound				
Group A	30	155.9333	8.43610	1.54021	152.7832	159.0834	145.00	170.00		
Group B	30	150.6667	7.15991	1.30722	147.9931	153.3402	140.00	165.00	196.9	.00
Group C	30	122.6667	4.86602	.88841	120.8497	124.4837	115.00	130.00	48	0
Total	90	143.0889	16.22222	1.70997	139.6912	146.4866	115.00	170.00		

Table 2: Mean and standard deviation of systolic BP in Group A, B and C.



The mean and SD Pre value for systolic blood pressure for Group A (HTN + DM-2) was (155.93 ± 8.43), for Group B (HTN + Pre diabetes) was (150.66 ± 7.15) and for Group C (Normal) it was (122 ± 4.86). The f value was 196.94 and P value was .000 which was (P

< 0.005). There was significant difference between Group A, Group B and Group C.



Descriptives										
Systolic BP										
					95% Confidence					
	N	Mean	Std. deviation	Std. error	Interval for Mean		Minimum	Maximum	F	Sig
					Lower bound	Upper bound				
Group A	30	93.4667	6.14611	1.12212	91.1717	95.7617	70.00	105.00		
Group B	30	93.3333	3.30447	.60330	92.0994	94.5672	90.00	100.00	73.951	.000
Group C	30	80.3333	4.53594	.82814	78.6396	82.0271	70.00	85.00		

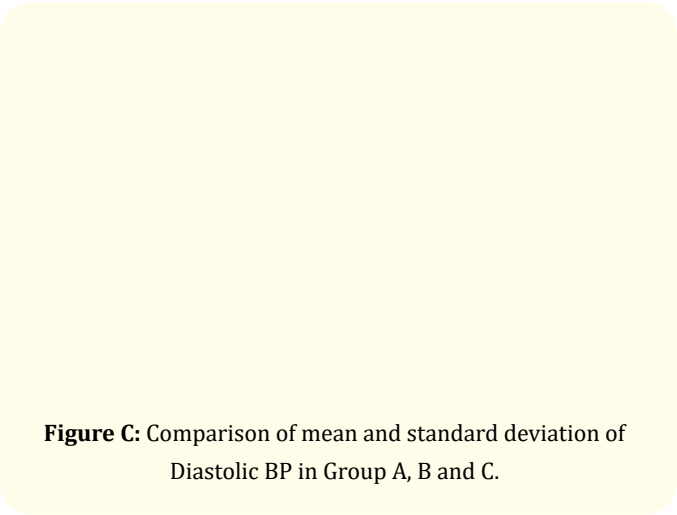
Table 3: Mean and standard deviation of Diastolic BP in Group A, B and C.

The mean and SD value of diastolic blood pressure for Group A (HTN + DM) was (93.46 ± 6.14), for Group B (HTN + Pre diabetes) was (93.33 ± 3.3.) and for Group C it was (80.33 ± 4.53). The f value

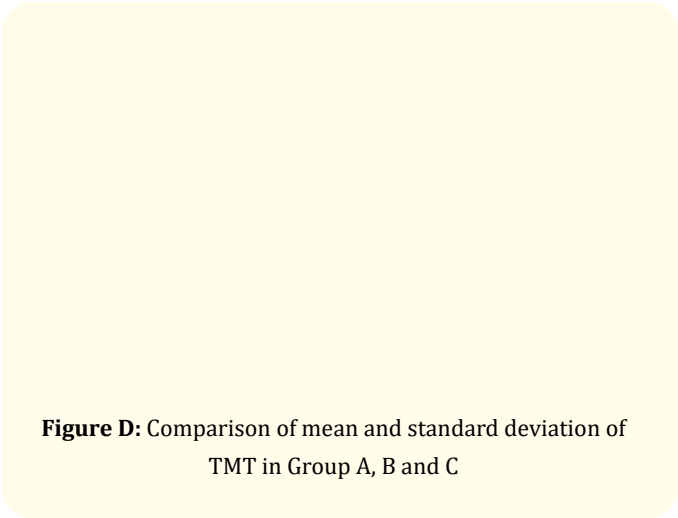
was 73.951 and P value was .000 which was (P < 0.005). So there was significant difference between Group A, Group B and Group C.

Descriptives										
Systolic BP										
					95% Confidence					
	N	Mean	Std. deviation	Std. error	Interval for Mean		Minimum	Maximum	F	Sig
					Lower bound	Upper bound				
Group A	30	67.07	12.171	2.222	64.52	73.61	52	103		
Group B	30	57.03	11.577	2.221	52.71	61.36	38	80	27.32	.00
Group C	30	46.63	11.533	2.106	42.33	50.94	23	72	2	0
Total	90	57.58	14.841	1.564	54.47	60.69	23	103		

Table 4: Mean and standard deviation of Executive Functions in Group A, B and C.



