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Association between Retinal Microvascular Changes and Severity of Coronary Heart Disease in Hypertensive Patients

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Abstract:

Background : The prevalence of coronary artery disease is increasing day by day. In many cases it is undiagnosed. Hypertension is one of the risk factors of coronary artery disease. Hypertension also causes some changes in retina which is easy to diagnose in clinical practice. So the aim of this study is to predict coronary artery disease by seeing hypertensive retinal changes.

Methods: A total of 100 patients with hypertension presenting to the emergency department with ischemic chest pain who underwent coronary angiography were studied. Presence or absence of coronary artery disease was determined. Optic fundi were assessed for hypertensive retinopathy which were photographed.

Results: Mean ± SD age of the study population was 56.23±10.76 years. There were 75 men (75%) and 25 women (25%). Prevalence of coronary artery disease and hypertensive retinopathy were 84% and 44% respectively. There was association between coronary artery disease and retinopathy (P< 0.017). Age (P= 0.019), smoking (P=0.011) and dyslipidaemia (0.039) were identified as risk factors for coronary artery disease.

Conclusion: Important observations from this study are that hypertensive retinopathy has an association with coronary artery disease. Retinal change can be used in predicting coronary artery disease in patients with hypertension which can be used as screening tool for diagnosing coronary artery disease in resource poor settings.

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Introduction:

Coronary heart disease (CHD) remains the leading cause of death worldwide and leads to substantial economic burden.[27] Traditional risk factors such as smoking, hypertension hyperlipidemia and diabetes are thought to explain most CHD,[8] although, 15-20% of those with CHD have no identified traditional risk factors and miss the opportunity for primary prevention.[5] The retinal vessels can be observed directly and non-invasively, and are therefore, clinically useful for assessing the systemic microvasculature.[35]

Retinal micro vascular abnormalities, such as generalized and focal arteriolar narrowing, arteriovenous nipping and retinopathy, reflect cumulative vascular damage from hypertension.[15] There are data supporting an association between retinal micro vascular abnormalities and stroke, but there is no convincing evidence of an independent or direct association with hypertensive retinal change and coronary artery disease severity.[2] When reliably quantified, retinal micro vascular abnormalities may be useful as risk indicators for cardiovascular diseases.

However, to the best of our knowledge, the relationship between changes in the retinal micro vascular structure and severity and extent of coronary heart disease (CHD) estimated by coronary angiography, has yet to be thoroughly investigated. The present study was undertaken to assess whether retinal micro vascular signs are associated with CHD severity and extent, among patients presenting with suspected CHD. The data from this study will add to new knowledge by determining the potential

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value of retinal micro vascular changes as prognostic markers of CHD risk, and whether there is a role for non-invasive retinal imaging of CHD suspects that could add to or precede coronary angiography.

Materials and methods:

Place of study: University Cardiac Center (UCC) and department of Ophthalmology, Bangabandhu Sheikh Mujib Medical University (BSMMU), Dhaka.

Study period: July 2015 to June 2016

Study design: Cross-sectional observational study.

Study population: Hypertensive patients admitted with typical ischemic chest pain in University Cardiac Center of BSMMU during the study period. Both male and female patients were included after taking informed written consent.

Selection criteria:

Inclusion criteria

1. Hypertension (as per JNC VII guideline)
2. Patients with typical ischemic chest pain.
3. Who underwent coronary angiography according to ACC/AHA guideline.
4. Who agreed for ophthalmoscopic examination.

Exclusion criteria

1. Diabetes mellitus/ impaired glucose tolerance, as defined by the American Diabetes Association
2. Presence of overt nephropathy (creatinine ≥1.5 mg/dL) or CKD
3. Known patients with CAD and were on treatment.
4. Who were managed medically without angiogram.
5. Presence of cataract

Variables

•Age• sex • BMI • smoking •Blood pressure (mmHg) level and duration•LVH on Echocardiography •Coronary artery lesion •Retinopathy• Family history of CHD

Ethical clearance was obtained from the Institutional Review Board (IRB) of BSMMU. According to Helsinki declaration for Medical Research involving Human Subjects 1964, all the patients be informed about the study design, the underlying hypothesis and the right for the participants to withdraw themselves from the projects at any time, for any reason, what so ever which will not hamper the standard duty of care anyway. Written informed consent will be obtained from each subject who will voluntarily provide consent to participate in the study. The ethical issues will be addressed accordingly.

