



## Elevated anticardiolipin titer as a stroke factor in young patients in kirkuk city

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### ABSTRACT

Stroke is a common cause of morbidity and mortality worldwide, and it is the third leading cause of medical death in developed countries. Stroke can be classified into ischemic disease (80%) and hemorrhagic disease (20). A case-control study done in the period extending from November 2013 to April 2014 in neuro medicine department in Azadi teaching hospital in Kirkuk city in Iraq. This study involving 2 study groups, each one of them, including 50 patients. The first group (cases) included 50 patients diagnosed as having an ischemic stroke by neurologist their ages were less than 45 years .in another group (control), 50 patients involved admitted to the same hospital with no history of prior ischemic stroke. Fifty patients with stroke of ischemic origin and 50 controls included in the study. Table 1 summarize demographic and clinical characteristics of patients and control groups, control was older than ischemic stroke patient with no significant correlation (P-value=0.33). Gender distribution showing a significant correlation in regarding female sex in both groups (P-value=0.001). Ischemic stroke according to our findings is more prevalent in those patients with Hypertension with 66% of patients in comparison to 42% of control patients with P-value of 0.0001, diabetic patients with double percentage (72%) to those in control group (36%) with P-value of 0.0001,coronary arterial disease ,valvular heart disease and rhythm disease such as atrial fibrillation seen to be more popular in those patients with ischemic stroke with no significant value in regarding to patients having coronary and valvular heart disease (P-value=0.11,0.21) and strongly associated with those patient presented with atrial fibrillation (P-value=0.0001). Elevated anticardiolipin antibodies are seen to be as an independent risk factor for ischemic stroke.

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### INTRODUCTION

Stroke is a common cause of morbidity and mortality worldwide, and it is the third leading cause of medical death in developed countries. Stroke can be classified into ischemic disease (80%) and hemorrhagic disease (20). Ischemic stroke is the result of interruption of blood supply to a part of the brain, so brain cells will die due to the reduction of oxygen and nutrients supply, and as it is a medical emergency an early action is required to minimize brain damage and potential complications (Colledge *et al.*, 2017) (Armitage, 2008).

A stroke occurs in older age more frequently than younger patients, as there are risk factors that play an essential role in stroke pathology, such as diabetes mellitus, hypertension, hyperlipidemia, smoking and the ageing process. Although, stroke can occur uncommonly in young patients and can lead to severe disability to the victim. Recent studies showed an increased incidence of stroke in young adults. (Dan *et al.*, 2012) (Kumar *et al.*, 2005) (Ashar *et al.*, 2012).

There are particular factors that might predispose to stroke in young patients, such as inherited coagulopathies; i.e. protein C and S deficiencies, factor III leaden. A lot of studies revealed a significant relationship between auto-antibodies and increased incidence of stroke (S, 2015) (Tuhim *et al.*, 1999a) (Ginsburg *et al.*, 1992a).

Cardiolipin antibodies (ACA) are autoantibodies produced by the immune system that mistakenly target the body's cardiolipins, substances found in the outermost layer of cells (cell membranes) and platelets and can lead to a clot formation or thrombosis and occlusion of an artery or vein and this can lead to severe complications, such as cerebral infarction. (Lien *et al.*, 2006).

ACA antibodies are quite common in the general population and are not always associated with the anti-phospholipid syndrome (APS). Studies indicate that there is a higher prevalence of IgM positives than IgG in the general population with these isotypes occurring in 9.4% and 6.5% of the people, respectively (Weingarten and Filippi, 1997) (Tuhim *et al.*, 1999b).

This study is conducted to assess the ACA titer as a stroke risk factor in young patients in Kirkuk city in Iraq.

## MATERIALS AND METHODS

### Subject and methods

A case-control study done in the period extending from November 2013 to April 2014 in neuro medicine department in Azadi teaching hospital in Kirkuk city in Iraq. This study involving 2 study groups, each one of them, including 50 patients. The first group (cases) included 50 patients diagnosed as having an ischemic stroke by neurologist their ages were less than 45 years .in another group (control), 50 patients involved admitted to the same hospital with no history of prior ischemic stroke. Sera collected from both groups and froze up to -70 C until Anticardiolipin were measured by using Enzyme-linked immunosorbent assay with standard commercial lab kit (BIOLABO).

Anticardiolipin IgM, IgG isotypes were measured, normal expected values were Negative with less than 15.0 MPL Units for IgM isotype and 15.0 GPL units For IgG isotype, 15.0 – 22.9 represented as a low positive test,  $\geq 23.0$  is categorized as a high positive test.

