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Assessment of plasma D-dimer level and its correlation with disease severity among hypertensive patients

Endeshaw Chekol[1*], Solomon Genet[2], Menakath Menon[2], Zeleke Geto[3], Tadesse Asmamaw[4], Tadesse Lejisa[5], Wossene Habtu[5], Tigist Getahun[5] and Yosef Tolcha[5]

[1]Department of Biochemistry, College of Health sciences; Debre Tabor University, Debre Tabor, Ethiopia
[2]Department of Biochemistry, Addis Ababa University, Addis Ababa, Ethiopia
[3]Department of Biomedical Science, Wollo University, Wollo, Ethiopia;
[4]Department of Biochemistry, Gondar, Ethiopia;
[5]National Reference Laboratory for Clinical Chemistry, Addis Ababa, Ethiopia
[*]Corresponding author: endeshawchekole@gmail.com

Abstract

It has been reported that inappropriate acute thrombus formation is the pathophysiological substrate underlying increased risk and severity of target organ damage in hypertension. However, the relationship between severity of hypertension and D-dimer has not been well characterized. This study was aimed to assess plasma D-dimer level and its correlation with disease severity among hypertensive at Yikatit 12 Hospital Medical College (Y12HMC), Ethiopia. A comparative cross-sectional study was conducted at Y12HMC among 100 participants (60 hypertensive and 40 controls). The correlations between variables were determined using correlation coefficients, regression analysis, and different parametric and non-parametric tests. We observed higher D-dimer levels among hypertensive compared to the healthy controls ($P<0.001$). The D-dimer levels were found to be increased significantly with the severity of hypertension ($P<0.001$). D-dimer was found to have a diagnostic power of 86.9% in differentiating complicated from uncomplicated hypertension at 0.83mg/l cut-off value. This study suggests that D-dimer level was higher among hypertensive than control groups and it was also increasing significantly with the severity of hypertension. This suggests that hypercoagulability of fibrin plays a role in the pathogenesis of cardiovascular disorders and thromboembolic complications of hypertensive patients. Further studies need be done on larger scale and using more robust study designs such as cohort to establish the causality of the association between severity of hypertension and D-dimer level.

Keywords: Hypertension, D-dimer, Disease Severity, Cardiovascular disorders

Introduction

Hypertension is the most important modifiable cardiovascular risk factor that, in long-term, leads to target organ damage (TOD) or thromboembolic complications associated with heart, brain, kidney and peripheral arteries, results in increased morbidity and mortality (Daniel and John, 2004; Foe and Sear, 2004; Macmahon et al., 1990). Hypertension doubles the risk of stroke, coronary heart disease (CHD), Peripheral Arterial Disease (PAD) and End Stage Renal Disease (ESRD) (Daniel and John, 2004; Foe and Sear, 2004). Plethora of studies have examined that essential hypertension, independently or by clustering with the coexisting risk factors such as age, gender, smoking, obesity, diabetes, and dyslipidemia, is involved in the development of TOD (Macmahon et al., 1990); with complications predominantly occurring as a result of thrombotic rather than hemorrhagic factors (Dell'omo et al. 2003; Beevers et al., 2001).

The risk of Cardiovascular disorders CVD resulting from hypercoagulability due to endothelial injury in hypertensive disorder can be proven by measuring D-dimer (D-DI) level which is more sensitive, highly predictive and noninvasive procedure though elevated D-DI has little specificity and low positive predictive value (Olson, 2015). D-DI is reportedly a good independent biochemical risk marker of thrombogenesis and fibrin turnover (Wells et al., 2003). In patients without evidence of coagulopathy, the D-DI may represent microvascular thrombosis and the elevated levels of which may provide clinical utility in predicting risk of future myocardial infarction, stroke, and PAD in the general population (Smith et al., 1997; Fowkes et al., 1993).

Although the relationship between hypertension and D-DI level has been reported previously and gained great interest among researchers worldwide in recent years, to the best of our knowledge, studies addressing the severity of hypertension and D-DI level are rare worldwide. The primary aim of this study was to assess plasma D-dimer level and its correlation with disease severity among hypertensive patients. Specifically, we sought to compare plasma D-dimer level in hypertensive patients with apparently healthy individuals and also to evaluate the correlation between plasma D-dimer level and the severity of hypertension. Besides, we aimed to determine predictive ability of plasma D-dimer to differentiate between complicated and non-complicated hypertension.

Methods and materials

Study area, design and period

A comparative cross-sectional study was designed and conducted in Yikatit 12 Hospital Medical College (Y12HMC) in Addis Ababa, Ethiopia from May 03 to June 09, 2019.