Results:

A total 100 hypertensive patients with typical ischaemic chest pain admitted into University Cardiac Centre, BSMMU, who underwent coronary angiography were included into the study. Fundal photography were taken in retinal clinic of BSMMU. Based on coronary angiography 84 patients had coronary artery disease, 16 patients had normal coronary arteries or insignificant lesion. Based on ophthalmoscopicfindings 44 patients had hypertensive retinal changes and 66 patients had normal findings. The details of the study results are described below

Table-I

Demographic characteristics of the patients. (n=100)

Characteristics	CAD		P value
	Significant (n= 84)	No or Insignificant (n=16)	
Mean age* (yrs)	58.5±9.0	49.7±10.9	0.019^{s}
Sex**			
Male	63 (75)	12 (75)	1.000^{ns}
Female	21 (25	4 (25)	

*Data were analyzed using unpaired t-Test and were presented as mean±SD
n = Number of study population
s= significant
ns = non significant
**X^2 Test was done to analyze the data; Figure in the parentheses indicate corresponding percentage.

Patients with significant CAD were on an average older than those who did not suffer from significant CAD. There was no significant difference between two groups in terms of sex.

Table-II

Distribution of the study patients according to stage of hypertension (n=100)

Stage of hypertension	CAD		P value
	Significant (n= 84)	No or Insignificant (n=16)	
JNC VII stage I	60 (71)	12 (75)	0.693^{ns}
JNC VII stage II	24 (29)	4 (25)	0.732^{ns}

X^2 Test was done to analyze the data; Figure in the parentheses indicate corresponding percentage.
n = Number of study population
ns= non significant

Table II compared stage of hypertension between two groups. There was no significant difference between groups.

Table-III

Association between hypertensive retinopathy and Gensini score (n=100)

Stages of hypertensive retinopathy	Gensini scoremean±SD	P value
Normal findings (n=42)	8.16±4.17	
Stage 1 hypertensive retinopathy (n=22)	16.34±6.31	<0.001[s]
Stage 2 hypertensive retinopathy (n=16)	28.43±9.23	
Stage 3 hypertensive retinopathy (n=3)	37.51±11.12	
Stage 4 hypertensive retinopathy (n=1)	48.23±15.65	

n = Number of study population
s = significant
P value reached from Chi square test
Data were analyzed using one way ANOVA statistics and were presented as mean±SD

Table III showed more the grade of hypertensive retinopathy, the more is the Gensini score.

Table-IV

Gensini score in patients with or without hypertensive retinopathy (n=100)

	Hypertensive retinopathy present (n=44)	Hypertensive retinopathy absent (n=56)	P value
Gensini score	32.54±13.67	14.31±10.26	0.041[s]

n = Number of study population
s = significant
P value reached from t test

There is significant difference in Gensini score in patients with retinopathy than without retinopathy.
r=+.686, p<0.001

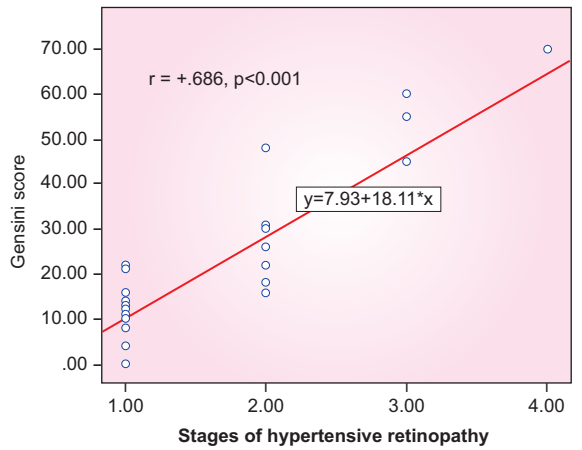

Fig.-1: *Scatter diagram showing correlation between Gensini score and stages of hypertensive retinopathy*

Spearman's correlation test showed significant positive correlation between hypertensive retinopathy and coronary artery disease.

Table-V

Regression analysis showing predictors of CAD (N=100)

Variable	Univariate analysis (p value)	Multivariate analysis Odds ratio (95% CI)	P value
Age	0.019	1.2 (0.9-1.4)	0.052[ns]
Smoking	0.011	0.29 (0.03-2.71)	0.283[ns]
Dyslipidaemia	0.039	0.28 (0.03-2.41)	0.249[ns]
Retinopathy	0.017	3.60 (1.53- 8.49)	0.003[s]

n= Number of the study population
ns=Not significant
CI= confidence interval

Multivariate analysis was performed using stepwise logistic regression and retinopathy found as independent predictors CAD.

