RISK FACTORS FOR CEREBROVASCULAR ISCHEMIA IN YOUNG AGE

THESIS
Submitted for partial fulfillment of
The M.D. Degree in
Neurology

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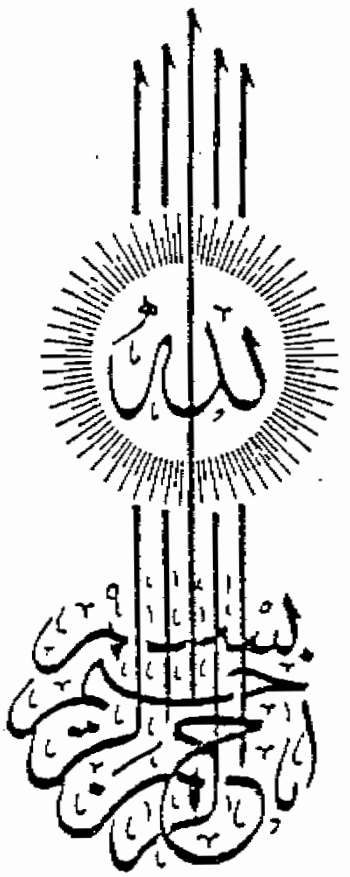
1995



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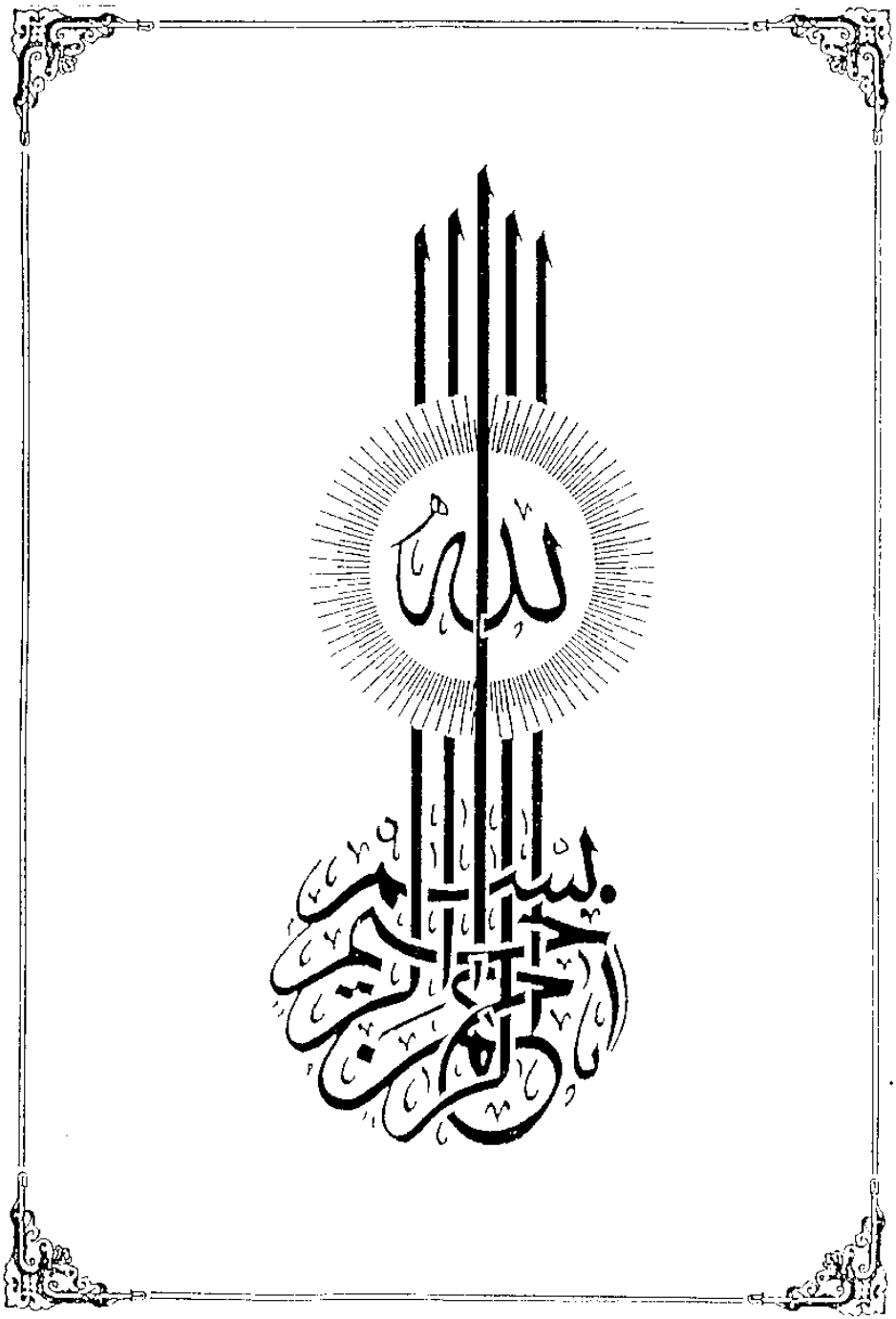

