THE SIGNIFICANCE OF ANTIPHOSPHOLIPID ANTIBODIES IN ISCHAEMIC BRAIN DISEASE IN ADULTS SUDANESE PATIENTS

A thesis submitted in partial fulfillment for the requirements of the Degree of M.D in Clinical Medicine

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أَستَغْفِرُ لِلَّهِ وَأَنتَ أَشْفَى، أَذْهَبُ، أَنَّاسُ رَبَّنَا لَنْ يَقْدِرَ عَلَيْكُمْ شَفَاءً إِلَّا سَقَمَاءً يَغِدُّرُ إِلَّا شَفَاءً إِلَّا سَقَمَاءً
Dedication

To

The soul of my Father …

Kind Mother …

And all members of my beloved Family …

Rasha
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## CHAPTER ONE

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ACKNOWLEDGEMENT

I would like to express my deep gratitude to my supervisor Dr. Hassab El Rasoul Siddig. Without his continued enthusiasm, leading advices and critical comments, this work could not have been put forward.

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I would particularly thank all my colleagues who have helped me in the preparation of this thesis, these include: Dr. Sharief, Dr. Baha, Dr. Mauz and Dr. Randa.

I am indebted to the patients and their families who made this study a reality.

Thanks to Mr. Hassan and Miss. Shereen who helped with the statistical work and typing of the thesis.
This study is a hospital based, case controlled, cross-sectional study, carried out during the period from July 2003 till January 2005 in ElShaab and Khartoum Teaching Hospitals, to assess the prevalence of Antiphospholipid antibodies (APLAs) in ischaemic brain disease (IBD) patients and to find out their special features.

160 individuals were studied; 89 with IBD (48 females and 41 males), 35 with other diseases (13 females, 22 males), 36 healthy control (18 females, 18 males).

Patients were studied using a simple direct, standardized questionnaire including, history, physical examination and investigations.

All individual were tested for APLAs, IBD patients were examined by CT brain, ESR and platelets, lipid profile and blood sugars.

Antinuclear factor (ANF) was done in 24 patients, anti double stranded DNA in 18, partial thrombo blastin time (PTT) in 16 and VDRL in 14 patients. Echocardiography was done in eight patients, echocardiography and carotid Doppler’s in six patients. Follow-up CT scan brain six weeks following stroke was done in four APLAs +ve patients.

APLAs +ve patients with IBD showed a female : males ratio of 2 : 1.5 and increased incidence in the age group 20-29 years.
APLAs +ve patients at presentation tend to have more headache and fits but have less disturbance of consciousness, speech disturbance or motor weakness compared to those who were APLA –ve. They were also found to have more frequent history of DVT, migraine and abortion.

APLAs were found to be strongly associated with elevated ESR and low platelets, +ve VDRL, carotid stenosis, ANF and prolonged PTT.

Follow-up CT brain six weeks following stroke was done in four patients and found to return to normal in three of them.

The study demonstrated higher local incidence of APLAs in IBD than that reported worldwide, and they tends to occur more commonly in young females with IBD, suggesting a possible causal relationship.

The study also suggested a better prognosis in stroke patients for motor weakness and CT changes.
منظور الدراسة

かれالية من موجبة في عام 2005، حيث كانت فترة الدراسة هي 8 أشياء، تم التفاعل مع هذه الأشياء، وتصل في النهاية إلى النتائج.

أثناء فترة عام 2003-2005، حيث تم تقدير الأحداث من خلال الأحداث، تم التفاعل مع الأحداث، وتصل في النهاية إلى النتائج.

تمت الدراسة من خلال الأحداث، وتمت الردود على الأحداث، وتصل في النهاية إلى النتائج.

 Keeper للفترة، حيث تبين أنه تم الاستماع إلى الأحداث، وتصل في النهاية إلى النتائج.

