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ROLE OF ALTERED LIPID PROFILE AND OTHER ASSOCIATED RISK FACTORS IN ISCHEMIC STROKE IN KOSI REGION, BIHAR, INDIA.

Medicine

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ABSTRACT

Objectives: This study was to evaluate the incidence, various risk factors, and clinical profile of ischemic stroke patients in Kosi region, Bihar, India. **Methods:** A detail history, clinical examinations and relevant investigations were performed to all ischemic stroke patients. Investigations were performed like as routine: complete hemogram, fasting blood sugar, urea, creatinine and urine for RE. Biochemistry: serum lipid profile (TCh ,LDL-C, HDL-C,TG,VLDL-C), serum lipoprotein(a). serum homocysteine, plasma fibrinogen. Comprehensive lipid Tetrad index:- TCh X TG x Lp(a), HDL. Cardiovascular: Chest X-ray PA view, ECG and Echo Doppler study. Neuroimaging: CT scan of Brain, MRI and MRA (where needed). Results: Data was analysed by using simple statistical methods with the help of MS-Office software. All data was tabulated and percentages were calculated. Conclusions: Patients in the above 5th to 7th decades of life are the most vulnerable to suffer ischaemic stroke. Males were commonly suffered. Hypertension is one of the most prevalent risk factors for ischemic stroke . And comprehensive lipid tetrad index has a direct relation with the incidence of ischemic stroke. So that, awareness regarding dietary habit and life style modifications are necessary for prevention from the risk of ischemic stroke.

KEYWORDS

Ischemic stroke, age group, gender, risk factors, comprehensive lipid tetrad index.

INTRODUCTION

A stroke, or cerebrovascular accident, is defined as an abrupt onset of a neurologic deficit that is attributable to a focal vascular cause. Thus, the definition of stroke is clinical, and laboratory studies including brain imaging are used to support the diagnosis. The clinical manifestations of stroke are highly variable because of the complex anatomy of the brain and its vasculature. Cerebral ischemia is caused by a reduction in blood flow that lasts longer than several seconds. Neurologic symptoms are manifest within seconds because neurons lack glycogen, so energy failure is rapid. If the cessation of flow lasts for more than a few minutes, infarction or death of brain tissue results (Harrisons 20th edition) [1].

In our country, crude prevalence rate (CPR) of stroke is estimated is be around 220 per 100,000 people. In the elderly (55- 65 yrs), crude prevelance rate (CPR) is 700 per 100,000 excluding sudden death and TIA. With increasing elderly population in most countries (including India), we are to face an increase of around 30% in number of acute strokes in next 20 years. (P.M Dalal : Stroke Prevention Strategies for India [1]

Lipoprotein (a) consists of apoprotein (a) molecule bound by a SH link to the apoliprotein B moiety of LDL particle. Apoprotein (a) has homology with plasminogen and may inhibit fibrinolysis by competing with plasminogen. Patients with high serum Lp (a) appear to have a higher risk of ischaemic stroke (Harrison : 20th edition) [1]. Thrombosis ultimately causes the gravest complications of atherosclerosis. Elevated fibrinogen levels might promote a thrombotic diathesis and is an independent risk factor for the development of cerebral infarction (Bradley : 3rd ed.) [3].

Objectives of our study was to evaluate the incidence, age, sex ratio and risk factors of ischaemic stroke with special reference to dyslipidemia and other unidentified risk factors of stroke patients like lipoprotein(a), homocysteine and fibrinogen in Kosi region, Bihar.

MATERIALS & METHODS

This study was conducted in departments of General Medicine and Neurology, Katihar Medical College and Hospital, Katihar, Bihar, India during a period from November 2018 to April 2020. Attendants of entire subjects signed an informed consent approved by institutional ethical committee of KMCH, Bihar was sought.

A detail history, clinical examinations and relevant investigation were performed to all patients. Patients who had hemorrhagic stroke or TIA or had potential sources of embolism from heart were excluded from this study.

METHODS:

History:

The patients were enquired about the date of onset of stroke, family history of hypertension, stroke, AMI/IHD, premature death and diabetes symptoms like- weakness of extremities, headache, vomiting, impaired consciousness, convulsions, loss of speech, CNS abnormalities like ptosis, diplopia, blurring of vision, facial weakness, nasal intonation, regurgitation; pain paraesthesia, bladder and bowel habits, fever and neck pain.

Patients were also enquired about risk factors like hypertension, diabetes, heart disease, dyslipidaemia, addiction like smoking, drug history like oral contraceptive pills, sedentary habits and past history of stroke or TIA.