Acknowledgment

All due thanks to GOD who enabled me to accomplish this work, and above all offered me the scientific guidance of Prof. Dr. Anwar El Etrebi, who was always there paving the way for me whenever I faced any obstacles. His wisdom, support and encouragement were far beyond any expectations. I am also honoured by the supervision of Prof. Dr. Fathy Tamara who made many of the tools for this research, available. To my fortune, I was supervised by Dr. Osama Abdulghani, as he guided me and dedicated much of his time revising this work meticulously, and Prof. Dr. Nevine Kassem who tried to connect me with the laboratory, thus making a hard task easier.

I am particularly grateful to Prof. Dr. Samiha Abdul Moneim and Prof. Dr. Amira Zaki for their generous supply with review articles.

I always find myself indebted to Dr. Hany Aref, for his endless help.

My thanks to Dr. Nihad Amer, Lecturer of Int. Medicine, Dr. Zeinab Galal, from the Rheumatology Department, Dr. Hany Foad and my colleagues in the Cardiology Department and to Mr. Ahmed Kamal Nazeer for their sincere efforts, and to all my colleagues in the Neuropsychiatry Department.

I can never let a chance go without expressing my deep feelings of love, respect and appreciation to my great professors in the Neuropsychiatry Department.

Last but never least, I am forever grateful to my family, a family that is always behind my achievement.

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LIST OF ABBREVIATION

ACA	Anticardiolipin antibodies
AF	Atrial fibrillation
ANA	Antinuclear antibodies
APA	Antiphospholipid antibodies
APL	Antiphospholipid
ASD	Atrial septal defect
ATIII	Antithrombin III
CICs	Circulating immune complexes
CIPs	Coagulation inhibitory proteins
CNS	Central nervous system
DVT	Deep venous thrombosis
EC	Endothelial cell
GANS	Granulomatous angiitis of the nervous system
HDL	High density lip oprotein
HZO	Herpes zoster ophthalmicus
IEC	Infective endocarditis
LA	Lupus anticoagulants
LA	Left atrium
LDL	Low density lipoprotein
LVH	Left ventricular hypertrophy
MCA	Middle cerebral artery
MI	Myocardial infarction
MVP	Mitral valve prolapse
PAN	Polyarteritis nodosa
PC	Protein C
PFO	Patent foramen ovale
PS	Protein S
RA	Rheumatoid arthritis
SEC	Spontaneous echocontrast
SLE	Systemic lupus erythematosis
SMC	Smooth muscle cell
TEE	Transesophageal echocardiography
TIAs	Transient ischemic attacks
TSC	Total serum cholesterol
TTE	Transthoracic echocardiography

INTRODUCTION
AND
AIM OF THE WORK

INTRODUCTION

Increasing age is considered as the single most important factor that forecasts ischemic stroke, yet cerebrovascular ischemia is no longer rare among adolescents and young adults (Hart and Miller, 1983 ; Adams et al., 1995). In some reports it is estimated that the incidence of stroke is approximately six cases per 100.000 aged 15 to 39 years and 38 per 100.000 aged 40 to 44 years (Kittner et al., 1993).

This appears to have stimulated an interest in ischemic stroke in young aged patients over the past few years. This seems logical because stroke in a young subject implies a degree of disability, if not mortality in the most productive years of his life. Hence, the concern with the factors predisposing to ischemic strokes. Determination of these factors may , in the near future , lead to designing prevention programs.

It is known that the leading causes of ischemic stroke among the elderly persons are extracranial or intracranial atherosclerosis and cardioembolism, often in a setting of non valvular atrial fibrillation (Hart and Miller, 1983 ; Gorelick, 1995) However, the causes of stroke in young adults are more diverse. Cardioembolism was considered to be one of the commonest risk factors in young adults (Bogousslavsky et al., 1987). Rheumatic heart disease dominated the cardioembolic

causes in most studies (Cerebral Embolism Task Force, 1989 ; Toole, 1990), to the extent that it might have masked other causes which are becoming more and more important in recent studies (Adams et al., 1995). New investigations as transesophageal echocardiography (TEE) showed the importance of the disorders of the interatrial septum and spontaneous left atrial contrast and mitral valve prolapse (MVP), (Gorelick, 1995), especially in young adults with undetermined etiology for their strokes.