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ﺍﻟﺼﻔﺎﺋﺢ، ﺍﳊﻤﺮﺍﺀ ﺍﻟﻜﺮﻭﻳﺎﺕ ﻣﻌﺪﻝ ﺑﺎﺭﺗﻔﺎﻉ ﺑﻘﻮﺓ ﻣﺮﺗﺒﻂ ﺍﳌﻀﺎﺩ ﺍﻟﻌﺎﻣﻞ ﺍﳚﺎﺏ، ﺍﻟﺴﺒﺎintendent ﻏﺾ ﺍﳚﺎﺏ، ﺍﻟﺰﻫﺮﻱ ﻓﺤﺺ ﺍﳚﺎﺏ، ﺍﻟﺪﻣﻮﻳﺔ ﺩﺭﺍﺳﺔ ﻣﺼﺎﺑﲔ ﻣﺮﺽ ﻋﻨﺪ ﺍﻟﻄﺒﻴﻌﻲ ﺑﺎﻟﺴﻜﺘﺔ ﻣﺼﺎﺑﲔ ﻣﺮﺽ ﹾﺍﻟﺪﻣﺎﻏﻴﺔ ﺑﺎﻟﺴﻜﺘﺔ ﻣﺮﺽ ﻋﻨﺪ ﺍﻟﻄﺒﻴﻌﻲ ﺑﺎﻟﺴﻜﺘﺔ ﻣﺼﺎﺑﲔ ﻣﺮﺽ ﹾﺍﻟﺪﻣﺎﻏﻴﺔ ﺑﺎﻟﺴﻜﺘﺔ ﻣﺮﺽ ﻋﻨﺪ ﺍﻟﻄﺒﻴﻌﻲ ﺑﺎﻟﺴﻜﺘﺔ ﻣﺼﺎﺑﲔ ﻣﺮﺽ ﹾﺍﻟﺪﻣﺎﻏﻴﺔ ﺑﺎﻟﺴﻜﺘﺔ ﻣﺮﺽ ﻋﻨﺪ ﺍﻟﻄﺒﻴﻌﻲ ﺑﺎﻟﺴﻜﺘﺔ ﻣﺼﺎﺑﲔ ﻣﺮﺽ ﹾﺍﻟﺪﻣﺎﻏﻴﺔ ﺑﺎﻟﺴﻜﺘﺔ ﻣﺮﺽ ﻋﻨﺪ ﺍﻟﻄﺒﻴﻌﻴ
## ABBREVIATIONS

<table>
<thead>
<tr>
<th>Abbreviation</th>
<th>Definition</th>
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<tr>
<td>APS</td>
<td>Antiphospholipid syndrome.</td>
</tr>
<tr>
<td>APASS</td>
<td>Antiphospholipid antibodies stroke study.</td>
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<td>APLAS</td>
<td>Antiphospholipid antibodies.</td>
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<tr>
<td>ACL</td>
<td>Anticardiolipin.</td>
</tr>
<tr>
<td>ABS</td>
<td>Antiphosphatidylserine.</td>
</tr>
<tr>
<td>B2GPI</td>
<td>Beta2 glycoprotein 1.</td>
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<tr>
<td>CTscan</td>
<td>Computerized tomography.</td>
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<tr>
<td>DVT</td>
<td>Deep vein thrombosis.</td>
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<tr>
<td>D.M</td>
<td>Diabetes mellitus.</td>
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<tr>
<td>ELISA</td>
<td>Enzymelinked immunosorbant assay.</td>
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<tr>
<td>ECG</td>
<td>Electrocardiography.</td>
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<tr>
<td>GABA</td>
<td>Gamma aminobutyric acid.</td>
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<tr>
<td>HIV</td>
<td>Human immunodeficiency virus.</td>
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<tr>
<td>HLA</td>
<td>Human leucocytes antigen.</td>
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<tr>
<td>HDL</td>
<td>High density lipoproteins.</td>
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<tr>
<td>HELLP</td>
<td>Haemolysis, elevated liver enzymes &amp; low platelets.</td>
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<tr>
<td>HT</td>
<td>Hypertension.</td>
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<tr>
<td>IBD</td>
<td>Ischaemic brain disease.</td>
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<tr>
<td>ITP</td>
<td>Immune thrombocytopenic purpura.</td>
</tr>
<tr>
<td>LE</td>
<td>Lupus erythematous.</td>
</tr>
<tr>
<td>LDL</td>
<td>Low density lipoproteins.</td>
</tr>
<tr>
<td>LA</td>
<td>Lupus anticoagulant.</td>
</tr>
<tr>
<td>MRI</td>
<td>Magnetic resonance image.</td>
</tr>
<tr>
<td>U/S</td>
<td>Ultrasonography.</td>
</tr>
<tr>
<td>SLE</td>
<td>Systemic lupus erythematosus.</td>
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<tr>
<td>TIA</td>
<td>Transient ischaemic attacks.</td>
</tr>
<tr>
<td>WMH</td>
<td>White matter hyperintense lesions.</td>
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INTRODUCTION

Most of the early work leading to the detailed description of APS was carried out in the early 1980s by Dr. Graham Hughes and his colleagues while studying lupus. It became clear that some patients had a tendency to form blood clots in arteries and veins. This clotting was associated with a particular antibody which attacks phospholipids, Hence the term antiphospholipid antibodies. \(^1\)

**Definition:**

Antiphospholipid syndrome (APS) is a disorder characterized by recurrent arterial or venous thrombosis, recurrent fetal loss, and autoimmune thrombocytopenia associated with the presence of antibodies against the cellular component phospholipids. \(^2\)

**Types:**

1. *Primary APS;*
   
   Not associated with systemic lupus or other autoimmune disease.

2. *Secondary APS;*
   
   Associated commonly with systemic lupus erythematosus.

**Occurrence:**

It can affect a number of different organs in the body. All age groups can be affected; from infants to elderly. However, the majority of people with APS are aged between 20 and 50 years. The female to male ratio is 2 : 1.
Clinical features:

A. Pregnancy loss:

Obstetric complications include recurrent fetal loss, often but not always in the late second or third trimester, severe pre-eclampsia, premature delivery; chorea gravidarum; intrauterine growth retardation or postpartum syndrome manifested by pleuropericarditis and fever.