Population, sample size and sampling procedure

Due to budget and reagent constraint, we were obliged to measure plasma D-dimer level from 60 hypertensive patients attending Y12HMC and 40 volunteer healthy individuals during the study period using purposive sampling technique. But, study participants with suspected deep venous thrombosis (DVT), pulmonary embolism(PE), disseminated intravascular coagulation (DIC), recent surgery/trauma (in the last 3 months), pregnancy, early age (<20 year) and advanced age (>80 year), known history of diabetes mellitus, renal failure, or liver disease, those on anticoagulatory (heparin or warfarin) or thrombolytic treatment (streptokinase or urokinase) were excluded from the study by reviewing patient's card and historically from the participants as well as through interview.

Study variables

Plasma D-dimer level was dependent (criterion) variable while socio demographic factors (age, sex, marital status, residence, occupation, education); behavioral factors (smoking, alcohol use, physical activity); family history of hypertension; anthropometric parameter (BMI, weight, height) and clinical factors (BP, duration of HTN, number of drugs used, presence of complication) were independent (predictor) variables in this study.

Data collection procedures

After informed written consent, sociodemographic data, medical data and risk factors were collected from the selected participants using structured questionnaire through face to face interview, reviewing patient's card and direct measurement of variables like weight, height, and Blood Pressure (BP). BP was measured in the morning (before taking antihypertensive drug) at sitting positions from right arm in a quiet room using an Omron automatic device after making patient comfortable and after 15 minutes of rest. A mean of 2 measurements was used to determine Systolic blood pressure (SBP) and diastolic blood pressure (DBP) in each participant. The weight of the participants was measured using a standard balance while the height was measured using a height measuring scale with light clothing and without shoes. Body Mass

Index (BMI) was then calculated based on the formula: BMI=Weight (in kg)/ (Height in m^2) (Tambe et al., 2010). Using classification by De Lorenzo et al. (2016), four categories of BMI were identified: underweight, <18.5 kg/m^2; normal, 18.5–24.9 kg/m^2 overweight, 25.0–29.9 kg/m^2; and obese, ≥30 kg/m^2.

Blood sample collection, preparation and laboratory analysis

After then, 4 ml of venous blood was drawn from each participant via venipuncture from the antecubital vein and was poured into EDTA tube. After it was thoroughly mixed with the anticoagulant inside the tube, blood was centrifuged for 15 minutes at 3,000 rpm within 4 hours after collection at room temperature to obtain platelet-poor plasma (PPP). Plasma was separated from cells into Nunc tube using micropipette and then PPP was stored and refrigerated at -20^oC until assayed. One ml plasma was taken into sample tube for analysis and plasma D-dimer was measured by fully automated immunoturbidometric assay, using a Roche COBAS INTEGRA 6000 analyzer using the Tina-quant D-dimer Gen.2 test. The Tina-quant D-dimer test was then performed using a cutoff of 0.5 mg FEU/l.

Statistical data analysis

Data was statistically analyzed using SPSS version 25.0. Independent samples t-test and Wilcoxon Mann Whitney U-tests were used to see the difference in the mean values of continuous variable between hypertensive and control groups as well as between study variables with two responses, accordingly. One-way ANOVA and Kruskal-Wallis tests were also used to see the difference in the mean values of D-dimer level among the three stages of HTN and other study variables with three or more responses. The correlation between continuous variables that met the assumptions was computed using the Pearson's correlation coefficient. A point-biserial correlation coefficient was used for the dichotomous variables. Correlations between the ordinal variables and continuous variables that didn't meet the normality assumptions were assessed by Spearman nonparametric test. Simple and multivariate regression analyses were performed to examine the predictive variables and odds ratio. Adjusted Odds Ratio (AOR) with 95% CI was used to show the strength of association. Those variables with two-sided P-values of less than 0.05 were considered as statistically significant. The diagnostic performance of D-dimer levels for HTN related complications was evaluated using a receiver operating characteristic (ROC) curves analysis.

Ethical approval and informed consent

Ethical clearance was obtained from Research Ethical Committees of Biochemistry Department, College of Health Sciences, Addis Ababa University after review was conducted, and approval was obtained by a letter DRERC 04/14. A formal collaboration letter for data collection was obtained from the Department of Biochemistry to Y12HMC. A written informed consent was obtained from each eligible study participants before the data and blood sample were collected. Confidentiality of the information taken was kept secret and code numbers were used during sample collection.

