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Malondialdehyde Levels in Ischemic Stroke

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Abstract:
Background: *Cerebrovascular accident occurs due to obstructed or decreased blood flow to a part of brain leading to death of brain tissue due to lack of supply of oxygen and nutrients.Early detection and treatment can decrease the damage to the brain tissue. Many studies indicated oxidative stress as a risk factor in pathogenesis of stroke. Oxidative stress, is the imbalance between free radical formation and antioxidant defense mechanism in body. Lipid peroxidation, the process of oxidative degradation of lipids in cell membrane is caused by free radicals.*
Malondialdehyde (MDA) is a product of lipid perodixation. The measurement of serum MDA levels as a parameter of oxidative stress in CVA would be extremely important for a better understanding of its Pathophysiology.
Materials and Methods: *Prospective randomised controlled study was done with 60 patients of ischemic stroke and 30 healthy controls who are age matched and sex matched with patients. Serum malondialdehyde, lipid profile, Serum Creatinine and blood sugar were done with fasting blood sample for patients and controls.*
Results: *The mean MDA level in cases is 5.18 + 1.26. The mean MDA level in controls is 3.27 + 1.26.The difference between cases and controls is found to be statistically significant with P < 0.001.*
Conclusion: *Stroke patients have showed raised MDA levels compared to controls suggesting oxidative stress as an independent risk factor in ischemic stroke.*
Key Word: *Cerebrovascular accident; oxidative stress;lipid peroxidation; malondialdehyde.*

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I. Introduction

"Cerebrovascular accident" is defined as abrupt onset of a neurologic deficit that is attributable to a focal vascular origin [1]. Cerebrovascular accident is more commonly known as "stroke". Stroke is the second mortality in the world wide and may soon become the leading cause of death [2]. In India it is the third largest killer after MI and malignancy. It is ranked as the sixth leading cause of Disability adjusted life year (DALY, one DALY being equal to one year of health lost due to disease) in 1990 and is projected to rank fourth by the year 2020 [3]. Annually 15 million people worldwide suffer a stroke of these approximately 5 million die and another 5 million are left permanently disabled, placing a great socio economic burden on the family and society [4]. Strokes can be classified into two major categories ischemic and hemorrhagic. Ischemic is due to interruption of blood supply and hemorrhagic is due to rupture of a blood vessel or an abnormal vascular structure. Growing evidence indicate oxidative stress as an independent risk factor in pathogenesis of stroke [5, 6].

Oxidative stress, is the imbalance between free radical formation and antioxidant defense mechanism in body [7].

Currently, there is evidence from both animal and human studies demonstrating that oxidative damage to membrane lipids and proteins is increasing during cerebral ischemia and reperfusion (IR) [8,9,10,11]. Lipid peroxidation is the mechanism involved in neuronal damage induced by Ischemia and Reperfusion [12]. The brain being rich in lipids is particularly vulnerable to damage by Lipid Peroxidation [13].The role of lipid peroxides like F2 – isopropanes and 8- Hydroxy – 2 – deoxyguanosine were not adequately evaluated in stroke.

Malondialdehyde is a product of lipid peroxidation [14]. It is formed due to degradation of polyunsaturated fatty acids, in the cell membrane which are particularly vulnerable to free radical attack by losing hydrogen ions [15]. Malondialdehyde is widely used as a biomarker to measure the level of oxidative stress [16] [17]. Studies on stroke clearly demonstrated that serum MDA levels correlates with clinical outcome and size of infarct. The measurement of serum MDA levels as a parameter of oxidative stress in CVA would be extremely important for a better understanding of its Pathophysiology.

A number of studies have clearly demonstrated the involvement of free radicals in lipid peroxidation and eventual neuronal damage occurring in the brain and spinal cord [18]. Linnik reported increased level of lipid peroxidation products in ischemic stroke [19].

Santos et al (1980) discovered higher values of SMDA in stroke [20].Huang et al in 1988 hypothesised rise in lipid peroxide in stroke [21]. Sharpe PC and his colleagues detected higher levels of Malondialdehye in subjects with ischemic stroke than in controls [22]. M. Beg, S Ahmad, S Gandhi, N Akhtar Z Ahmad in 2005 studied the raised serum levels of MDA in patients of cerebrovascular accident [23].Plasma levels of raised MDA, in CVA was also noticed by Recep AYGUL, Dilcan, KOTAN, Abdul Kadir YIL DIRIM, Hizir ULVI, Fatih AKCAY [24].These studies encouraged us to do a comparative study of SMDA levels in patients of stroke and the controls as a measure of lipid peroxidation.