B. Thrombosis:

All venous and arterial systems can be involved; commonly DVT and strokes.

C. Other features:

Migraine, haemolytic anaemia, livedo- reticularis and thrombocytopenia. Antiphospholipid antibodies are an extremely heterogenous group of antibodies directed against a variety of antigenic determinants platelets; coagulation proteins. and endothelial cells. Cerebral ischemia associated with apl is the most common arterial manifestation, However, the importance of apl as a cardiovascular risk factor is controversial. In many studies apl is associated with an increased risk for incidence and recurrence of cerebral ischaemia; myocardial infarction; and venous thrombosis. Intracardiac thrombus has been reported. Regardless of age; patients with cerebral ischaemia often have other risk factors for cerebrovascular disease. APL may act in concert with other vascular risk factors that damage endothelial cells. A variety of cardiac valvular lesions have been associated with apl; and cardiac emboli are a possible cause of cerebrovascular symptoms.
Situations in which antiphospholipid antibodies may be detected; Infections; Syphilis; malaria; H.I.V; Hepatitis C.

Rheumatic and collagen vascular disease; S.L.E; systemic sclerosis; rheumatoid arthritis; temporal arteritis; psoriatic arthorathy; sjogren syndrome.

**Thrombatic disease:**

Venous thromboembolic disease; peripheral arterial occlusion; ischeamic heart disease; after coronary bypass graft surgery; valvular heart disease; pulmonary hypertension.

**Disorders of the nervous system and eye:**

Thrombotic stroke; transient ischemic attaks; sagittal sinus thrombosis; ischemic optic atrophy; multi-infarct dementia; chorea; guillian barre syndrome.

**Drugs:**

Phenothiazines, procainamide, hydralazine, phenytoin, quinidine.

**Miscellaneous:**

Autoimmune thrombocytopenia and haemolytic anaemia; Behcet syndrome; sickle cell anaemia, intravenous drug abuse.

The diagnosis of antiphospholipid antibody syndrome requires the antiphospholipid antibody panel, lupus anticoagulant, anticardiolipin antibody on two separate occasions, at least 6 weeks a part, in the presence of thrombosis, thrombocytopenia or recurrent miscarriage.
LITERATURE REVIEW

Antibodies to phospholipids were probably first described by Wasserman in 1906, who had developed a laboratory assay for detection of syphilis, and later by Pangborn in 1941, whose laboratory assays for syphilis utilized a prepared extract of bovine heart muscle which is rich in phospholipids that he called cardolipin. During the Second World War, laboratory assays for syphilis were being performed on military and non-military personnel; doctors discovered a number of people with positive syphilis test results, but with no clinical evidence of disease. In follow-up studies of false positive patients, it was found that they could be divided into two groups, transient false positive (usually due to infection) and long term false positive, where there was a high prevalence of autoimmune disorders including systemic lupus erythematosus (LE). This was the first hint that there was an association between unusual antibodies (which cause a false positive syphilis test) and autoimmune disease.

In 1952, Conley and Hartmann reported two LE patients with bleeding disorders and a false positive syphilis test. The laboratory studies suggested that there was a relationship between the presence of these unusual antibodies and bleeding tendencies, because the patient blood did not clot as rapidly as normal; the term lupus anticoagulant was used to describe this clinical condition.
It has been shown that this antibody is only present in a small number of LE patients and that blood-clotting complications occur in patients with these antibodies rather than the bleeding complications one would expect from the laboratory results. Although the actual mechanisms remains to be determined, antiphospholipid antibodies can attack platelets or blood vessel cells which may cause the formation of small blood clots.\textsuperscript{5}

The association between the presence of the lupus anticoagulant and blood clots has stimulated the development of more sensitive tests for the detection of antiphospholipid antibodies. Studies suggest that prolonged increased levels of antiphospholipid antibodies are associated with a potential risk of both arterial and venous blood clots or are a consequence of some other previous clinical event remains controversial.

The lupus anticoagulants, anticardioliopin antibodies and anti beta 2 glycoprotein 1 antibodies are autoimmune antibodies against phospholipids or plasma proteins bound to anionic phospholipids and are a cause of a clinical paradox of thromboembolic disease called the antiphospholipid syndrome (APS).

Antiphospholipid antibodies are found among young, apparently healthy individuals at a prevalence of 1-5 % for both anticadioliopin antibodies and lupus anticoagulant. The presence of antiphospholipid antibodies increases with age and with co-existent chronic disease. The prevalence of antiphospholipid antibodies is considerably higher in patients with SLE.\textsuperscript{6}
Pathogenesis of thrombosis in APS:
The following mechanisms have been demonstrated in vitro:

- Binding to vascular endothelium.
- Inhibition of prostaglandin I release.
- Inhibition of fibrinolysis.
- Interference with the phospholipids-dependent protein C activation.
- Interference with the anticoagulant effect of activated protein C.