Results

Plasma D-dimer levels between the hypertensive patients and controls

The concentrations of D-DI exceeded the normal range (>0.5mg/l FEU) in 38(63.3%) of hypertensives and 8 (20.0%) of controls. From independent sample t-test, it was observed that a significantly higher (P<0.001) mean value of D-DI levels among hypertensives (1.1±2.0 mg/l) compared to control groups (0.37±0.3mg/l) (Table 1).

Table 1 Plasma D-Dimer levels between the hypertensive patients and controls in Y12HMC, May 2019

	Control (40)	Case (60)	P-value
D-DI (mg FEU/l), mean ±SD	0.37±0.3	1.1±2.0	<0.001

Comparison of D-DI levels between different independent variables

Independent sample t-test (Table 2**)**, showed that there was statistically significant higher mean levels of plasma D-DI (P<0.05) in poorly controlled hypertensives compared to the well-controlled hypertensive patients. In addition, results showed that complicated hypertensives had significantly elevated plasma D-DI level than uncomplicated patients (P<0.001).

Table 2 Comparison of D-DI levels among hypertensive between groups of independent variables in Y12HMC, May 2019

Variables		D-DI level, mean ± SD, mg/l	P-value
Sex	Male	0.96±0.75	0.346
	Female	0..86±0.71	
Alcohol consumption	Yes	1.46±0.71	0.149
	No	0.88±0.72	
Physical activity	Yes	0.84±0.81	0.432
	No	0.92±0.70	
Family history of HTN	Yes	0.96±0.71	0.606
	No	0.87±0.73	
BP control status	Well controlled	0.73±0.83	0.029
	Poorly controlled	1.14±0.63	
Presence of complication	Yes	1.60±0.87	<0.001
	No	0.65±0.46	

P-values written in bold are significant (2-tailed)

One-way analysis of variance (ANOVA) showed that there were statistically significant differences in mean plasma D-DI level ($P < 0.05$) among different groups of age, BMI, BP and number of antihypertensive drugs. (Table 3 and Figure 1**)**.

Table 3 ANOVA of D-DI levels (mg/l FEU) according to different independent variables in Y12HMC, May 2019

		Sum of Squares	Df	Mean Square	F	P-value
Age group						
Plasma D-dimer	Between Groups	6.292	5	1.258	3.578	0.035[a]
	Within Groups	33.058	94	.352		
Marital status						
Plasma D-dimer	Between Groups	2.560	3	.853	2.227	0.090
	Within Groups	36.790	96	.383		
Educational status						
Plasma D-dimer	Between Groups	1.586	3	.529	1.344	0.265
	Within Groups	37.764	96	.393		
Occupation						
Plasma D-dimer	Between Groups	2.636	7	.377	.944	0.477
	Within Groups	36.714	92	.399		
Body Mass Index (BMI) classification						
Plasma D-dimer	Between Groups	5.133	3	1.711	4.800	0.004[b]
	Within Groups	34.217	96	.356		
Smoking						
Plasma D-dimer	Between Groups	.220	2	.110	.273	0.762
	Within Groups	39.130	97	.403		
Blood Pressure (BP) classification						
Plasma D-dimer	Between Groups	5.403	2	2.702	7.720	0.001[c]
	Within Groups	33.947	97	.350		
Number of drugs						
Plasma D-dimer	Between Groups	4.041	3	1.347	2.842	0.025[d]
	Within Groups	26.541	56	.474		

*From Tukey HSD Post hoc analysis: **a**-indicates significant difference ($p<0.05$) in D-DI level between 20-29 and 70-80 years age; **b**-significant difference in D-DI level between obese vs normal; **c**-indicate significant difference in D-DI level among all groups except normotensive vs stage 1 HTN; d-significant difference between mono- vs quadruple therapy.*