Family history of hypertension, stroke, AMI/IHD, premature death and diabetes is enquired.

Examinations of the patient:

General survey was done concentrating on waist- hip ratio, carotid pulse, blood pressure, and peripheral signs of atherosclerosis like xanthoma, xanthelesma and locomotor brachialis. Detail examination of nervous system was done- whether the patients were conscious, alert and cooperative, drowsy or unconscious. Speech and articulator and handedness (Right/ left) were examined. Spine and cranium were examined and whether there were any meningeal sings was noted. The cranial nerves were examined in details specially 2nd and 7th cranial nerves. Motor functions were examined including nutrition, power, tone and coordination of upper and lower limbs. Frank hemiplegia/hemiparesis, and hemianesthesia, visual field defects were specially noted. Test for superficial sensation (pain, touch, and temperature), deep sensation (vibration sense, muscle, position joint and pressure sense) and cortical sensation (2 - point discrimination, stereognosis, graphaesthsia) were done. Reflexes including superficial like plantar and deep tendon reflexes were elicited. Test for cerebellar functions were done Gait was noted.

Bladder and bowel functions were examined. Any trophic changes like bed sore, trophic ulcer, charcoat joints were noted. Examinations of other systems like CVS, Respiratory, GI, and Haematopoetic system were also examined.

The following investigations were done:

1) Routine: Complete Hemogram, Fasting Blood sugar, Urea, Creatinine and Urine for RE. 2). Biochemistry: Serum lipid profile (TCh ,LDL-C, HDL-C,TG,VLDL-C), Serum lipoprotein(a). Serum Homocysteine, Plasma Fibrinogen. Comprehensive lipid Tetrad index:- TChX TG xLp(a), HDL. 3). Cardiovascular: Chest X-ray PA view, ECG and Echo Doppler study. 4) Neuroimaging: CT scan of Brain, MRI and MRA (where needed)

STATISTICALANALYSIS

Data was analysed by using simple statistical methods with the help of MS-Office software. All data was tabulated and percentages were calculated.

OBSERVATIONS

In this present study, age groups of patients had 30 to >70 years. Mean age of patients was 53.43 years and standard deviations was 7.84. Most of the patients 24(30%) were in age group 50-59 years. Most of the patients 48(60%) were male. Male and female ratio was 3:2.

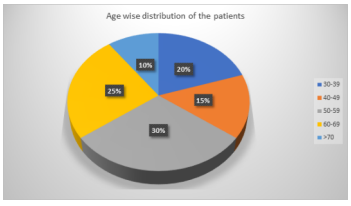

Figure.1. Age wise distribution of patients.

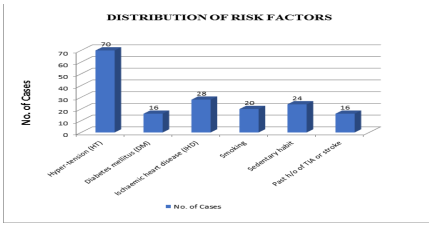

Figure.2. Risk factors of ischemic stroke patients.

In this study, hypertension 70(87.5%) was the most common risk factors of ischemic stroke patients. Other risk factors were Ischaemic heart disease (IHD) 28(35%), sedentary habit 24(30%), smoking 20(25%), diabetes mellitus (DM) and past h/o of TIA or stroke 16(20%). Most common family history of ischemic stroke was AMI/IHD and multiple risk factors 30(37.5%). And other associated family history were stroke 26(32.5%), hypertension 24(30%), diabetes mellitus 20(25%) and premature death 12(15%).

In this present study, rt-sided hemiplegia was commonest comprising 44(55%) while Lt-sided hemiplegia comprised 32(40%).

Mean ± S.D levels of total cholesterol, HDL-C, LDL-C, TG were 196.6±46.8, 43.2±7.79, 118.85±36.46 and 196.43±128.79 mg/dl respectively. 36(45%) patients had TCh above 200mg/dl. 38(47.5%) had LDL-C level above 100mg/dl. 44(55%) patients had TG levels above 150 mg/dl. 24 out of 40 cases i.e. 30 % had HDL-C level below 40 mg/dl.

This study shown that 36(45%) cases had TCh: HDL- C ratio more than 4.5. 20(25%) of the study group had LDL-C / HDL-C ratio >3.5.

In this study, only 6 cases i.e. 7.5% of the study group had comprehensive lipid tetrad index below 10,000. 16 cases i.e. 20% had comprehensive lipid tetrad index between 10,000 & 20,000 while 58 cases comprising 72.5% of the study group had above 20,000.

