Serum D-Dimer in Lacunar Stroke

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Abstract

Background: *Stroke is the third most common cause of death in the developed world as well as is the most common cause of severe physical disability. A good number of studies have shown elevated serum D-Dimer level in acute ischemic stroke. Approximately one quarter of ischemic strokes are caused by lacunar infarct. This study demonstrated serum D-Dimer in Lacunar Stroke. The purpose of the study to find out serum D-Dimer in Lacunar Stroke.*

Materials and methods: *This cross-sectional study was conducted in Medicine Department, Dhaka Medical College, Dhaka on the patients with diagnosis of first ever acute lacunar Ischemic (LACI) stroke presented within 2 days of onset of symptoms. In this study, total 45 acute LACI cases irrespective of their gender were included and examined in presence of consultant physician, who were admitted from March 2014 to September 2014.*

Results: *An overall male predominance with a male to female ratio was 2:1 with the mean (SD) age of the study population of lacunar stroke was 57.60 (12.68) years. At the distribution of common risk factors in this study, there were hypertension (n=26, 57%), smoking (n=18, 40%) Diabetes mellitus (n=14, 31.1%), dyslipidemia (n=12, 26.6%) and ischemic heart disease (n=9, 20. %). Accounting the focus point of our study, the mean (SD) value of serum D-Dimer was 0.37 (0.20) mg/L with gender difference in male and female [0.39 (0.20) mg/L Vs. 0.31 (0.19) mg/L]. A regression analysis was done to find the association of D-Dimer category group (Dependent variable) which were categorized as Normal range [D-Dimer level <0.5 mg/L (n=29)] and Increased level [D-Dimer level ≥0.5 mg/L (n=16)] according to normal cutoff point of D-Dimer (<0.5 mg/L). It shows there was no statistically significant difference among normal and raised D-Dimer with gender, age, smoking, Tobacco, family history of CVD, hypertension, Diabetes mellitus, and dyslipidemia (p value > 0.05). But here, male and dyslipidemia patients were respectively 3.23 and 3.84 times more prone to develop increased level of D-Dimer, but it was statistically non-significant.*

Conclusion: *In this study, it was found that serum D-Dimer was not significantly raised with Lacunar stoke patients. Though lacunar stroke is diagnosed specially by imaging methods, serum D-Dimer may play a role in diagnosis process to exclude from non-lacunar stoke.*

Key words: Brain CT/MRI; D-Dimer; Lacunar stroke.

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INTRODUCTION

Stroke is a common medical emergency with an annual incidence of between 180 and 300 per 1,00,000. Among all types of ischemic strokes, about one quarter are caused by lacunar infarct.[1] Moreover, it is not a benign condition, 30% of patients are left dependent and scant long-term data suggest that up to 25% of patients have a second stroke within 5 years.[2] Though it is well-known that plasma d-dimer level is increased in ischemic stroke but in case of lacunar stroke, it is not established.

Clinical as well as laboratory tests differentiation of lacunar from non-lacunar strokes in the very early phase could help to exclude patients with lacunar stroke from pharmacologic trials designed for non-lacunar strokes including thrombolytic agents. This study is one of the research projects to fill the gap. Serum D-dimer in this regard can be an important tool in understanding the disease and the patient, which is not usually practiced.

Therefore, this study was conducted in all units of Medicine Department of Dhaka Medical College Hospital and serum D-dimer level was measured in lacunar stroke patients within 48 hours of onset of symptoms. Limited data are available regarding this topic in our country.The results of the study would create baseline data regarding the Bangladeshi population that can be used by the relevant health care providers in the early diagnosis and the researchers in building a larger data base for future use. Health planners will also benefit by the results in planning future health care system. The purpose of the study to find out serum D-Dimer in Lacunar Stroke.