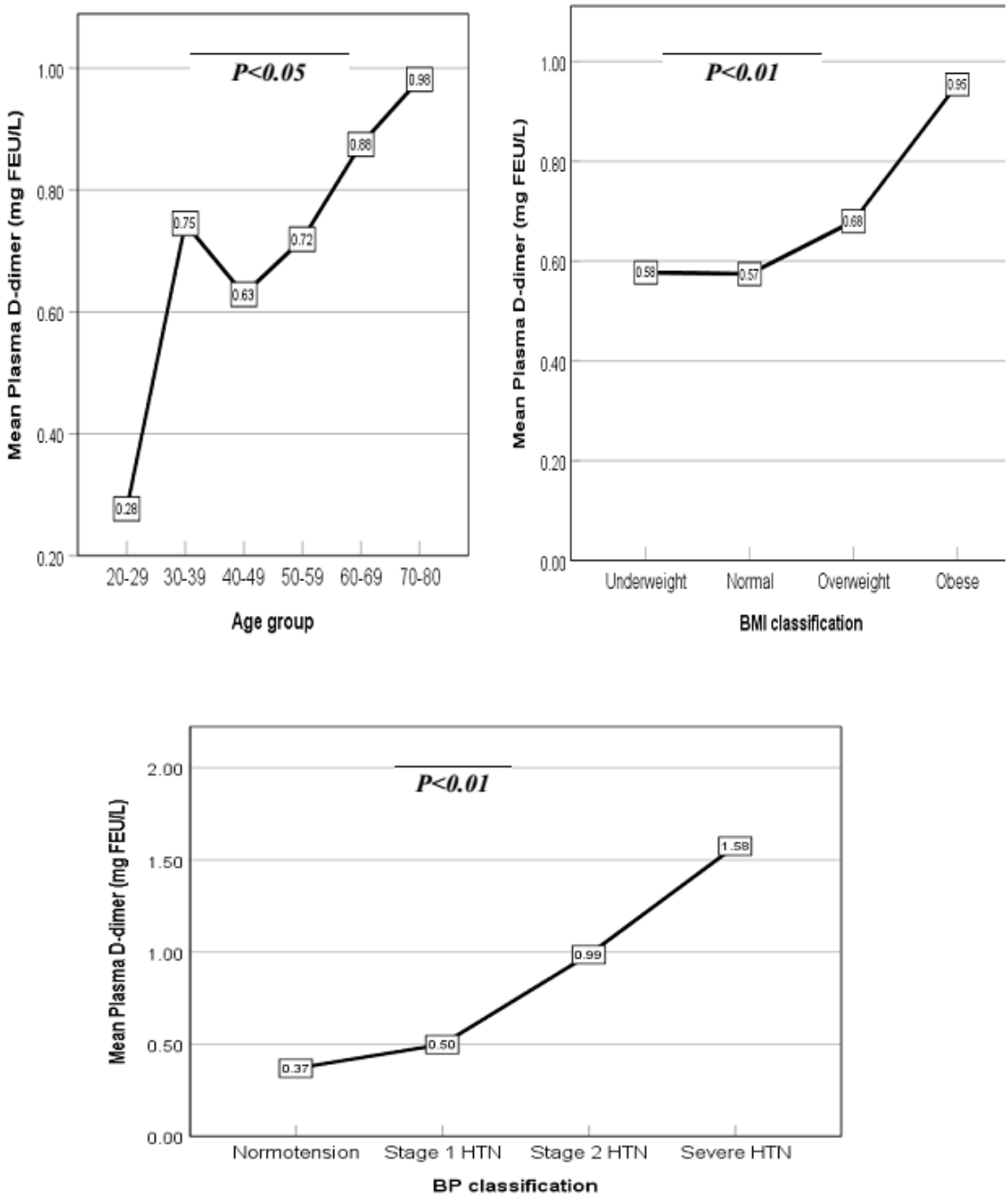

Figure 1 Mean plot showing the relationship between mean plasma D-DI levels with age group, BMI and BP classification, in Y12HMC, May 2019

Comparison of D-DI levels according to the severity of hypertension

Plasma D-DI levels were increased significantly with the severity of HTN ($p<0.001$), in which the mean D-DI level of severe HTN (1.6 ± 0.87mg FEU/l) were significantly higher compared to

both stage 1 HTN (0.50±0.25 mg FEU/l) and stage 2 HTN (0.99±0.63 mg FEU/l) from one way ANOVA (Table 4 and Figure 2**)**.

Table 4 Comparison of Plasma D-Dimer according to the severity of hypertension in Y12HMC, May 2019

	Stage 1 HTN (30)	Stage 2 HTN (14)	Severe HTN (16)	P-value
D-DI (mg FEU/l), mean ±SD	0.50±0.25	0.99±0.63	1.6±0.87	<0.001