(46.63 ± 11.53). The f value was 27.322 and P value was .000 which was (P < 0.005). There was significant difference between Group A, Group B and Group C.



The mean and SD value of Executive functioning by TMT for Group A (HTN + DM) was (69.07 ± 12.17), for Group B ( HTN + Pre diabetes) was (57.03 ± 11.57) and for Group C (Normal) it was

Post hoc test

Multiple Comparisons						
Dependent Variable: TMT Tukey HSD						
(I) Group	(J) Group	Mean Difference (I-J)	Std. Error	Sig.	95% Confidence Interval	
					Lower Bound	Upper Bound
Group A	Group B	12.033*	3.037	.000	4.79	19.28
	Group C	22.433*	3.037	.000	15.19	29.68
Group B	Group A	-12.033*	3.037	.000	-19.28	-4.79
	Group C	10.400*	3.037	.003	3.16	17.64
Group C	Group A	-22.433*	3.037	.000	-29.68	-15.19
	Group B	-10.400*	3.037	.003	-17.64	-3.16

Table 5

\*. The mean difference is significant at the 0.05 level.

By using one way ANOVA for Group A, Group B and Group C was statistically significant, But to check which one was more significant in the variable of Systolic BP, Diastolic BP and TMT. Post hock test is done by tukey’s method.

On Comparison of Group A with Group B and Group C there were significant difference between both groups but on comparing Group B with Group C, Group C was more significant with mean difference (22.433), which is greater than the mean difference of Group B (12.033).

On Comparing Group B with Group A and Group C there were significant difference between both the groups but on comparing Group A and Group C, Group A is more significant with mean difference (12.033) which is greater than the mean difference of Group B (10.400).

On Comparing Group C with Group A and Group B there were significant difference between both the groups but on comparing Group A and Group B, Group A is more significant with mean difference (22.433) which is greater than the mean difference of Group B (10.400).



## Results and Discussion

Mean and standard deviation in demographic profile (Age and Gender) in three different Groups: Group A (HTN + DM-2), Group B (HTN + Pre diabetes) and Group C (Normal) subjects. The mean age of participants with HTN + DM-2 was more than pre diabetics and normal subjects, so it stated that diabetes with hypertension occurs with aging. P Value was .002 ( $P < 0.05$ ). It shows significant difference in gender and age between these three groups.

Table 2 showed the mean and standard deviation for systolic BP in Group A, Group B and Group C. The P value for systolic blood pressure among three groups was .000 ( $P < 0.005$ ). So there was significant difference between Group A, Group B and Group C.

Table 3 showed the mean and standard deviation for diastolic BP in Group A, Group B and Group C. The P value for diastolic BP among these three groups was .000 ( $P < 0.005$ ). So there was significant difference between Group A, Group B and Group C.

Table 4 showed the mean and SD value of Executive functioning by TMT for Group A (HTN + DM) was ( $69.07 \pm 12.17$ ), for Group B (HTN + Pre diabetes) was ( $57.03 \pm 11.57$ ) and for Group C (Normal) it was ( $46.63 \pm 11.53$ ). The f value was 27.322 and P value was .000 which was ( $P < 0.005$ ). So there was significant difference between Group A, Group B and Group C. It indicated that in Group A (HTN + DM-2) executive functions are more affected than group B (HTN + Prediabetes) and in between Group B and Group C, executive functions were more affected in group B than group C (Normal).

Table 5 showed post hoc analysis of Group A, group B and group C, to rule out which group is more significant in variable systolic BP, diastolic BP and executive functions. On Comparison of Group A with Group B and Group C there were significant difference between both groups but on comparing Group B with Group C, Group C was more significant with mean difference (22.433), which is greater than the mean difference of Group B (12.033).

On Comparing Group B with Group A and Group C there were significant difference between both the groups but on comparing Group A and Group C, Group A is more significant with mean difference (12.033) which is greater than the mean difference of Group B (10.400).

On Comparing Group C with Group A and Group B there were significant difference between both the groups but on comparing Group A and Group B, Group A is more significant with mean difference (22.433) which is greater than the mean difference of Group B (10.400).

Final result stated that Group A (HTN + DM-2) was most affected in executive functioning as compared to group B and group C.

The focus of the study was to see effect of hypertension on executive functions in patients with Diabetes Mellitus Type-2 and pre diabetes, people with age 45-65 years old were taken in the study. Three groups were there- group A (HTN + DM-2), group B (HTN + Prediabetes) and group C (Normal) subjects. All the participants were measured for executive functions by Neuropsychological Test Trail Making Test TMT A and B. There was significant difference in Results between all the three groups. Many studies support this relationship.