MATERIALS AND METHODS

An observational, cross-sectional study with analytic component was conducted with 45 Consecutive patients with diagnosis of LACS (Lacunar Stroke)presented within first 2 days in Medicine Department of Dhaka Medical College Hospital (DMCH) at age more than 14 years, was included after taking informed written consent and following exclusion criteria in between 6months from March 2014 to September 2014. Each patient was diagnosed as LACS by Oxfordshire Community Stroke Project classification (OCSP) criteria and confirmed by neuroimaging [Brain CT/MRI] and exclude hemorrhagic stroke or other intracerebral diseases. Blood samples was taken for D-dimer measurement from each patient within the first 2 days of the onset of stroke symptoms and before the anticoagulant treatment were started and serum samples were stored at -32℃ till estimation in Department of Hematology, DMCH. The medical records and demographic, clinical, laboratory and radiological records of each patient was examined.

Purposive sampling technique was used. Every available patient who fulfilled the inclusion criteria was included in the study until target sample size was achieved. A pre-designed semi-structured form was used for data collection. The instrument was prepared keeping in view the objectives of the study. The instrument was pre-tested on fifteen respondents in place other than the study area. No sensitive questions were asked. They were interviewed after the informed consent form.

Data were analyzed by computer with the help of SPSS version 21.0 software package. All data were recorded in a preformed data collection sheet. Qualitative variables were expressed by frequency and percentage and quantative variables as mean (SD). Association between categorical variables were analyzed by chi-squared test and continuous variable by t-test used. Binary logistic regression analysis was done to assess the factors and expressed by adjusted odds ratios with 95% confidence interval. For all statistical tests, we considered p value <0.05 as statistically significant.Prior to the commencement of this study, the research protocol was approved by the Ethical Review Board of Bangladesh College of Physician & Surgeons (BCPS), Dhaka.
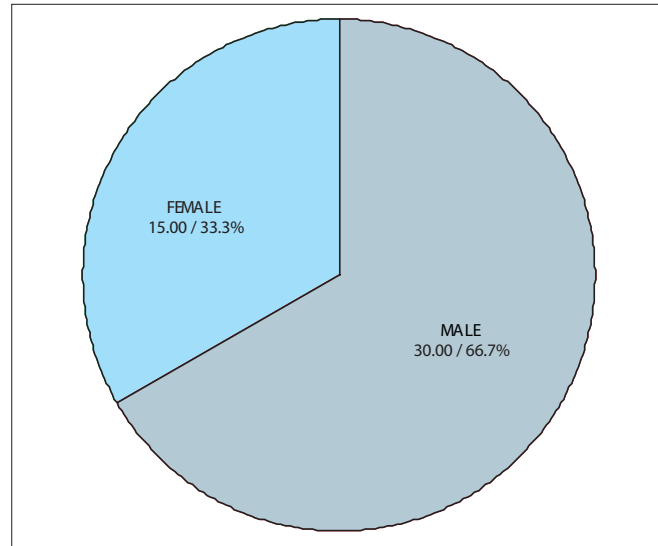
RESULTS

Figure 1 Distribution of LACI patients according to gender (n=45)

It shows there were an overall male predominance with a male to female ratio was 2:1 (male=30, female=15).

Table I Distribution of age of LACI patients (n=45)

	Mean ± SD	Min - Max
AGE (Years)	57.60 ± 12.68	25.00- 85.00

Table I shows mean (SD) age of the study population of lacunar stroke was 57.60 (12.68) years with the age range of 25 to 65 years.

Table II Distribution of LACI patients in relation with age category (n=45)