Recently, it has been shown that phospholipids may not be the target antigen for many of these antibodies, but a protein on which epitops become exposed only when the protein itself becomes bound to negatively charged antibodies. Beta 2 glycoprotein I is such a phospholipids binding protein that also has anticoagulant properties. 7 Several theories exist in an attempt to explain the cellular and molecular mechanisms by which antiphospholipid antibodies promote thrombosis; activated endothelial cells, oxidant-mediated injury to the vascular endothelium, direct interference in the phospholipids mediated regulation of coagulation and a mechanism similar to the paradoxical thrombosis of heparin-induced thrombocytopenia. The common pathology, however, is a characteristic thrombotic microangiopathy with minimal vascular or perivascular inflammation. This change in the architecture of both small and
large arteries is the nidus for in situ thrombosis from which emboli can originate.

There are two types of APS; primary and secondary. While people with primary APS have no other associated condition, the secondary form is associated with another immune disorder, such as SLE, viral infections or induced by medication e.g. chlorpromazine.

In different studies, 8-65 per cent of people with lupus have the lupus anticoagulant, and 25-61 per cent have anticardiolipin antibodies, these antibodies were first discovered in people who have lupus, but it is not necessary to have lupus to have these antibodies.  

**Prevalence of antiphospholipid antibodies:**

Although antiphospholipid antibodies are associated with a propensity for thrombosis and with various autoimmune disorders, they can sometimes be found in normal asymptomatic individuals. Normal individuals occasionally have elevated levels of either IgG or IgM acl. In one study, the prevalence was five percent on a first test but only two percent on retesting. Increased levels of IgG or IgM acl have been observed in 12 to 52 percent of the elderly.  

Recently the antiphospholipid in stroke study group demonstrated an extremely high prevalence among subjects older than 65 years. The significance of this finding is still unclear. It had been suggested that acL in the middle-aged and elderly partly belong to a class of natural autoantibodies without pathogenic complications. Conceivably, they could also be associated with clinically unexpected ischemic brain damage some state of hypercoagulability. Focal changes of the brain
parenchyma are a common MRI observation in normal subjects, and their frequency is strongly age related. Only recently has the presence of such abnormalities been linked to slowing of mental processing, which may be another accompaniment of aging. It might therefore be speculated that an association exists between the presence of acL, silent cerebral damage, and cognitive impairment in older persons.

**Associated disorders:**

Antiphospholipid antibodies have been noted in increased frequency in patients with SLE. Approximately 31% of patients have LA, 23-47% have acl, & 20% have antibodies glycoprotein 1. on the other hand roughly 50% of patients with LA have SLE.APA also occur with increase frequency (5-10%), in women with greater than three spontaneous recurrent abortions.

**Autoimmune and rheumatic diseases:**

- Haemolytic anaemia.
- Idiopathic thrombocytopenic purpura.
- Juvenile arthritis.
- Rheumatoid arthritis (7-50%).
- Psoriatic arthritis (28%).
- Scleroderma (25%).
- Sjogren syndrome (25-42%).
- Behcet syndrome (7-20%).
- Mixed connective tissue disease (22%).
- Polymyositis and dermatomyositis.
- Polymyalgia rhumatica (20%).
- Osteoarthritis (less than 14%).
• Occasionally in gout and in multiple sclerosis.
• Chronic discoid lupus.
• Esinophilia myalgia and toxic oil syndrome.
• Raynaud's phenomenon.

**Infections and drugs:**

These are usually IgM acL antibodies but not anti beta-2 glycoprotein 1 antibodies, they may occasionally result in thrombotic events.

These infections include hepatitis A and C virus; pneumocystis crani; infectious mononucleosis rubella; syphilis; leptospirosis; and kalazar. Among the drugs that are implicated are phenothiazines; phenytoin; hydralazine; procainamide; quinidine; quinine; dilantin; alpha interferon; amoxicillin and propranolol.\(^{11}\)

**Genetic predisposition:**

Relatives of patients with APS are more likely to have these antibodies. One report; evaluated 83 relatives of 23 patients; 29 (33 percent) had acl. In addition; there is a strong association of APL with HLA-DR in canadaiian; German; Italian; and Mexican patients and with HLA-DQ7 in American and Spanish patients\(^{12}\).

APS may be associated with genetic or acquired activated protein C resistance. Some studies suggest that activated protein C resistance can act synergistically with antiphospholipid antibodies to be prothrombotic in children with SLE.\(^{12}\)


**Clinical features:**

The APS can lead to a variety of clinical manifestations; including venous and arterial thrombosis; recurrent spontaneous miscarriages; and thrombocytopenia. Infrequently, primary antiphospholipid syndrome can result in multiorgan failure because of multiple vessel occlusion.