The range of comprehensive lipid tetrad index was 105,551, and the mean was 37,150.7. Mean ± S.D of serum Lp(a) level was 38.10 mg/dl ± 16.41.

Incidence of raised lipo protein(a): 42(52.5%) patients of the study group had their Lp(a) level above 30 mg/dl. 38(47.5%) patients of the study group had their Lp(a) level below 30 mg/dl.

Serum homocystein level: mean ± S.D of serum homocysteine level was 15.34 ± 9.43 mol/L. Age group 50-59 years patients had higher level of mean serum Homocysteine (17.13mol/L).

Table.1. Level of homocysteine according to age group [n=80].

Age group	Mean Hcy level mol/L	Range
30 – 39	14.1	6 – 29
40 – 49	13.9	7.5 – 22
50 – 59	17.13	7 – 33.6
60 – 69	16.38	6 – 58.9
> 70	13.85	8 – 20

Only 26(32.5%) patients of the study group had hyperhomocysteinemia (>15 mol/L). 54(67.5%) patients had hypohomocysteinemia (<15 mol/L). Mean ± S.D of plasma fibrinogen level was 312. 4±90.79 mg /dl.

Incidence of hyperfibrinogenemia: Only 12(15%) of the study group had their plasma fibrinogen level above 400 mg/dl. And 68(85%) patients had fibrinogen level less than 400 mg/dl.

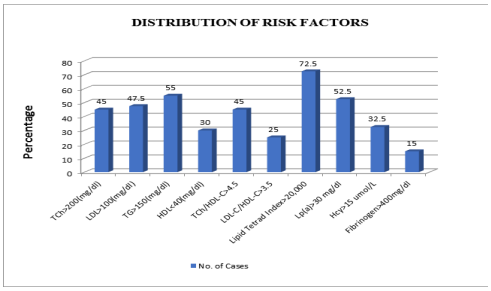

Figure.3. Distribution of risk factors in ischemic stroke patients.

In this present study, major risk factors of ischemic stroke was lipid tetrad index > 20000 (72.5%). Others risk factors were TG>150mg/dl (55%), Lp(a)>30 mg/dl (52.5%), LDL>1000 mg/dl (47.5%), TCh/HDL-C>4.5 and TCh>200 mg/dl (45%), HCy>15 umol/L (32.5%), HDL<40 MG/DL (30%), LDL-C/HDL-C>3.5 (25%) and fibrinogen>400 mg/dl (15%).

Table.2. Anatomic site of cerebral infarction as revealed by CT Scan/MRI [n=80].

Site of infarction	No. of cases	Percentage
Frontal lobe	6	7.5
Parietal lobe	10	12.5
Occipital lobe	8	10
Temporal lobe	-	-
Thalamic	10	12.5
Basal ganglion	20	25
Paraventricular	36	45
Pons	6	7.5
Mid Brain	-	-
Medulla	2	2.5
Cerebellum	2	2.5

In this present study, most of the patients had paraventricular infarction 36(46%). 20(25%) had basal ganglion infarction. 6(7.5%) patients had frontal lobe infarct. 10(12.5%) patients had parietal lobe infarct and similar number had thalamic infarct. 8(10%) had occipital infarct. 6(7.5%) had pontine infarct. Only 2(2.5%) patients had medullary and cerebellar Infarct. Most of the patients 56(70%) had anterior circulation territory infarct. Posterior circulation territory Infarct was seen in 10(12.5%) patients. 14(17.5%) patients had combine territory Infarct.

Table.3. Distribution of infarction according to side and number (CT findings) [n=80].

	Right	Left	Bilateral	Single lesion	Multiple lesion
No. of cases	28	24	28	36	44
percentage	35	30	35	45	55

In this present study, 28(35%) patients had Rt-sided infarct, 24(30%) patients had Lt-sided infarct while 28(35%) patients had bilateral infarct. 36(45%) patients had single lesion, while 44(55%) patients had multiple lesion.

Table.4. Distribution of infarction according to vesselwise (based on CT/MRI findings) [n=80].

	Small vessel	Large vessel	Combined
No. of cases	60	12	8
Percentage	75	15	10

In this present study, most of the patients 60(75%) had infarction in small vessels. Infarction in large vessel was seen in 12(15%) patients. And combined infarct was seen in 8(10%) patients.

DISCUSSIONS

This present study was enrolled a total of 80 ischemic stroke patients. Laboratory investigations were performed including serum lipid profile, serum lipoprotein(a) and serum homocysteine. Most of the patients were males 48(60%). Male and female ratio was 3:2.