II. Materials and methods

The present study was conducted on patients of ischemic stroke admitted in medical wards and casualty of Government General Hospital, Vijayawada, during the period of 2018-2019. Informed consent was taken from the study group in their own language. This study was approved by Ethics Committee of Siddhartha Medical College Vijayawada. Sixty (60) patients of ischemic stroke (with mean age 55.95 years) were taken for study. Out of sixty (60) cases, thirty eight (38) are men and twenty two (22) are women.The study also included thirty (30) healthy control subjects who are age matched (mean age 56.2 years) and sex matched with patients. Out of thirty (30) twenty are men and ten (10) are women.

Fasting blood sample collected for serum malondialdehyde, lipid profile, Serum Creatinine and blood sugar within 24-72 hours of admission .A detailed history taken about risk factors for stroke and previous history of stroke from study group. All the samples collected are analysed immediately.

Inclusion criteria:
Diagnosed patients with ischemic stroke were included for the study.

Exclusion criteria:
Patients with Hemorrhagic stroke, trauma, space occupying lesions of cerebrovascular disease, cerebral embolism, TIA are excluded from the study .Cases and controls with conditions known to be associated with free radical activity such as rheumatoid arthritis, coronary artery disease and congestive heart failure were also excluded from the study.

Estimation of Blood Glucose was done by GOD–POD (Monozyme Kit) method [25],
Normal Range: Fasting: 70-110 mg%,Post prandial : < 140 mg%.
Total Cholesterol by CHOD – POD method [26] Normal Range: 130-200mg%.

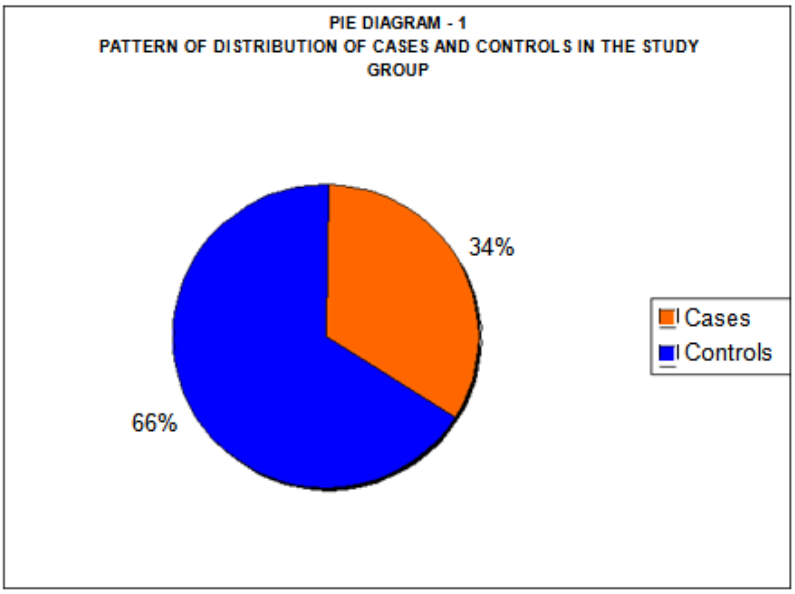
HDL Cholesterol by Phosphotungstic acid method [27],
Normal Range: Male-30 to 63 mg% Female-35 to 75 mg%.
Triglycerides by GPO/ESPAS method 1973 [28, 29], Normal upto 150 mg%.
LDL Cholesterol was calculated indirectly by using Friedewald's formula, LDLC = Total Cholesterol – HDL – T.G/5.
Serum Creatinine by Jaffe's method.
Normal Range: Male-0.5-1.1 mg%, Female-0.4-0.8 mg%.

Serum malondialdehyde estimated by measurement of thiobarbituric acid (TBA) reactive substances, Okhawa et al., 1979 method.