Discussion:

Analysis of baseline differences between patients with and without coronary heart disease was done using t test which showed significant difference in age, smoking, dyslipidaemia and retinopathy between groups. GhanshyamPalamaner et al. 2009 showed in their study no significance difference in smoking and dyslipidaemia between two groups but showed significant difference in sex and retinopathy. Among patients with coronary heart disease (n=84), there was coexistent hypertensive retinopathy in 42 patients (50%). This result is similar in previous study in which GhanshyamPalamaner et al. 2009 showed 55.2% patients of coronary heart disease had hypertensive retinopathy. In our study among patients without coronary heart disease (n=16), retinopathy was present in 2 patients (12.5%) which was 14% in previous study.

Data of this study support the hypothesis that hypertensive retinopathy is positively associated with significant

coronary heart disease. Previous reports have noted an association between hypertensive retinopathy and coronary heart disease.[3]

This study results found that hypertensive retinopathy is not only a simple marker of atherosclerosis, but also correlates with the coronary angiographic Gensini score, which was calculated to yield a measure of the extent and severity of coronary atherosclerosis.

Thus the study opinions, patients with hypertensive retinopathy had higher gensini scores because they had both more significant coronary lesion and a higher incidence of double and triple vessel disease.

Previous studies have suggested that the presence of hypertensive retinopathy is a marker of cardiovascular morbidity.[7] This study results support this finding. And hypertensive retinopathy may serve as a window showing the atherosclerotic burden of the coronaty arteries which can be used as a non invasive marker of CHD.

Conclusion:

Coronary heart disease showed an association with retinopathy. Hypertensive retinal changes can be used in predicting CHD .Fundoscopy is a non invasive test that can be performed in short time in physician's chamber. It costs nothing and hence may be used as an early screening tool in a resource poor setting for predicting CHD in hypertensive patients.

Recommendation

1.Hypertensive retinopathy may be used as a screening tool to predict coronary heart disease

2. Further studies are needed in large scale to evaluate the role of Hypertensive retinopathy as a screening tool.

Limitation of the Study:

Grade I retinopathy can occur as a consequence of ageing and hence cannot be clearly attributed to hypertension.

Sample size was small.

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References:

1. Akman A. &Kadayifcilar S. Effects of hypertension on the retinal vein width at the retinal arterio-venous crossings. European Journal of Ophthalmology, 1998;8:71–75.
2. Aoki N. Epidemiological evaluation of funduscopic findings in cerebrovascular diseases. Fundoscopic findings as risk factors for cerebrovascular diseases. JpnCirc J 1975;39:257–69.
3. American Diabetes Association. 2017 Standard of medical care in diabetes; V 40 S1 P 1-35.
4. B. B. Duncan, T. Y. Wong, H. A. Tyroler, C. E. Davis, F. D. Fuchs. Hypertensive retinopathy and incident coronary heart disease in high risk men. Br J Ophthalmol, 2002;86:1002–1006.
5. Benfante R & Reed D. Is elevated serum cholesterol a risk factor for coronary disease in the elderly? JAMA 1990;19;263(3): 393-96
6. Breslin DJ, Gifford RW Jr, Fairbairn JF, Kearns TP. Prognostic importance of ophthalmoscopic findings in essential hypertension. JAMA 1996;195:335–38.
7. Couper DJ. Reliability of retinal photography in the assessment of retinal microvascularcharacteristics : the atherosclerosis risk in communities study. Am J Ophthalmol; 2002;133:78–88.
8. Dawber TR. The Framingham study: the epidemiology of atherosclerotic disease. JAMA. 1980;245(5):512
9. Dodson PM, Katsuki S, Ikui H, Kimoto K, Mimatsu T, Hypertensive retinopathy: a review of existing classification systems and a suggestion for a simplified grading system. J Hum Hypertens; 1996;10:93–98.
10. Garner A, Ashton N, Tripathi R, Kohner EM, Bulpitt CJ, Dollery CT. Pathogenesis of hypertensive retinopathy. An experimental study. Br J Ophthalmol; 1975;59:3–44.
11. Gensini GG. 1975, Coronary Angiography. New York: Futura Publishing, 1975:4.
12. GhanshyamPalamaner, YadavSrinivasan, Anita A, Kumar ShihasSalim, Suhas et al. Can retinal changes predict coronary artery disease in elderly hypertensive patients presenting with angina. The American Journal of Emergency Medicine. 2009;132: 78–88.
13. Goto I, Katsuki S, Ikui H, Kimoto K, Mimatsu T. Pathological studies on the intracerebral and retinal arteries in cerebrovascular and non cerebrovascular diseases. Stroke; 1975;6:263-9
14. Hayreh SS, Classification of hypertensive fundus changes and their order of appearance. Ophthalmologica, 1989 ;198:247–260.
15. Hiller R &Sperduto RD. Diabetic retinopathy and cardiovascular disease in type II diabetics. The Framingham Heart Study and the Framingham Eye Study, Am J Epidemiol; 1988;128:402-9.
16. Hitha B, Pappachan,JM, Pillai HB, Sujathan P, Ramakrishna CD, Jayaprakash, K. Microalbuminuria in patients with essential hypertension and its relationship to target organ damage, an Indian experience. Saudi J Kidney Dis Transpl, 2008;19(3):411-9
17. Hubbard LD, Brothers RJ, King WN. Methods for evaluation of retinal micro vascular abnormalities associated with hypertension/ sclerosis in the Atherosclerosis Risk in Communities Study. Ophthalmology; 1999;106:2269–80.
18. Hurst's The Heart . 13th edition. p. 1287,1472