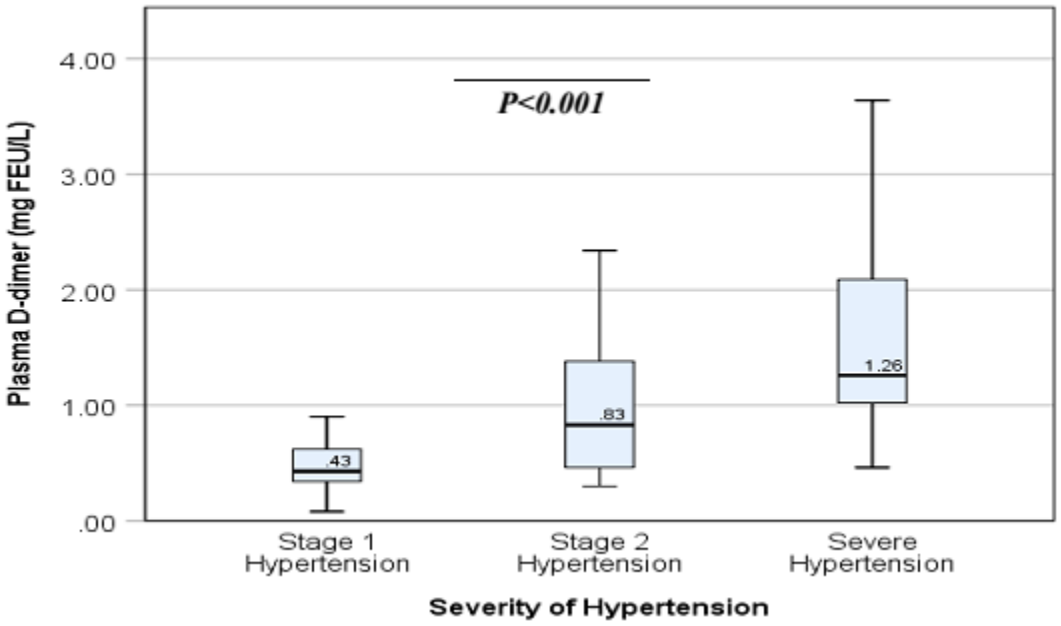

Figure 2 Box and Whisker plot showing the trend of D-DI Levels across the severity of HTN.

The Tukey HSD post hoc analysis showed that there was statistically significant difference ($p<0.05$) in mean plasma D-DI level in any of pair combinations among the clinical stages of HTN i.e. between stage 1 HTN versus stage 2 HTN and severe HTN as well as between stage 2 HTN and severe HTN (Table 5).

Table 5 Tukey HSD Post hoc analyses for pairwise multiple comparison of plasma D-DI across clinical stages of HTN in Y12HMC, May 2019.

Severity of HTN (I)	Severity of HTN (J)	Mean Difference (I-J)	Std. Error	Sig.	95% CI
Stage 1 Hypertension	Stage 2 HTN	-0.48705	0.184	0.028	(-0.9304, -0.0437)
	Severe HTN	-1.07633	0.176	<0.001	(-1.5004, -0.6523)
Stage 2 Hypertension	Stage 1 HTN	0.48705	0.184	0.028	(0.0437, 0.9304)
	Severe HTN	-0.58929	0.208	0.017	(-1.0906, -0.0880)
Severe Hypertension	Stage 1 HTN	1.07633	0.176	<0.001	(0.6523, 1.5004)
	Stage 2 HTN	0.58929	0.208	0.017	(0.0880, 1.0906)

Correlation and regression analysis of D-DI level with independent variables

Depending on the nature of variables, Pearson's, point biserial and spearman's rank correlation was performed. Among hypertensive patients, age ($r = 0.285$, $p = 0.004$), BMI ($r = 0.214$, $P = 0.032$), SBP ($r = 0.312$, $p = 0.002$), DBP ($r = 0.221$, $P = 0.027$), presence of complication ($r_b = 0.57$, $P < 0.001$) and severity of HTN ($\rho = 0.66$, $P < 0.001$) were found to have statistically significant positive correlation with D-DI values (Table 6). The mean plasma D-DI level was increased with age, SBP (Figure 3), severity of HTN and DBP. In contrary, the number of antihypertensive drugs ($r = -0.238$, $P = 0.007$) and BP control status ($r = -0.804$, $P = 0.033$) were negatively correlated with D-DI levels. However, no significant correlations existed between D-DI values and sex, smoking status, alcohol consumption, physical activity, family history of HTN or duration of HTN (Table 6).

Table 6 Correlation between plasma D-dimer level and independent variables in Y12HMC, May 2019

Variables	Correlation coefficient	P-value
Age (year)	0.285 [r]	0.004**
Sex	-0.071 [rb]	0.591
Smoking status	0.095 [ρ]	0.350
Alcohol Consumption	-0.146 [rb]	0.267
Physical activity	0.047 [rb]	0.722
BMI (kg/m^2)	0.214 [r]	0.032 *
Family history of hypertension	-0.053 [r]	0.685
Number of antihypertensive drugs	-0.238 [r]	0.007**
SBP (mmHg)	0.312 [r]	0.002**
DBP (mmHg)	0.221 [r]	0.027 *
Duration of HTN (year)	0.147 [r]	0.263
Complication	0.570 [rb]	<0.001***
Severity of HTN	0.660 [ρ]	<0.001***
Controlled BP	-0.804 [ρ]	0.033*