Our study is collaborating with the study by Kelkar et al 1996[4], where also male (69%) was more than female (31%), the ratio of male and female being 2.22 (out of 81 patients).

In this present study, mean age of patients was 53.43 years. Most of the patients 24(30%) were belonged in age group of 50-59 years. This was similar to the findings of Sachdeva et al (1977), Jolly et al (1971) [5,6]. Most of the older age group (>40 years) patients 70(87.5%) had hypertension. Hypertension was the commonest risk factors.

P.M. Dalal (1997) were observed that high blood pressure was major risk factor in both sexes at all ages of stroke [2].

In this present study,16(20%) of all ischaemic stroke patients had diabetic. Data from Northern Manhattan Study showed that the prevalence of diabetes to be as high as 22% and 20% among elderly blacks and Hispanics respectively [7]. Our findings were supported similar to their findings.

In this present study, 28(35% of all ischaemic stroke patients had an evidence of Ischaemic Heart Disease. In Framingham Study, after 36 years of follow up, 32.7% patients had prior Coronary heart disease (Stroke 3rd edition). This suggests that atherosclerosis is a generalised disorder affecting both cardiovascular and Cerebrovascular system. In this present study, 25% ischemic stroke patients were smokers. Cigarette smoking increases the risk of thrombotic stroke and has been clearly linked to brain infarction (Stroke 3rd edition). Only 24(30%) patients had sedentary. In age group below 40, onl. Physical activity exerts a beneficial influence on risk factors for atherosclerosis by reducing blood pressure and weight, raising HDL-C and lowering LDL-C, decreasing platelet aggregability and increasing insulin sensitivity. Increasing physical activities have now been rather convincingly associated with reduced incidence of stroke (Stroke 3rd edition)[8].

In this present study, 16(20%) patients had past history of TIA / stroke. According to Walker et al 1981 18% to 26% patients had an past history. Which was similar to our study [9].

In this present study, paraventricular and basal ganglion infarction was the commonest findings. 28 cases had right-sided infarction, 24 cases had left-sided infarction while 28 cases had bilateral infarction. Single lesion comprises of 36(45%), while multiple lesion was present in 44(55%). 44(55%) patients had right-sided hemiplegia while 40% had left-sided hemiplegia.

Anterior circulation territory involvement was the commonest 56(70%) while posterior circulation comprised 10(12.5%) while 14(17.5%) belong to combined territories. Approximately 80% of ischaemic stroke occurs in carotid or anterior circulation and 20% occur in vertebrobasilar or posterior circulation (Bradley 2000) [3]. Small vessel disease was the commonest 60(75%) while large vessel infarct comprised 12(15%) while combined lesion comprised 8(10%) cases.

In our study, we found that the mean serum cholesterol was 196.6 mg/dl, range was from 130 to 306 mg/dl. Mean HDL-C was 43.2 mg/ dl, LDL-C mean was 118.85 and mean TG was 196.43 mg/dl.

In this present study, most of cases 36(45%) had hypercholesterolemia. 38 cases had LDL-C above 100 mg/dl i.e. 47.5% of the study group had adverse LDL-C level. (Enas A Enas et al) [10].

TCh/HDL ratio was more that 4.5 in 36 patients cases i.e., 45% of cases had this adverse lipid ratio.

The ratio of total cholesterol to HDL-C was significantly higher and concentration of HDL was lower in stroke cases in Madras, India (Sridharan et al) [11].

LDL/HDL ratio was more than 3.5 in 20 cases in 25%of the study group had this adverse lipid ratio.

42 cases had serum lipoprotein (a) level above 30mg/dl i.e. 52.5% of the study group had raised Lp(a) level. The mean Lp(a) of study group was high i.e., 38.10 and range was from 10.5-88 mg/dl.

58 cases had their comprehensive lipid tetrad index greater than 20,000 i.e. 72.5% of the study group had high adverse Comprehensive Lipid tetrad index. 16 cases had their index borderline between 10,000-20000 constituting 20% while only 6 patients comprising only 7.5% had their index favourable i.e., less than 10,000. The mean comprehensive lipid tetrad index was high i.e., 37,150.70.

Enas observed that abnormal i.e., more than 20,000 index predicts coronary risk due to dyslipidemia. So similar to coronary risk as observed by Enas, 72.5% ischaemic stroke patients have unfavourable index [10].

In our study, we found mean serum total cholesterol was 196.6 mg/dl i.e. in the upper limit of normal, mean LDL-C was 118.85 i.e., slightly raised, mean TG 196.43 mg/dl that is raised and mean HDL-C was 43.2 mg/dl that is normal. Therefore, the values of serum total cholesterol, LDL-C and TG tallies with the observation of Manoria et al [12].