19. Kannel WB, Blood pressure as a cardiovascular risk factor: prevention and treatment. J Am Med Ass. 1996;275: 1571-76.

20. Keith NM, Wagener HP, Barker NW, Some different types of essential hypertension: their course and prognosis. Am J Med Science; 1939;197:332-43.

21. Klein R. Retinopathy in a population-based study. Trans Am OphthalmolSociety. 1992;90:561–94.

22. Levy D, Garrison RJ, Savage DD, Kannel WB, Castelli WP. Prognostic implications of echocardiographically determined left ventricular mass in the Framingham Heart Study. New England Journal of Medicine; 1990;322:1561-66.

23. Leung H, Wang JJ, Rochtchina E, Wong TY, Klein R, Mitchell P. 2004, Impact of current and past blood pressure on retinal arteriolar diameter in an older population. Journal of Hypertension; 22:1543–49.

24. Mancia G, Laurent S, AgabitiRosei E, Ambrosioni E, Burnier M, Caulfield MJ, Nov. Reappraisal of European guidelines on hypertension management: a European Society of Hypertension Task Force document, Journal of hypertension., 2009;27(11): 2121-58.

25. McInnes GT, Hypertension and coronary artery disease: cause and effect; Journal of Hypertension; 1995;13:S49-S56.

26. McMahon S & Rodgers A, The effects of blood pressure reduction in older patients: an overview of five randomized controlled trials in elderly hypertensives, Clinical Experience of Hypertension; 1993;15: 967-78.

27. Okrainec K & Banerjee D. Coronary artery disease in the developing world. American Heart Journal; 2004;148:7-15.

28. Sharrett AR,. Retinal arteriolar diameters and elevated blood pressure: the atherosclerosis risk in communities study. American Journal of Epidemiology; 1999;150:263–70.

29. Schwartzkopff B, Motz W, Frenzel H, Vogt M, Knauer S, Strauer BE. Structural and functional alterations of the intramyocardial coronary arterioles in patients with arterial hypertension. Circulation. 1993;88: 993-1003.

30. The JNC 7 Report. The seventh report of the joint national committee on prevention, detection, evaluation and treatment of high blood pressure. JAMA, 2003;289:2560-72.

31. The Washington Manual of Echocardiography, 1st edition p.44

32. Third report of the National Cholesterol Education Programme (NECP) Expert Panel on Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults (Adult Treatment Panel III) final report. Circulation, 2002;106:3143-3421

33. Tso MO, Jampol LM. Pathophysiology of hypertensive retinopathy. Ophthalmology. 1982;89:1132–45.

34. Walsh JB. Hypertensive retinopathy: description, classification and prognosis. Ophthalmology; 1982;8:1127–1131.

35. Wong TY & McIntosh R. Systemic associations of retinal micro vascular signs: a review of recent population-based studies. Ophthalmic Physioogyl.; 2005;25:195–204

36. World Health Organization, 2000, Obesity: Preventing and Managing the Global Epidemic, World Health Organization, Geneva, Switzerland,