******** Correlation is significant at the 0.001 level; ****** significant at 0.01; ***** significant at 0.05 level (2-tailed).*
[r] Pearson's correlation coefficient; [rb] Point biserial correlation Coefficient; [ρ] Spearman's correlation coefficient

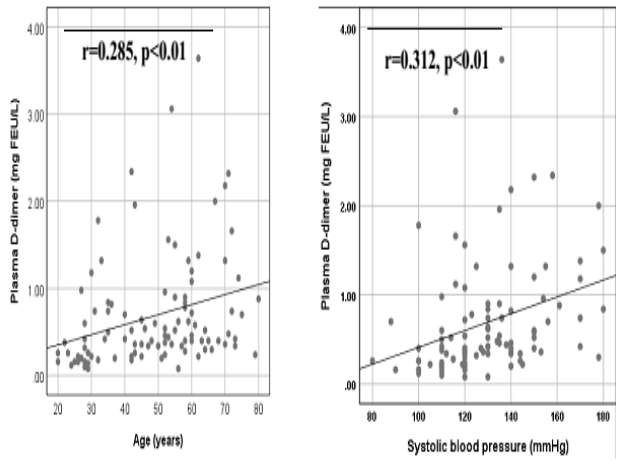

Figure 3 Scatter plot depicting the trend of correlations between D-DI level vs age and SBP, in Y12HMC, May 2019

As illustrated in Table 7, after adjusting for the effects of other variables, SBP, severity of HTN, presence of complication and BP control status were found to have independently significant association with plasma D-DI level. Systolic BP was found to be a significant predictors of plasma D-DI level in HTN in which one unit increase in SBP elevates the D-DI level by 0.001(B = 0.001, $p < 0.023$). It was also observed that there was a significant change in the level of plasma D-DI across the clinical stages (severity) of HTN. Accordingly, for a one unit increase to a higher-level clinical stage, there was an increase in D-DI level by 0.569 (B = 0.569, $p < 0.001$). While all other independent variables are held constant, the presence of complication, such as stroke or heart diseases, significantly increased the plasma D-DI level by factor of 1.048 (B= .048, $p < 0.001$). Poorly controlled HTN has 0.41 higher D-DI levels than well-controlled HTN.

Table 7 Multiple linear regression analysis to see the factors affecting D-DI level in hypertensive patients

Variables	Plasma D-dimer (mg FEU/L)			
	B*	95% CI for B		P-value
		Lower	Upper	
Age, year	0.003	-0.010	0.016	0.636
BMI (kg/m^2)	0.024	-0.008	0.056	0.136
SBP (mmHg)	0.001	0.008	0.013	0.023
DBP (mmHg)	0.004	-0.019	0.021	0.736
Presence of complication	1.048	0.691	1.405	<0.001
No. of antihypertensive drugs	0.211	-0.015	0.438	0.067
Severity of hypertension	0.569	0.373	0.764	<0.001
BP control status	0.410	0.262	0.543	0.020

**B indicates unstandardized model coefficients to indicate how much the dependent variable varies with an independent variable when all other independent variables are held constant. P-values written in bold are significant at<0.05.*

Diagnostic performance of D-dimer levels for disease severity in hypertension

The diagnostic performance of D-DI for presence of thromboembolic complication in hypertensive patients was further investigated using a receiver operating characteristic (ROC) curve. We found that the area under the curve (AUC), measuring the overall diagnostic

performance of the D-DI test, was 0.869 (95% CI: 0.773–0.964) at p<0.001 which indicated AUC is significantly different from 0.5.