**Thrombosis:**

Thrombosis can occur in virtually any vascular bed in the body. Venous thrombosis are more common than arterial thrombosis; commonly affecting the calf causing deep venous thrombosis which is the presenting feature in 32 % of people diagnosed with APS and antiphospholipid antibodies can be detected in 10 % of all patients with venous thrombosis.\(^{13}\)

Renal, hepatic, axillary, subclavian and retinal veins or the vena cava may be involved. The most common site of arterial thrombosis is the cerebral circulation, but the coronary, renal, and mesenteric artery and arterial bypass graft occlusions have also been noted.

Recurrent events are common in APS. Initial arterial thrombosis tend to be followed by an arterial events and initial venous thrombosis by venous events. The factors that determine the predilection for the venous or arterial circulation are not known.\(^{14}\)

A prospective study of 360 patients with APS noted that 34 experienced a recurrent thrombotic event during a median follow up period of approximately four years. Thrombotic events were responsible for five of eight deaths. Another prospective study of 81 patients with apl found that 31 % had recurrent ischaemic strokes; patients with high titers of acl had a shorter time to recurrence. A second prospective study of 412 patients presenting with a first
episode of venous thromboembolism found that the risk of recurrence was twice as high among patients with acl compared to those without such antibodies.¹⁵

**Cerebrovascular:**

Single or multiple transient ischaemic attacks and or strokes occur and often recur in the APS, resulting in a variety of temporary or permanent neurologic deficits. These include transverse myelopathy; epilepsy; chorea; dementia; Gillian bare syndrome, transient global amnesia, seizures, motor neuron disease, depression, amaurosis fugax and pseudotumor cerebri. Some of these features results from arterial thrombi; while others are caused by cerebral emboli due to libmansacks endocarditis.

Central nervous system involvement in APS is strongly associated with small high-density lesions on MRI suggestive of a vasculopathy; they are difficult to be distinguished from multiple sclerosis which may also have apl antibodies. The APS should be particularly suspected when stroke occurs in a young patient without significant risk factors. In one report antiphospholipid antibodies were found in 25% of patients under the age of 45 with a cerebrovascular accidents of unclear aetiology.¹⁶

The relative risk of stroke associated with the presence of antiphospholipid was assessed using clinical data and frozen sera from 2000 subjects, there was a modestly increased risk of stroke associated with the presence of antibodies of antibodies of the IgG type that were dependent upon the presence of beta–2 glycoprotein 1. The presence of antibodies that bind beta–2 glycoprotein 1 in the absence of phospholipids, or those that
bound to phospholipid in the absence of beta-2 glycoprotein 1 were not associated with an increased risk of cerebrovascular events. 17

Neurologic events associated with antiphospholipid antibodies (APAS) include transient ischaemic attacks; stroke and vascular dementia in individuals much younger than is typically observed with these disorders.

A study conducted in Detroit; USA evaluated 27 non-elderly adults with APAS but without concurrent disease process or history of neurologic events and 27 age and education-matched controls. It indicated group differences in executive functioning; verbal learning and memory; and visuospatial ability. In contrast; gross attentional processes and fine motor skills appeared unaffected by the syndrome. Moreover, the frequency of impaired neuropsychologic performance was greater among individuals with APAS than among controls. The presence of cognitive deficits in otherwise asymptomatic patients with APAS indicates a preclinical phase of neurologic involvement and may prove to be the most sensitive markers of the syndrome.18

**Ocular findings:**

Retinal findings in APAS include venous tortuosity; cotton-wool spots; retinal vein occlusions; and retinal artery occlusions. Other fundal findings may include optic nerve edema, vitreous haemorrhage, choroidal vascular occlusions, conjunctival telengectasia, episcleritis, and keratitis have also been reported. Visual acuity may
be reduced. These symptoms are caused by thrombotic tendency of patients with APAS.  

Stroke is often the initial manifestation and is the best described. Echocardiographic evidence of mitral valvular lesions, aortic valvular abnormalities have been implicated as sources for cerebrovascular events. However, many patients show no evidence of cardiac pathology following cerebrovascular events, suggesting the role of in situ thrombosis as a causative mechanism.

In the antiphospholipid antibodies in stroke study group (APASS), angiography was done in 49 of 128 patients, half of those studied had intracranial lesions, middle CA occlusion were the most common arterial ischaemic events were responsible for most strokes with haemorrhage being distinctly uncommon, in this patient, a haemorrhagic infarction was most likely due to necrosis after an intravascular thrombus.

A study conducted in San Carlo, Milano, Italy, assessing the prevalence of APA in young patients with cerebral ischemia of undetermined cause; it studied 77 patients, 34 were positive for apL to 1 or more phospholipids. A significant number of patients had apL to anionic phospholipids. A small number of cases showed apL with specificity to neutral phospholipids, in 17 cases positivity for only 1 phospholipid was demonstrated, in contrast, the remaining 17 cases showed positivity for multiple phospholipids and more than 1 isotype was demonstrated. Fifty-nine patients were acL negative, of these subjects, 18 showed positivity for apL to epitopes other than cardiolipin.
Antiphospholipid–related clinical events were also present in aCL negative aPL positive patients, two patients who had multiple strokes both had an isolated anti-pi antibody. It concluded that, no statistically significant differences in age, sex, diagnosis (stroke or TIA), or cerebrovascular risk factors were observed between patients who had aPL to a single phospholipids and 1 or 2 isotypes and those with aPL to multiple phospholipids and multiple isotypes.  