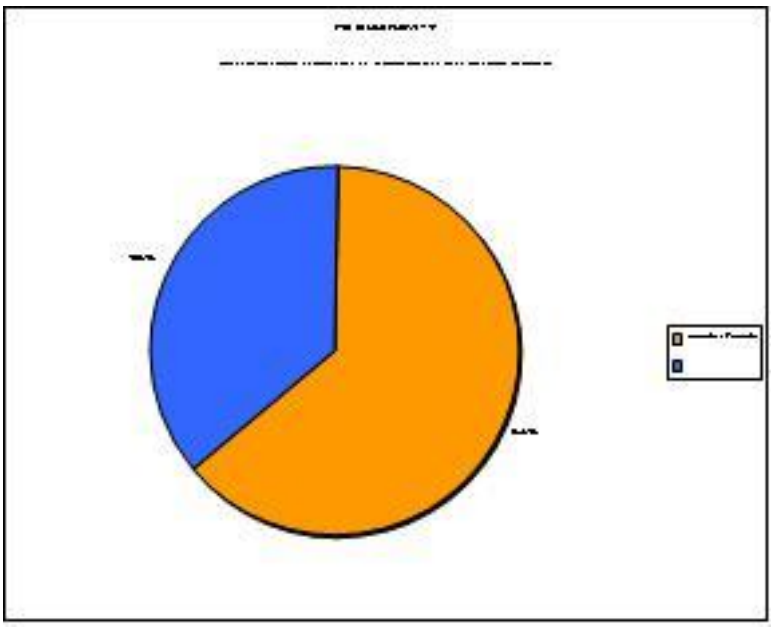
Statistical analysis:
Analysis of data was done using SPSS Software [version 20.0]. Student's t-test, ANOVA test, Pearson's correlation coefficient were used to compare data. $p<0.05$ was considered as statistically significant.

III. Result

The present study comprises of sixty (60) cases of ischemic stroke and thirty (30) healthy controls.



The mean age of controls (56.20) is slightly higher than that of cases (55.95) but the difference is however not statistically significant (P = 0.88; NS). Similarly slightly higher proportion of males was found in controls (66.7% vs 65.0 %) compared to cases but the difference was however not statistically significant (P=0.87; NS). Thus the cases are comparable with controls in respect of age and sex distribution.



The mean fasting blood sugar level was found to be significantly higher in cases (108.33 vs 77.26) compared to controls. The mean serum creatinine level was however comparable in both the groups (0.91 vs 0.99), the difference being not statistically significant (P=0.72; NS).

Baseline parameters of Cases & Controls

S.No	Parameter	Cases (n=60)	Controls (n=30)	Statistical significance
1	Age (Mean ± SD)	55.95 ± 7.98	56.20 ± 7.48	t = 0.14; P = 0.88; NS
2.	Sex			
	(a) Male	39 (65.0)	20 (66.7)	$\chi 2$ = 0.02; df=1; P=0.87; NS
	(b) Female	21 (35.0)	10 (33.3)	
3.	Fasting Blood sugar (Mean ± SD)	108.83 ± 27.18	77.26 ± 9.25	t = 6.16; P<0.001; S
4.	Serum creatinine (Mean ± SD)	0.91 ± 0.20	0.99 ± 1.71	t = 0.35; P = 0.72; NS

The mean total cholesterol, triglycerides, LDL and VLDL levels were found to be significantly higher in cases compared to controls.

The mean HDL levels were found to be significantly higher in controls compared to cases.