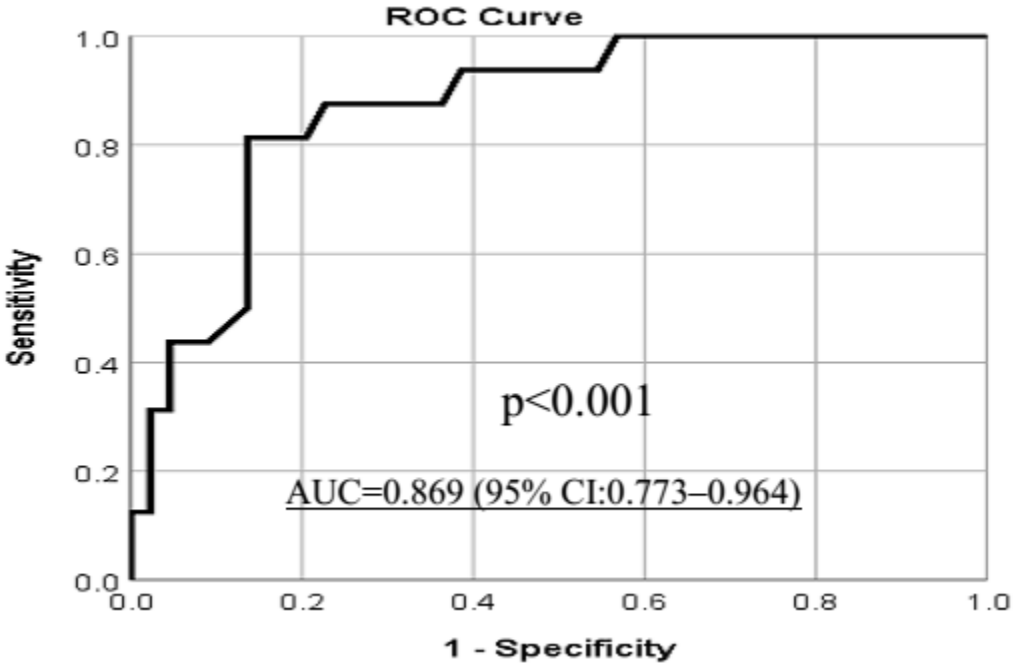

Figure 4: ROC curve analysis for the prediction of thromboembolic complications in Y12HMC, May 2019.

The optimal cut-off value for the D-DI concentration (0.83 mg/l FEU) was selected based on ROC curve analysis. The amount of D-DI was determined to be an effective diagnostic marker for severe (complicated) HTN. At a cut-off value of 0.83mg/l, the D-DI concentration had a sensitivity of 87.5%, a specificity of 77.5% with a PPV of 87.5% and NPV of 77.3%. The D-DI test also had an accuracy of 80.0% (Table 8).

Table 8. The diagnostic power of D-DI in differentiating complicated HTN from uncomplicated in Y12HMC, May 2019

Cut off value	Sensitivity, %	Specificity, %	PPV, %	NPV, %	Accuracy, %
D-DI (0.83mg/l)	87.5	77.5	87.5	77.3	80.0

N-number of patients; PPV-Positive Predictive Value; NPV-Negative Predictive Value

Discussion

The association between HTN and the activation of blood coagulation was elucidated in different literatures. Commonly observed in hypertensive patients, the hypercoagulable state appears to act as an important risk factor for thrombotic complications and may play a role in disease progression (Armas-Herna´Ndez et al., 2007). Among the degradation products resulting from the proteolytic actions of plasmin on fibrin, D-dimer is the smallest fibrin degradation by-product, exhibiting unique characteristics. D-DI can be used to estimate the state of activation of the coagulation system, which is elevated by increasing fibrin formation and fibrinolysis (Riley et al., 2016).

This study, therefore, strived to assess plasma D-DI level and its correlation with disease severity among hypertensive patients. We utilized a fully automated quantitative approach for the determination of D-DI level in 60 hypertensive patients and the values were compared with 40 unmatched normal subjects. Our data demonstrated that about 63.3% of hypertensive had excessive concentrations of plasma D-DI level. The study also indicated that plasma D-DI levels significantly increased among hypertensive patients compared to healthy controls. This finding is consistent with a number of studies that have found elevated plasma D-DI levels in essential hypertension and white coat hypertension (WCHT) groups than in healthy controls (Ibrahim and Abdalla, 2014; Coban et al., 2004; Chi et al., 2002; Catena et al., 2000). A comparative cross-sectional study has also supported this finding showed that hypertensive patients tended to have an unbalanced fibrinolytic system and tendency towards a hypercoagulability and a more frequent thrombotic complication compared to normotensive subjects (Armas-Herna´Ndez et al., 2007). Finding of high fibrin D-DI in patients with HTN suggests hypercoagulable state and ongoing intravascular fibrin formation (and possibly early thrombus formation) that plays a role in the pathogenesis of CVDs and complications of HTN. However, this finding was conflicting

with another study done in Sudan (Osman and Muddathir, 2013) and a study by Sechi et al. (2000) who showed that the D-DI level was insignificantly increased in hypertensive patients when compared with healthy controls. This discrepancy may probably be related to a difference in sample size and study design.