Age group (Years)	Frequency	Percentage (%)
<45	6	13.3
45-60	22	48.9
>60	17	37.8

Table II shows maximum patients were among the groups of 45 to 60 and > 60 years of age accounting 48.9% and 37.8% respectively. The least frequency of age group was observed in < 45 years which was 13.3%.
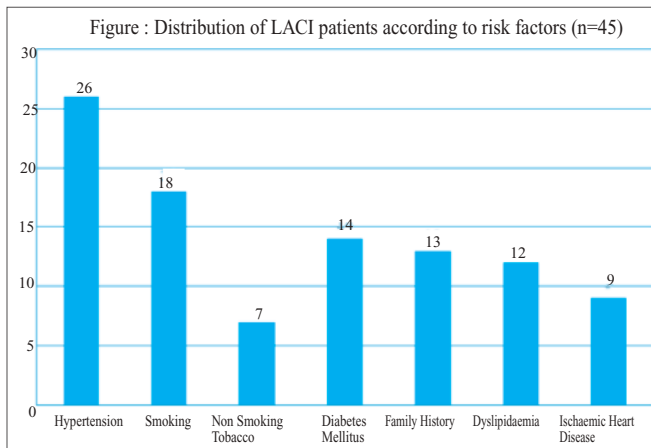
Figure 2 Distribution of Lacunar stroke patients according to risk factors (n=45)

*multiple response

It shows common risk factors were hypertension (n=26, 57%), smoking (n=18, 40%), non-smoke tobacco (n=7, 15.5%), Diabetes mellitus (n=14, 31.1%), family history (n=13, 28.8%), dyslipidaemia (n=12 26.6%) and ischaemic heart disease (n=9, 20.%).

Table III Distribution of serum D-dimer of lacunar stroke patients (n=45)

D-DIMER (mg/L)	Mean ± SD	Min - Max
In total	0.37 ± 0.20	0.01 - 0.70

This table shows distribution of serum d-dimer level of lacunar stroke patients. The mean (SD) value of serumd-dimer was 0.37 (0.20) mg/L with maximum 0.70 and minimum 0.01 mg/L (Table III).

Table IV Distribution of lacunar stroke patients according to D-dimer level in case of gender (n=45)

Gender	D DIMER(mg/L) (Mean ± SD)	p-value*
Male (n=30)	0.39 ± 0.20	0.15[ns]
Female (n=15)	0.31 ± 0.19	

*p value derived from independent sample t-test.

This table shows distribution of lacunar stroke patients according to D-dimer level in case of gender. The mean (SD) value of male counter gender was found 0.39 (0.20) mg/L and that of in female was 0.31 (0.19) mg/L. Though the mean (SD) value in male was mildly higher in female, there was no statistical significant difference (p > 0.05) (Table IV).

Table V Distribution of lacunar stroke patients according to grouping based on D-dimer level (n=45)

D-Dimer level group	Frequency	Percentage (%)
Normal range [D-Dimer level <0.5 mg/L (n=29)]	29	64.4
Increased level [D-dimer level ≥ 0.5 mg/L (n=16)]	16	35.6

Table V shows distribution of patients according to grouping based on D-dimer level. As D-dimer normal cut-off point <0.50 mg/L, we considered two group of lacunar stroke patients reminding this value. In our study, 64.4% patients had normal range of D-dimer level which was <0.5mg/L. On the other hand, 35.6% patients had increased value of D-dimer which was ≥ 0.5 mg/L.

Table VI Distribution of lacunar stroke patients according to mean (SD) value of grouping based on D-dimer level (n=45)

Type of patients of D-Dimer level group (mg/L)	Mean ± SD	p-value#
Normal range [D-Dimer level <0.5 mg/L (n=29)]	0.24 ± 0.13	< 0.0001[s]
Increased level[D-dimer level 0.5 mg/L (n=16)]	0.59 ± 0.04	
In Total (n=45)	0.37 ± 0.20	

S=significant.

#p value derived from independent sample t-test.

This table shows mean (SD) value of grouping based on D-dimer level of lacunar stroke patients. The mean (SD) value of the two groups of patients having D-Dimer level <0.5 mg/L and ≥ 0.5 mg/L, were 0.24 (0.13) mg/L and 0.59(0.04) mg/L respectively. There was statistical significant difference in between two groups considering mean value. But in total the mean (SD) value of Lacunar stroke patients was found within normal range which was 0.37 (0.20) mg/L. (Table VI).