Similarly, stroke is also attributed to newly described conditions such as the antiphospholipid (APL) syndrome, where the patient is liable to recurrent thrombotic events (Asherson et al., 1989), including cerebrovascular thrombosis, especially in young adults (Brey et al., 1990).

Also, the different vasculitic disorders can involve the central nervous system vasculature leading to ischemic episodes (Nadeau and Watson, 1992). These vasculitides can either primarily ivolve the central nervous system or else the central nervous system can be secondarily involved as a part of the systemic vasculitic process (Sigal, 1987).

In acute stroke, usually the routine hematological and coagulation tests reveal no abnormalities. Hence the importance of studying the naturally occuring coagulation inhibitory proteins (CIPs), the prevalence of which among young stroke

patients is still controversial (Buruma et al., 1984; Mertinez et al., 1993)

Atherosclerosis, although a known risk factor for old age (Szirmai et al., 1993), still some other factors can predispose to early onset of atherosclerosis (Petersdorf et al. , 1983)

There are many other cause for ischemic stroke. Some studies detected 60 different potential causes (Adams et al., 1995). They included 329 young adults with ischemic stroke in their study over 15 years. They determined the presumed cause for stroke using clinical information according to which diagnostic tests were tailored. In each case, a second causative diagnosis was made using the TOAST (Trial of Org 10172 in Acute Stroke Treatment) criteria. Graph (VI) shows their results.

In our study, some of the most important risk factors will be looked for in young stroke patients in contradistinction to old ones.

AIM OF THE WORK:

- To detect the risk factors for cerebrovascular ischemia in young patients as compared to old ones.

- To determine a workup of investigations most appropriate for young patients with ischemic strokes, that enables us to reach a causative diagnosis.

Hypothesis:

We started this study with the hypothesis that there are specific risk factors for cerebrovascular ischemia in young age that are not commonly found in old age , and the opposite is true. While still there are factors predisposing to ischemic stroke common to both age groups.

CARDIOEMBOLIC CAUSES FOR ISCHEMIC STROKE

It is estimated that 12% to one third of strokes are due to cardioembolic phenomena in adults younger than 50 years (Bogousslavsky et al., 1987), an approximately similar figure 10-20% was reported by Hwang et al, (1992). And in more than half the patients dying of heart diseases the autopsy revealed cerebral infarctions (Toole, 1990).

Overall, cardioembolism is one of the three most common causes of stroke in young, namely, dissection, arterial diseases and cardioembolism (Bogousslavsky, 1992).

Cardiac diseases can result in stroke in a variety of ways. First, a diseased heart valve or endocardium can be the locus for thrombus that can embolize to the brain. Atrial thrombi can be layered or floating and may attach to the posterior wall of the atrium or the interatrial septum. Left atrial thrombi are commonly associated with mitral stenosis, prosthetic valves, atrial fibrillation, and cardiomyopathy. They may be associated with smoky echoes in the left atrium, a condition of stasis that is closely associated with embolic disease (Obeid, 1992).

Second, impaired cardiac output caused by rhythm disorders or decompensation can reduce cerebral perfusion to critical levels. Finally, medications or surgery for the

management of circulatory disorders can impair normal brain function (Toole, 1990).

Some studies delineated the criteria for diagnosing an embolic stroke:

1-Newly developed neurological deficit and presence of a certain embolic source in the heart, including valvular heart disease, prosthetic valves, cardiomyopathy, myocardial infarction or atrial fibrillation. 2-Sudden onset clinical symptoms with the maximal focal neurological deficit. 3-Evidence of embolization in other parts of the body. 4-Angiographic features such as visualization of an embolic shadow and reopening of the previously occluded vessels, and 5-CT features such as hemorrhagic infarction and a sharply marginated hypodense area involving the cortex (Yasaka et al., 1993).

Whereas Toole, (1990) mentioned similar criteria but with some practical additions:

Features suggestive of cerebral embolism:

1-Abrupt onset of maximal deficit.

2-Begins during waking hours.

3-No previous TIA in the same vascular territory (however, 10% of embolic infarctions have a progressive course, secondary to distal migration of embolic fragments.

4-Potential embolic source.