A study done in Austria studied one-hundered eighty subjects, 77.3 % had negative, 15 % low positive aCL positive and 7.7 % moderately high positive aCL titers. aCL positive patients were slightly older and had a somewhat higher rate of cardiac disease than aCL negative subjects. Migraine without aura was reported by (8.3 % ) with negative , (11.4 % ) with low positive, and (11.1 % ) with moderately high positive titers. The aCL status of subjects had no influence on the MRI results, overall, silent ischaemic brain damage defined as either infarcts, lacunes or WMH was noted in 51 % with negative , 51.4 % with low positive and 66.7 % with moderately high positive titers . In the neuropsychological test, aCL positive study participants obtained worse scores than their aCL negative counterparts on almost all tests.

Preliminary data also suggest that antibodies directed against phosphatidylserine may react directly with central nervous system tissue and may be more specifically associated with ischaemic stroke.
Immunological factors may contribute not only to thrombosis but also to atherosclerosis, mediated by APsL, patients with APS have increased levels of antibodies to oxidized LDL, associated with progression of atherosclerosis and risk of thrombo-occlusive event. Antibody responses to phospholipids, oxidized LDL, beta-2 glycoprotein 1, prothrombin, and endothelial cells partially overlap and may reflect a broadening spectrum of antibody associated atherosclerotic disease. 23

Recent reports demonstrating that the presence of antibodies against phospholipids, oxidized LDL, and prothrombin is a predictor of myocardial infarction support an important role of APL in the pathogenesis of thrombo-occlusive events. It is possible that the presence of certain APL alters the threshold for thrombosis and thus creates a permissive thrombotic environment.

In a study reported in stroke, high prevalence of antiphosphatidylinositol antibodies was identified in young population of cryptogenic stroke or transient ischaemic attacks patients, high prevalence of antibodies directed to 1 or more of these phospholipids was found in this population. 23

In one report, APLAs were found in 25 percent of patients under the age of 45 with Cerebrovascular accident of unclear aetiology. A similar prevalence of approximately 20 percent positivity for APL was noted in a second report of stroke victims under age 50. 23

A study conducted in Texas studied strokes in young showed that, among the 160 stroke patients, 63 had at least 1 possible cause; large–artery atherosclerosis, 16; cardioembolism, 18; lacune and other causes. Fifty were indeterminate. Other causes
of stroke include haematologic disorders and nonatherosclerotic vasculopathy (e.g. vasculitis and dissection), migraine, oral contraceptive use, drug abuse, and stroke associated with the postpartum state.\textsuperscript{24}

Anticardiolipin IgG antibody was the isotype most strongly associated with stroke. acL of any type was seen in 43 cases and 62 controls, LA in 29 cases and 38 controls, and either acL or LA in 61 cases and 86 controls.

There was no evidence for effect modification by age, current cigarette smoking, hypertension, diabetes, angina, ethnicity, body mass index, and HDL levels. After adjustment for these factors, the relative odd ratio of stroke for women with acL immunoreactivity of any isotype or a LA was 1.87.\textsuperscript{25}

To test the prevalence of antiphosphatiolylinositol antibodies in young patients with cerebral ischaemia of undetermined cause, a study was performed in san carlo, italy. Seventy–seven non–SLE for patients had apl to one or more of the following antigens, 23.4% to cl, 18.2% to ps, 15.6% to PG, 14.3% to PA, and 28.6% to pi. Fifty nine patients were acl negative of these subjects 23.4% showed apl to noncardiolipin epitopes. PI was the specificity with highest prevalence in all 6 patients anti – PI antibody were the only detectable apl. The binding of apl to the different antigens was B2-GPI dependent.\textsuperscript{26}

Data demonstrate a high prevalence of apl in young adults with cerebral ischaemia of undetermined cause PI was the specificity with highest prevalence, suggesting that anti PI antibodies may be an immunological marker in young patients with Cerebrovascular disease.\textsuperscript{26}
Lupus anticoagulant and antiphospholipid antibodies are associated with thromboembolic phenomena in individuals both with and without systemic lupus.