Bansal 1973 revealed that increased TG and VLDL-C were significant risk factor for stroke in young individuals [13].

In a large meta-analysis of 45 prospective studies which included 13000 strokes in 45,000 people, no association was found between blood cholesterol and stroke mortality (Prospective Studies Collaboration).

The Copenhagen Heart Study (Lindenstrom ES et al) [14] and Multiple Risk Factor Intervention Trial (Neaton et al)[15] found close association of high cholesterol levels with the increased incidence of stroke.

It is noteworthy that serum cholesterol levels impose low relative risk for ischaemic stroke with advancing age. Hypercholesterolemia as a risk factor for coronary heart disease too loses its importance beyond 70 years of age (Kemeboiz et al) [16].

The importance of knowing the status of lipid profile as a risk factor for stroke is that by manipulating it favourably through life style modifications and pharmacological interventions, one may hope to prevent many a thrombotic stroke.

In our study, we found that the mean serum lipoprotein (a) was 38.10 mg/dl, majorities of patients 42(52.5%) had Lp(a) level above 30mg/dl.

Sandholzer et al [17] observed that in Asian Indians the Lp(a) level varies between 15 mg/dl to 60 mg/dl which may go up to 100 mg/dl in rare cases.

Reddy, Enas EA et al. [18] found that Lp(a) level above 30 mg/dl was found in 25% Asian Indians as compared to 17% whites. In our study we found that 52.5% cases had Lp(a) level above 30 mg/dl i.e., our percentage was greater than their findings.

Lp (a) is a subfraction of LDL-C. It is 10 times more atherogenic as well as thrombogenic that LDL-C.

It has been observed that Lp(a) levels in Asian Indians settled in various countries are significantly elevated. Indeed Lp(a) levels in Asian Indians are higher compared to all the ethnic groups (with the exception of blacks). The adverse effect of high levels of Lp(a) are

somewhat blunted in blacks by other factors; low LDL-C and TG and high HDL-C, while the adverse effects of Lp(a) among Asian Indians are augmented by high TG and LDL-C, and low HDL-C (Enas EA et al).

In this present study, the mean serum homocysteine (Hcy) level was 15.34 µmol/L. 26(32.5%) patients had elevated homocysteine levels.

Graham et al [19] observed in a large multi-centric study that high homocysteine concentration was associated with premature atherosclerosis.

Elevated plasma Hcy levels seen to be a feature of south Asian population. In both SHARE and the UK study, the levels of Hcy is South Asians/ Indians were higher than those found in other ethnic group (Anand, Yousuf et al). It does not tally with our findings where only 32.5% of the study group have elevated Hcy level, mean Hcy being 15.34 µmol/L.

Clarke et al (1991) [20] cemented Hcy reputation when it revealed that in a 123 patients study), 42% of patients with stroke had Hcy levels >15 µmol/L. His findings are similar to our findings where 32.5% had Hcy above 15 µmol/L (Shaun D'Souza).

Plasma fibrinogen critically influences platelet aggregation and blood viscosity, interacts with plasminogen binding and in combination with thrombin mediates the final step in clot formation. In addition, fibrinogen associates positively with age, obesity, smoking, diabetes, and LDL –C and universally with HDL-C alcohol use, physical activity and exercise level (Braunwald 2001) [21].

In our study, the mean plasma fibrinogen level was 312.4 mg/dl. Among these cases, only 12(15%) patients had hyperfibrinogenemia. Kristensen et al [22] observed that mean plasma fibrinogen level was 312 mg/dl for ischaemic stroke patients and 234 mg/dl for control patients, which was similar to our observations.

SUMMARY & CONCLUSIONS

Ischemic stroke was commonly found in older age male group patients. Right-sided hemiplegia was more frequently found. Basal ganglion and paraventricular infarction were the commonest finding on CT scan. Most of the cases had right sided infarct. Anterior circulation territory and small vessel stroke was commonest findings. Most of the patients had abnormal comprehensive lipid tetrad index, high level of Lp(a), hypohomocysteinemia, hypertriglyceridemia, high level of LDL-C and hypercholesterolemia.

Hence, we concluded that the persons in the above 5th to 7th decades of life are the most vulnerable to suffer ischaemic stroke. Males are commonly suffered. Hypertension is one of the most prevalent risk factors. And comprehensive lipid tetrad index has a direct relation with the incidence of ischemic stroke. So that, awareness regarding dietary habit and life style modifications are necessary for prevention from the risk of ischemic stroke.

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