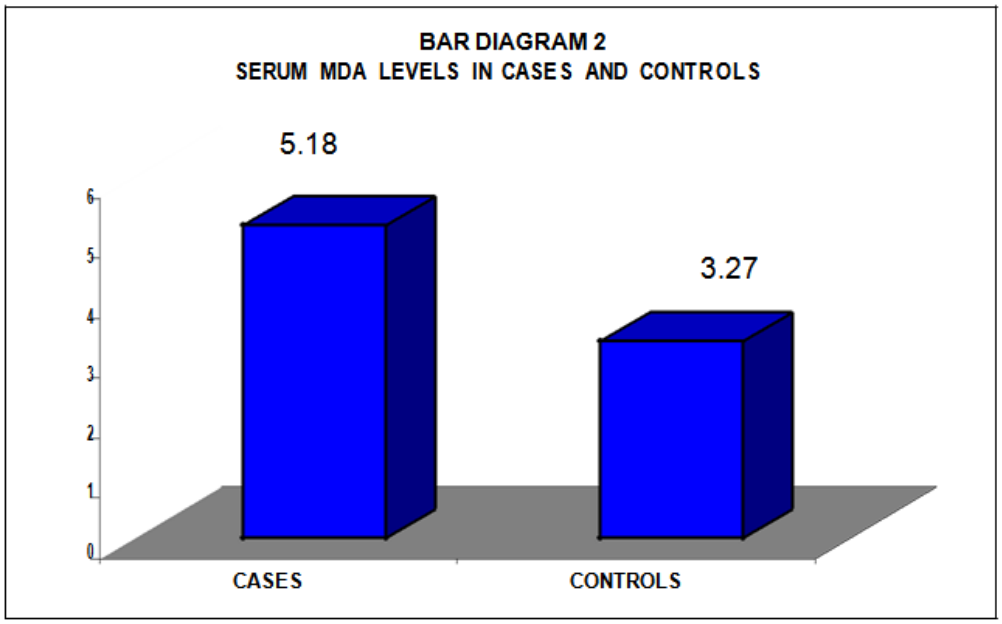
Lipid Profile of Cases & Controls

S.No	Parameter	Cases (n=60)	Controls (n=30)	Statistical significance
1	Total Cholesterol (Mean ± SD)	214.65± 29.41	181.40 ± 30.27	t = 5.00; P < 0.001; S
2.	Triglycerides (Mean ± SD)	145.98± 15.57	95.80 ± 15.12	t = 14.54; P < 0.001; S
3.	LDL (Mean ± SD)	145.08± 25.80	105.80 ± 25.61	t = 6.80; P<0.001; S
4.	HDL (Mean ± SD)	42.04 ± 3.57	59.24 ± 17.66	t = 8.36; P < 0.001; S
5.	VLDL (Mean ± SD)	29.13 ± 3.04	19.09 ± 3.13	t = 14.60; P < 0.001; S

The mean MDA level in cases is 5.18 + 1.26. The mean MDA level in controls is 3.27 + 1.26.
The difference between cases and controls is found to be statistically significant with P < 0.001; S.

MDA Levels of Cases & Controls

S.No	Parameter	Cases (n=60)	Controls (n=30)	Statistical significance
1	MDA (Mean ± SD)	5.18 ± 1.26	3.27 ± 0.52	t = 7.90; P < 0.001; S



IV. Discussion

Sixty (60) ischemic stroke patients for serum malondialdehyde as a measure of lipid peroxidation were studied. . Present study included thirty eight (38) male patients and twenty two (22) female patients. Age group varied from 41-70 years. Majority falling between 51-60 years.

Lipid peroxidation product – serum MDA levels:
The mean MDA level in the study group was 5.18 + 1.26 and in the control group was 3.27 + 0.52. The difference between means of two groups was statistically significant. Similar results have been reported by Linnik.

Lipid Profile
The mean total cholesterol level in the study group was 214.65 + 29.41 and in the control group was 181.40 + 30.27. The difference between two groups was statistically significant.

The mean LDL level in the study group was 145.08 + 25.80 and in the control was 105.80 + 25.6. The difference between two groups was statistically significant.

The mean HDL level in the study group was 42.04 + 3.57 and in the control was 59.24 + 17.66. The difference between two groups was statistically significant.

V. Conclusion

Stroke patients have showed raised MDA levels compared to controls suggesting oxidative stress as an independent risk factor in ischemic stroke.

References

[1]. Harrison's principle of internal medicine 17th edition: volume 2: 1501-09; 2513-2534.
[2]. Feigin VL (2005), "stoke epidemiology in the developing world" Lancet 365 (9478):2160-1.
[3]. Sethi PK Stroke – Incidence in India and management of ischemic stroke.
[4]. Neurosciences 2002, 6(3):139-43.
[5]. Mackay J, Mensah GA. The altas of heart disease and stroke published by WHO in collaboration with USA'S centers for disease control and prevention (CDC).
[6]. September 2004.
[7]. Mc cord JM .Oxygen-derived free radicals in post ischemic injury N Engl J Med. 1985, 312: 159-63. Braughler JM, Hall ED, Central nervous system trauma and stroke,
[8]. I: Biochemical considerations for oxygen radical formation and lipid peroxidation. Free radic Biol Med. 1989; 6:289-301.
[9]. Mohsen Muhammad Hussein El Kossi, Madeha Mahrous Zakhary (2000). Oxidative stress in the context of acute cerebrovascular stroke. Stroke 31: 1889.
[10]. Yoshida S, Inoh S, Aseno T, Sano K, Kubota M, Shimazaki H, Ueta N – Effect of transient ischemia on free fatty acids and phospholipids in the gerbil brain lipid peroxidation as possible cause of postischemic injury J Neurosurg, 1980;53:323-331.