A 32-year-old woman (the index case) with lupus anticoagulant, multiple cerebrovascular events, and a family history of premature stroke raised the possibility of a familial diathesis. Histories, interviews, examinations, and blood tests were obtained for 23 members of four generations of her family. Four individuals had suffered strokes three more had suffered neurologic symptoms, and five asymptomatic individuals had antiphospholipid activity in their blood. In addition, a cousin of the index case was found to have systemic lupus and antiphospholipid activity. Elevated concentrations of vonwillebrand factor antigen were found associated with some positive LA assays, the highest concentrations in the two individuals with stroke. The characteristic presentation of the index case and her good response to treatment suggest that further studies of families in whom antiphospholipid antibodies may present a risk factor for stroke is worthwhile.²⁷

A study conducted in Barcelona, Spain, 146 patients with cerebral ischaemia were studied, vascular risk factors for stroke with clinical and laboratory findings, particularly antiphospholipid antibodies were compared. Ten patients were positive for at least one antiphospholipid antibody, one patient had systemic lupus, one had rheumatoid arthritis and the remaining eight fulfilled the criteria for the diagnosis of primary antiphospholipid syndrome. These patients were predominantly males, not necessarily young, and 50% of them did not have any other vascular risk factor, there were no significant clinical or paraclinical differences between these patients and those without antiphospholipid antibodies.
Outcome in the 10 patients was good, and platelets antiaggregating drugs proved to be useful in preventing further cerebrovascular ischaemic events.28

To test the relation between thrombophilia and ischaemic stroke, a study was performed in Saint Antoine hospital, France, forty patients were tested, six cases of thrombophilia were found; 1 protein C deficiency, 1 protein S deficiency, and 4 activated protein C resistance. With heterozygous factor V laiden mutation only 1 case was found in the group 1 patients with idiopathic ischaemic stroke in the other 5 there was another cause or risk factor. three patients had increased anticardiolipin with SLE and 2 with primary antiphospholipid syndrome; 2 of these 3 patients also had factor V leiden mutation.

Congenital or acquired causes of thrombophilia are almost invariably associated with other predisposing factors, so these abnormalities should be looked for in patients with cerebral ischaemia, whether a cause is found or not, and their presence should not deter the search for other potential causes. The detection of such abnormalities has major practical consequences on the long–term management of patients to prevent further thrombotic episodes.29

55 young patients with ischaemic stroke were studied in Italy for LA and acl antibodies, ten patients, all with stroke had antiphospholipid antibodies. Antiphospholipid antibodies were significantly more frequent in women than in men, two patients had a new diagnosis of SLE, non of patients with antiphospholipid Abs had extracranial lesions on angiography. Patients with apl antibodies had significantly more prior cerebral events and by survival analysis,
higher probability of cerebral ischaemic or systemic thrombotic events.\textsuperscript{28}

A study was conducted in San carlo, where Doppler US was done in 32 patients, an ulcerated, non-stenosing atherosclerotic plaque of internal carotid artery was observed in three patients, one at the intracranial level, and two at the extracranial level, a stenosing (more than 50\% ) lesion of internal carotid artery at the extracranial level was found in one patient. Stenosis of more than 70\% are linearly associated with increased risk of distal brain infarct. Carotid endarterectomy is effective in reducing the risk of subsequent ipsilateral stroke.\textsuperscript{27} In fact an IgG –apl titer of higher than 10 GPL units has been shown to be an independent risk factor for the first stroke by the antiphospholipid antibodies in stroke study group (APAAS) Iran. It occurs mainly at a younger age than the typical atherothrombotic cerebrovascular events with women being affected slightly more than men. The median age of our cases was 30 years with 64\% within the age range of 29 – 37 years, the female to male ratio was 2: 1. Paresis was the most common presentation during both the acute and established stages. Secondly cerebellar signs which rarely reported in the literature. sensory disturbance (numbness and paresthesia) was the third most common presentation. INO, optic neuritis were found in two patients, motor dysphasia in three patients and disturbed level of consciousness in only one patient.\textsuperscript{30}

Epilepsy may occur in APS due to non-thromboembolic phenomena, apls have been demonstrated to bind directly to cat brain sera containing apl from SLE patients with seizure, has been shown to reduce a GABA receptors mediated chloride in snail neurons. Four of the patients had epilepsy,(grand mal seizures and myoclonic jerks in
one), motor dysphasia was present in three patients, and was the sole clinical manifestation in one.\textsuperscript{30}

The initial report linking antiphospholipid antibodies to seizures showed the presence of LA (but not acl) in patients with late onset seizures, subsequent reports have shown that LA has a stronger link to thrombotic events than do acl.

The incidence of stroke in young adults is estimated to be 62 per 100,000 with one study showing that 27% are idiopathic strokes and 31% are embolic with acl a possible cause for both. One study has shown that cerebrovascular events account for 14% of all late-onset seizures. Progressive cognitive impairment and mood changes have all been reported.\textsuperscript{31}

**Venous thrombosis:**

Antiphospholipid antibodies can be detected in approximately 10% of all patients with venous thrombosis. The incidence of venous thrombosis may correlate with the level of anticardiolipin antibodies. One study found that venous thrombosis occurred in 44% of patients with high titers of acl. Thrombosis occurred in 42% of those with antiphospholipid antibodies, 51% with lupus anticoagulants, 31% with anticardiolipin antibodies.\textsuperscript{32}

**Pulmonary disease:**

Multiple pulmonary complications can occur in patients with SLE and the APS including

- Pulmonary embolism and infarction, which occur approximately in one-third of patients with recurrent DVT.
- Thromboembolic and non-thromboembolic pulmonary hypertension, possibly leading to right-sided heart failure.
- Pulmonary arterial thrombosis.
- Pulmonary microthrombosis.
- Adult respiratory distress syndrome.
- Intra alveolar pulmonary haemorrhage.
- Fibrosing alveolitis.
- A postpartum syndrome, characterized by spiking fever, pleuritic chest pain, dyspnoea and pleural effusion and patchy infiltrates on chest radiographs.