Age, Gender, cigarette smoking, and history of chronic diseases such as hypertension, diabetes mellites, atrial fibrillation, valvular heart disease and coronary arterial disease (defined as patient have ischemic heart disease by form of Myocardial infarction ,Angina and percutaneous coronary intervention to revascularize stenosed diseased arteries ) For variables with is continuous and distributed non usually Mann Whitney test was used while those normally distributed continuous variables Student's unpaired t-test were used . In all issues,  $p < 0.05$  was represented as significant. Fischers exact test and chi-square test analysis were used to compare different variables to evaluate first-order interaction between risk factors of stroke and anticardiolipin value as positive or negative, All reports used methods of the Statistical Analysis System, version 6.12 (SAS Institute).

## RESULTS AND DISCUSSION

Fifty patients with stroke of ischemic origin and 50 controls included in the study. Table 1 summarize demographic and clinical characteristics of patients and control groups, power was older than ischemic stroke patient with no significant correlation (P-value=0.33). Gender distribution showing a significant correlation in regarding female sex in both groups (P-value=0.001). Ischemic stroke according to our findings is more prevalent in those patients with Hypertension with 66% of patients in comparison to 42% of control patients with P-value of 0.0001, diabetic patients with double percentage (72%) to those in control group (36%) with P-value of 0.0001, coronary arterial disease ,valvular heart disease and rhythm disease such as atrial fibrillation seen to be more prevalent in those patients with ischemic stroke with no significant value in regarding to patients having coronary and valvular heart disease (P-value=0.11,0.21) and strongly associated with those patient presented with atrial fibrillation (P-value=0.0001). No significant different appears between both study groups regarding smoking as a risk factor although it is more prevalent in control group (46%) than those in ischemic stroke patients group (32%) (P-value=0.11), sera were collected from all patients in both study groups and serum anticardiolipin titer both for IgM and IgG antibodies measured. Titters are clas-

sified into three categories: negative, low titter and high titters. No significant correlation seen in comparison between negative results of both IgM, IgG antibodies between patients and control study groups (P-value:0.66 and 0.8), current study shows significant rise of both low and high positive titters of anticardiolipin among stroke patients group than those control non stroke patients group (P-value:<0.0001,<0.0001,0.001,<0.0001). Table 1 and Table 2 as follows:

**Table 1: Demographic and Clinical Characteristics of Stroke Patients and Controls**

Parameter	Patients (n=50)	Control (n=50)	P-value
Age (mean±SD)	38±6.1	42±2.2	0.33
Sex(M/F)	(16/34)	(22/28)	0.001
Hypertension	33(66%)	21(42%)	0.0001
Diabetes mellites	36(72%)	18(36%)	0.0001
Coronary arterial disease	18(36%)	10(20%)	0.11
Valvular disease	6(12%)	2(4%)	0.21
Atrial fibrillation	14(28%)	1(2%)	0.0001
Current smocking	16(32%)	23(46%)	0.11

**Table 2: distribution of anticardiolipins titer among patients and control groups**

Anticardiolipin titer	Patients (n=50)	Control (n=50)	P-value
Negative IgM	28(56%)	38(76%)	0.66
Low + IgM	12(24%)	8(16%)	<0.0001
High + IgM	10(20%)	4(8%)	<0.0001
Negative IgG	32(64%)	42(84%)	0.08
Low + IgG	10(20%)	6(12%)	0.001
High + IgG	8(16%)	2(4%)	<0.0001

Stroke is a typical medical emergency in which early diagnosis and management are required. Otherwise, severe complications and disabilities can occur. In addition to the well-known medical diseases that can predispose to stroke (as DM, HT, dyslipidaemia) there are other risk factors that can jeopardize the young patient to the risk of stroke, one of these is the autoantibodies, and especially the anticardiolipin autoantibodies as it can lead to a hypercoagulable state by interaction with the endothelial cells. This leads to activation of an endothe-

lial type of cells, proinflammatory cytokines secretion mainly increased, tissue factor release, and profound activation of the coagulation cascade with the formation of clot and an ischemic stroke (Janardhan *et al.*, 2004) (Stallworth and Brey, 2001) (Petri, 2000).

This study has showed that there are statistically significant relationship between the finding of positive titters of anticardiolipin auto-antibodies: IgM and IgG ( low and high titters) in the participants and incidence of stroke. Although these auto-antiantibodies also present in the regular control participants, that was in non-significant number, this finding agrees with many studies published before about this subject (Ginsburg *et al.*, 1992b) (Ahmad *et al.*, 2000) (Brey *et al.*, 2001).

Our finding of the increased incidence of ischemic stroke in those patient with positive anticardiolipin autoantibodies without other risk factors for stroke like: DM, HT, dyslipidaemia, rises essential issues, like routine screening for these auto-antibodies and the role of prophylaxis in those who are positive (Levine *et al.*, 1997) (APASS, 1993) (Chakravarty *et al.*, 1990).

## CONCLUSIONS

Elevated anticardiolipin antibodies are seen to be as an independent risk factor for ischemic stroke.

## Recommendations

Screening for those with positive anti-cardiolipin antibodies and proper assessment of them to exclude anti-phospholipid antibodies syndrome and exclude the presence of other stroke risk factors, and proper prophylaxis.

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