[11]. Yamamoto M, Shima T, Uozumi T, Sogable T, Yamada K, Kawasaki T, A possible role of lipid peroxidation in cellular damages caused by cerebral ischemia and the protective effect of alpha-tocopherol administrative stroke, 1983; 14:977-982.
[12]. Polidori MC, Frei B, Cherubini A, Nelles G, Rodorf G, Keeney JF Jr, Schwamn L, Mecocci P, Koroshetz WJ, Beal MF. Increased plasma levels of lipid hydroperoxides in patients with ischemic stroke. Free radic Boil Med 1998; 25:561-567.
[13]. Watson BD, Busto R, Goldberg WJ, Santiso M, Yoshida S, Ginsberg MD, lipid peroxidation in vivo induced by reversible global ischemia in rat brain J. Neurochem. 1984; 42:268-274.
[14]. Dempoulos HB, Hamm ES, Pietronegroff seligman ML. Thr free radical pathology and microcirculation in major CNS disorders. Acta Physiolo scand suppl 1980; 492:91-113.
[15]. Rehncrona S, Siesjo BK, Mila L "Recovery of brain mitochondrial function in the rat after complete cerebral ischemia" Stroke 1979; 10:437-46.
[16]. Pryor WR, Stanley JP (1975), "letter: A suggested mechanism for the production of Malonaldehyde during the autoxidation of polyunsaturated fatty acids.
[17]. Nonenzymatic production of prostaglandin endoperoxides during auto oxidation". J.org. Chem 40 (24): 3615-7.
[18]. Halliwell B and Crutteridge JMC, Free radicals in biology and medicine 2nd Ed. Clarendon press, Oxford 1989.
[19]. Moore K, Roberts LJ (1998)."Measurement of lipid peroxidation" Free Radic, Res 28 (6): 659-71.
[20]. Del Rio D, Stewart AJ, Pellegrini N (2005) "A review of recent studies on melondialdehyde as toxic molecule and biological marker of oxidative stress". Nutr Metab cardiovasc Dis 15 (4): 316-28.
[21]. Halat G, Chavkok, lukacova Net al. Effect of partial ischemia on phospholipids and post ischemic lipid peroxdidation in rabbit spinal cord. Neurochem Research 1989; 14; 1089-97.
[22]. Cavalca V, cighetti G, loaldi Aetal. Oxidative stress and homocysteine in coronary artery disease clin chem...2001; 47:887-892.
[23]. Santos MT, waller J, Agnor J, Viknes J. Determination of plasma malondialdehyde like material and its clinical application in stroke patients J clin pathol 1980; 33;973-76
[24]. Huang Lu lee correlation between serum lipid peroxides and lesion size in cerebrovascular diseases clinical chem. Acta 1988; 173; 325-30.
[25]. Sharpe PC, Mulhollend C, Trinick T, Ascorbat and malondialdehyde in stroke patients I J Med Sci 1994; 163: 487-491
[26]. M Beg, S Ahmad, S Gandhi, N Akhatar, Z Ahmad, A study of serum Malondialdehyde levels in patients of cerebrovascular accident. JIACM 2005, 6(3):229-31.
[27]. Recep AYGUL, Dilcan KOTAN, Abdul kadir YILDRIM, Hizir ULVI, Fatih AKCAY, 'Plasma and cerebrospinal fluid Homocysteine, Nitric oxide and Malondialdehyde levels in acute ischemic stroke possible role of free radicals in the development of brain injury European journal of General Medicine . Vol 5, No:2,(2008).
[28]. Harold varley's practical clinical Biochemistry, Fourth edition.
[29]. Trinder, P. (1969) Annals clin. Bio chem. 6.24.
[30]. Burstein M., Schoinic HR Morfin R. (1970) J.Lipid Res,
[31]. Bucolo G, David M "clin chem. 19,476(1973).
[32]. Warner M. Gabriel son D.G; East man G. "Clin chem" 27,268(1981).

Dr. B. Haritha M D, et. al. "Malondialdehyde Levels in Ischemic Stroke." *IOSR Journal of Dental and Medical Sciences (IOSR-JDMS)*, 19(5), 2020, pp. 36-41.