After adjustment of confounders, through multiple linear regression, SBP, severity of HTN, presence of complication and BP control status were found to be possible predictor variables of D-DI level though the direction of causation was poorly defined which is the inherent property of cross-sectional study design. Unlike DBP, SBP was found to be the significant predictors of plasma D-DI level in HTN in which one unit increase in SBP elevates the D-DI level by 0.001. This is partially consistent with a report which indicated that high SBP and DBP were found to be independent predictors of plasma D-DI level (Pieper et al., 2000). Poorly controlled HTN has 0.41 higher D-DI levels than the well-controlled HTN suggesting controlling BP has a lowering effect on D-DI level.

The novel finding of the current study was the association of plasma D-DI with the severity of HTN where a more severe stage of HTN has a significantly higher D-DI value than the lower stages. The finding was unchanged after the adjustment for confounding variables in which a one level increase to the higher stage of HTN significantly increased the plasma D-DI level by factor of 0.569. This suggests that patients with elevated plasma D-DI level have more severe HTN compared to hypertensive patients with normal D-DI level though the poor positive predictive value of the test require supportive test to exclude other possible causes of elevated D-DI and arrive at conclusion. This is in corroboration with previous studies which showed that the level of D-DI increased by progression of HTN to higher or more severe stage (Sechi et al 2000; Zhang et al., 2003).

D-dimer level was significantly elevated (by a factor of 1.048) in patients with complicated HTN, such as stroke and heart diseases, compared with those patients without complication while all other independent variables were held constant. These results are consistent with findings from prior study by Chi et al. (2002) demonstrating that hypertensive patients with left ventricular hypertrophy, left ventricular enlargement, and left atrial enlargement, were found to have higher levels of D-DI. This was also supported by Sechi et al. (2000) who reported that higher D-DI levels were independently associated with advanced TOD in hypertensive patients. It has been suggested that thrombus formation is involved in HTN progression to complicated type as a

result of promoting vessel thrombus occlusion and embolism. Further studies with more laboratory investigations and clinical data are needed for logical interpretation and accurate conclusion of the association of an elevated D-DI level and TOD in hypertensive patients. This is an important finding with a benefit for a better management of hypertensive patients.

D-dimer also predicts the presence and severity of hypertension-related damage in different organs. D-dimer is a classic marker, which is easy and convenient to test and could be measured in prediction of thrombotic complications associated with hypertension. The ROC curve analysis and the corresponding area under the curve (AUC) in this study showed that plasma D-DI as a biomarker has a predictive ability to discriminate complicated hypertension from uncomplicated one. The level of D-DI was determined to be an effective diagnostic marker for thrombotic complications in hypertension with an AUC of 0.869 (95% CI:0.773–0.964) as well as with a sensitivity and a specificity of 87.5%, and 77.5% respectively at 0.83mg/l FEU cut-off value and an accuracy rate of 80.0%. To the best of our knowledge, ours is the first report from a comparative cross-sectional study demonstrating the diagnostic power of D-DI level in prediction of thrombotic complications in hypertension. This intriguing finding led us to suggest that D-DI measurement can be a useful method to screen for hypertension related TOD or complications resulting from hypercoagulability and can also be useful in identifying patients with higher risk of TOD progression whereas further data will be required to help substantiate the finding.

Conclusion

In conclusion, this work suggests that plasma levels of D-DI were higher in hypertensives than the control groups and confirmed the hypercoagulable state among hypertensive patients. Besides, this study concluded that the severities of HTN were found to have statistically significant positive correlation with D-DI values. High level of D-DI was associated independently with disease severity, patients with severe HTN tend to have higher concentrations of D-DI than those with stage 1 and stage 2 HTN. Our data demonstrate that plasma D-DI have been shown to have very good predictive power for thromboembolic complications like heart diseases and stroke, and this biomarker could serve as a valuable predictor of complication development in HTN. Moreover, the current diagnostic evidence shows that hypertensive patients having marked elevated concentrations of D-DI, is an indication of thrombotic complications related to HTN. This study was cross sectional and we strongly

believe that further studies need be done on larger scale using more robust case control and cohort studies to establish the causality of the association between the severity of HTN and DDI level and their diagnostic implications on prediction of complication associated with of HTN.

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Authors' contributions

ZG conceived the study idea and refined it with EC and SG. EC involved in proposal writing, designed the study and participated in all implementation stages of the project. SG and MM worked on the designing of the study and approved the proposal. EC, ZG, TL, WH, TG, YT and TA worked on the data collection, laboratory analysis, entry, cleaning, and analysis. EC analyzed the data and finalized the write up of the manuscript. SG and MM reviewed and approved the data analysis, and drafted, reviewed, and approved the final manuscript.

Conflicting interest

The authors report no conflicts of interest in this work.

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