As Group A (HTN + DM-2) showed poor executive functions in elderly people, Katherine Samaras, *et al.* explained in one of her study that Diabetes Mellitus type-2 have a sound relationship with elevated Body mass index so people who have these both the conditions together often poses low grade systemic inflammation. Inflammation enhances the risk of vascular sufferings such as HTN. In DM-2 it has been said that inflammatory protein cytokines is linked up with decline in cognitive functions which further lead to dementia because of microvascular changes [10]. Chronic hyperglycaemia has been said to show reduced regional blood flow increased membrane permeability leading to cells damage. DM type-2 lead to Gray matter perfusion and low macrovascular blood supply given by Jacobus F. A. Jansen [11].

Hsu Ko Kuo, *et al.* [12] stated that elevated Blood Pressure readings and DM in old age people effect executive functions. Pathways which interconnect various parts of frontal lobe with subcortical circuits are responsible for good execution. When BP keep rising all the time these circuits got tired of bearing pressure load and in return lead to small vessel injuries in cerebral areas [13]. S M Gold, *et al.* stated that in DM-2 there is damage to hippocampal regions and disintegrity that leads to brain complications. Further it results in poor memory and planning.

Ekaterina Tchistiakova, *et al.* [14] explained that HTN in combination with DM-2 lead to multiple brain issues such as decrease in cortical thickness and decrease in cerebrovascular reactivity. This study explained that higher order cognitive and executive functions were preserved with thickness of cortex in some of the areas such as temporal and frontal cortex. DM-2 leads to perfusion abnormalities, dysregulation of brain functions and decreased execution. HTN leads to vascular and functional irregularities. In combination these two leads to structural abnormalities. In this study they have



also compared HTN with HTN + DM-2 and have showed that cortical thickness was more decreased in participants suffering from HTN along with DM-2 that further leads to dysexecution.

Rucker, *et al.* [4] stated that people suffered from these metabolic issues showed diffuse brain atrophy and white matter lesions in magnetic resonance imaging. Patients showed poor performance in task shifting, working memory and visuospatial ability.

In group B (HTN + Prediabetes) of our study, executive functions showed diminished executive functions but not up to that extent as in group A (DM-2 + HTN). Marzieh Nazaribadie, *et al.* [15] stated in one of his study that people suffered from impaired glucose tolerance are on risk to develop diabetes mellitus 2 and mild cognitive changes has been seen in participants suffered from pre diabetes. Gulin Alkan, *et al.* said that early brain aging and decline in cognitive and executive functions are present even in pre diabetes stage. So vascular complication occurs and further chance to develop reduced cerebral blood flow in prediabetes patients. Iaedacola, *et al.* [16] in one of the study over hypertension stated that fat deposition in cerebral arteries occurred because of hypertension. This deposition of fats, lead to reduction in blood flow to brain and thrombogenesis. Proper amount of blood flow is very much important for accurate functioning of cellular activity. So this mismatch between blood flow and cellular activity in old age population lead to cognitive deterioration mainly memory problems, processing speed, sustained attention, working memory and stress.

In group C (Normal) of this study, population show better results on executive functions as compared to other groups suffering from HTN + DM-2 and HTN + Prediabetes. As per the many studies it has been said that with ageing human brain started shrinking and hyper density of white matter of the brain, effect on cortical thickness along with intellectual function deterioration that can lead to Alzheimer's in later life. Old age has said to be reflection of Central Nervous System said by J H Cohl [17].

As a final result, this research work concluded that there is for sure impact of Hypertension on Executive functions. Executive functions in Diabetes mellitus-2 have shown much reduced executive functions than normal old age population. People suffering from HTN with pre diabetes also showed reduced executive functions as compared to normal subjects but not as reduced as in DM type-2 participants.

## Conclusion

This study concluded that the executive functions mainly processing speed, sustained attention, hand eye coordination, visuospatial ability and working memory are most effected in patients with Hypertension and Diabetes Mellitus type 2. In patients with Hypertension and Prediabetes executive functions got affected but not up to that extent as in HTN&DM 2. Normal aged individuals are least affected in execution as compared to HTN in Diabetes type 2 and Pre diabetes. This study says that patients with these issues must focus on training their execution to prevent themselves from further sufferings such as Alzheimer's.

## Conflicts of Interest

There are no conflicts of interest of any sort.

## Acknowledgments

We are thankful to the Department of Physiotherapy, Lovely Professional University, India and Faculty of Physiotherapy, Jimma University, Ethiopia, for helping in carrying out this research to a fruitful outcome.

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**Volume 2 Issue 5 May 2019**

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