Table-VII Association between D-dimer category group and risk factors associated with stroke in logistic regression analysis in Enter model

Risk Factors	Odds Ratio	95% Confidence Interval	p-value
Gender			
Female[ref]	1		
Male	3.23	0.58-18.07	0.182
Age	1.03	0.97-1.10	0.29
Smoking			
No[ref]	1		
Yes	0.96	0.21-4.45	0.96
Tobacco			
No[ref]	1		
Yes	.533	0.02-8.05	0.53
Diabetes Mellitus			
No[ref]	1		
Yes	1.01	0.15-6.80	1.00
Hypertension			
No[ref]	1		
Yes	0.78	0.15-4.17	0.77
Dyslipidemia			
No[ref]	1		
Yes	3.84	0.57-25.76	0.17
Family History of CVD			
No[ref]	1		
Yes	0.53	0.10-2.79	0.45

Table VII shows association of D-dimer category group (Dependent variable) which were categorized as Normal range [D-Dimer level <0.5 mg/L (n=29)] and Increased level [D-dimer level ≥0.5 mg/L (n=16)] according to normal cutoff point of D-Dimer (<0.5 mg/L). It shows there was no statistically significant difference among normal and raised d-dimer with gender, age, smoking, Tobacco, family history of CVD, hypertension, Diabetes mellitus, and dyslipidaemia (p value > 0.05). But here, male were 3.23 times more prone to develop increased level of D-dimer but it was statistically non-significant (95% CI, 0.58-18.07, p value >0.05). Another risk factor, Dyslipidemic patients were 3.84 times more prone to develop Increased level of d-dimer (95% CI, 0.57-25.76, p value >0.05).

DISCUSSION

An overall male predominance with a male to female ratio was 2:1, was observed in all lacunar stroke patients. In correspond of our study findings, Dewan et al also found male predominance in their study about 63.33% male.[3] A study at Bangabandhu Sheikh Mujib Medical University, Bangladesh from July, 1997 to June, 1999 was carried out to find out relationship between blood lipids, lipoproteins and ischaemic stroke and revealed male to female ratio was 2.75 and explained the findings as male beds are more than that of females in that hospital as well as the cultural factor that are not give proper attention to female.[4] In that same study, it reported that age range from 35 to 79 years with mean 59.45 and majority of patients were in 7th decade (n=20, 33%) and 6th decade (n=16, 27%).[5] Considering mentionad study results are similar our findings.

Analysis of age distribution of the study found that mean (SD) age of the study population of lacunar stroke was 57.60 (12.68) years with the age range of 25 to 65 years. A major portion of patients were among the groups of 45 to 60 and > 60 years of age accounting 48.9% and 37.8% respectively. In a hospital-based study on lacunar stroke in Portugal found mean±SD age of 64.8±10.8 years with the range of 34 to 93 years.[6] This finding is about to have consistent with our study.

At the distribution of common risk factors in this study, there were hypertension (n=26, 57%), smoking (n=18, 40%), non-smoke tobacco (n=7, 15.5%), Diabetes mellitus (n=14, 31.1%), family history (n=13, 28.8%), dyslipidaemia (n=12 26.6%) and ischaemic heart disease (n=9, 20.%). Reminding these risk factors, cumulative risk factors categories were also observed. It shows most of them three or more risk factors (n=19, 42.2%) which was followed by two (n=15, 33.3%) and one risk factor (n=10, 22.2%) chronologically. According to Anwarullah et al in a review of 100 stroke patients', risk factors showed hypertension in 65%, smoking in 44%, IHD in 27%, family history of stroke in 26%, past history of stroke in 22% Diabetes mellitus in 21%, Rheumatic Heart Disease (RHD) with Atrial Fibrillation (AF) in 6%, lone AF in 2%.[4] According to

Rozenthal et al.(1996) found smoking 53.8%, hypertension 43.4%, hyperlipidaemia 22% and Diabetes mellitus 21 % as main risk factors for stroke.[7] According to Hannan et al hypertension was the commonest risk factor 58.7% and other common risk factors were age (50.97%), smoking (38.7%), family history of stroke in 21.29% followed by Diabetes mellitus (14.2%).[8] In a review of lacunar stoke findings was described as Hypertension and diabetes appeared commoner among patients with lacunar versus nonlacunar infarction. However, analyses confined to studies using risk factor–free ischemic subtype definitions found only a marginal excess of hypertension with lacunar versus nonlacunar infarction (RR, 1.11,95% CI, 1.04 to 1.19) and no difference for diabetes (RR, 0.95,95% CI, 0.83 to 1.09).[9]

Accounting the focus point of our study, the mean (SD) value of serumd-dimer was 0.37 (0.20) mg/L with maximum 0.70 and minimum 0.01 mg/L. In the context of gender, the mean (SD) value of male counter gender was found 0.39 (0.20) mg/L and that of in female was 0.31 (0.19) mg/L. Though the mean (SD) value in male was mildly higher in female, there was no statistical significant difference (p > 0.05).

As D-dimer normal cut-off point <0.50 mg/L, we considered two group of lacunar stroke patients reminding this value. In our study, 64.4% patients had normal range of D-dimer level which was <0.5mg/L. On the other hand, 35.6% patients had increased value of D-dimer which was ≥ 0.5 mg/L. There was highly statistical significant difference in between two groups considering mean value (0.24 (0.13) mg/L vs. 0.59(0.04) mg/L, p <0.0001).

In 1993, Yamazaki M et al in patients with cardioembolic stroke, D-dimer and alpha 2-antiplasmin-plasmin complex levels were higher during the acute and subacute phases, while thrombin-antithrombin III complex levels were higher during the acute phase than in patients with lacunar stroke and controls.[10] In contrast, only D-dimer levels were higher in atherothrombotic stroke patients than controls during the acute and chronic phases and no significant alterations in these markers were observed in the patients with lacunar stroke. In 2010 SkoloudÃk D et al there was no correlation between the changes in D-dimer or fibrinogen levels and age, gender, time to artery recanalization, risk factors, and the seriousness of neurologic deficits on admission (p > 0.05).[11] According to Üstünda et al D-dimer levels showed variations according to different stroke types.[12] However, no important difference was observed between lacunar stroke (1.28+0.32 ng/mL, p=0.306), TIA (0.43+0.25 ng/mL, p=1.000) and the control group. In a study of early diagnosis of ischemic stroke subtypes by serum D-dimer level, 0.67 ± 0.08 g/mL or mg/L was detected in lacunar stoke patients.[13-14] All these studies are consistent with our study findings.

A regression analysis was done to find the association of d-dimer category group (Dependent variable) which were categorized as Normal range [D-Dimer level <0.5 mg/L (n=29)] and Increased level [D-dimer level ≥0.5 mg/L (n=16)] according to normal cutoff point of D-Dimer (<0.5 mg/L). It shows there was no statistically significant difference among normal and raised d-dimer with gender, age, smoking, Tobacco, family history of CVD, hypertension, Diabetes mellitus, and dyslipidaemia (p value > 0.05). But here, male were 3.23 times more prone to develop increased level of D-dimer but it was statistically non-significant (95% CI, 0.58-18.07, p value >0.05). Another risk factor, Dyslipidemic patients were 3.84 times more prone to develop Increased level of d-dimer (95% CI, 0.57-25.76, p value >0.05).

CONCLUSION

In this study, it was found that serum D-Dimer was not significantly raised with Lacunar stoke patients. The mean (SD) value of serumD-Dimer was within normal range which was 0.37 (0.20) mg/L. This level was also statistical non-significant difference in male and female [0.39 (0.20) vs. 0.31 (0.19) mg/L, p> 0.05]. Though lacunar stroke is diagnosed specially by imaging methods, serum D-Dimer may play a role in diagnosis process to exclude from non-lacunar stroke. Clinical as well as laboratory tests differentiation of lacunar from non-lacunar strokes in the very early phase could help to exclude patients with lacunar stroke from pharmacologic trials designed for non-lacunar strokes including thrombolytic agents.

DISCLOSURE

All the authors declared no competing interest.

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