**Cardiovascular disease:**

Patients with APL commonly have cardiac disease, including valvular thickening and the development of vegetations. The mitral and aortic valves are most commonly affected, possibly leading to valvular insufficiency. Antiphospholipid antibodies have been incriminated in intracardiac thrombi, pericardial effusion, cardiomyopathy and peripheral vascular disease.

In one report, 20% of patients with nonautoimmune ischaemic heart disease had anticardiolipin antibodies of uncertain significance. In another study of 37 patients with unstable angina, 30% had antibodies to beta-2 glycoprotein-1. A study of nearly 2000 subjects strongly suggests a pathogenic role for beta-2 GPI dependent IgG type antiphospholipid antibodies in some patients with ischaemic heart disease. Up to 20% of younger people who have a heart attack have antiphospholipid antibodies. 33

A study conducted in San Carlo, where echocardiography was done in 61 patients and did not show any possible additional source of cardiac embolization such as atrial or appendage thrombi or valvular vegetation.
A study in stroke published by the American heart association stated that, cerebral infarction in patients with atrial fibrillation is presumed to result from embolization of intracardiac thrombi, which most commonly form in the left atrial appendage. Autopsy data indicate that stroke is a possibility throughout the life of persons with a history of atrial fibrillation.\textsuperscript{34}

**Haematologic:**

Thrombocytopenia and thrombotic thrombocytopenic purpura have both been reported in APS. A review of 13 studies of 869 patients with SLE found that thrombocytopenia was more common in those with antiphospholipid antibodies (37\%), the lupus anticoagulant (55\%), and anticardiolipin antibodies (29\%) than in those without these antibodies. The risk of developing the APS is increased in patients with ITP who have antiphospholipid antibodies or lupus anticoagulant activity. One prospective study of 82 patients presenting with ITP noted that only one–quarter to one-third of those with such antibodies remained free of thrombotic events during the subsequent five years compared to 96 to 98 percent in those who did not have these antibodies. Patients with ITP and persistent presence of a lupus anticoagulant appeared to be at highest risk, 45 percent of such patients developed APS during five years of follow–up.

**Bleeding episodes:**

The possible presence of prothrombin antibodies should be suspect when a patient with known antiphospholipid antibodies develops bleeding manifestations rather than thrombosis.\textsuperscript{35}

**Renal disease:**

The incidence of renal disease in the APS is unclear.

- Thrombi in the glomerulus and small arteries.
- Arterial or venous thrombosis in the intrarenal vessels or in large artery branches.
- An increased incidence of graft thrombosis in hemodialyzed patients.

**Gastrointestinal:**

Patients with APS antibodies may have ischaemia involving the oesophagus, stomach, duodenum, jejunoileum or colon resulting in gastrointestinal bleeding, abdominal pain, oesophageal necrosis with perforation, or giant gastric or a typical duodenal ulceration.

**Cutaneous:**

AP antibodies have been associated with many cutaneous abnormalities including livedo reticularis, livedo vasculitis, cutaneous necrosis and infarctions, thrombophlebitis, gangrene of digits, skin ulcerations, subungual splinter haemorrhages, and Degos disease (malignant atrophic papulosis).  

**APS and pregnancy:**

APA have been linked to poor reproductive performance e.g infertility, recurrent miscarriage, placental insufficiency, intrauterine growth retardation and early separation of the placenta and HELLP syndrome. An evidence has confirmed that patients who experience IVF failure, often have elevated APAs, also women with pelvic endometriosis or unexplained infertility tend to have elevated APAs.

It has been well established that APAs bind to human trophoblast, phosphatidylethanolamine and phosphatidylserine are two important phospholipids that serve as adhesion molecules, they bind to trophoblast, inhibiting its invasive potential and interfering with cytotrophoblast to syncitiotrophoblast differentiation. This phenomenon
has the effect of seriously compromising the respiratory, metabolic, and endocrine functions of cyntiotrophoblast. A 21 percent of women presenting with three or more pregnancy losses. 9 pregnant ladies with antiphospholipid antibodies are more prone to develop strokes or pulmonary embolism.

Risks for several complications are increased in women with apl and include; strokes, blood clots and pregnancy – induced hypertension (occurring in as many as 50% of women with apl).³⁶

A study published in up to date, stated that some patients with SLE have a false positive test for syphilis. Such patients have been noted to have fewer successful pregnancies, an increased number of thrombotic events, livedo reticularis and migraine.

It occurs because the syphilis antigen used in the test is embedded in cardiolipin so a reaction against this molecule will be incorrectly interpreted as being directed against the treponemal antigen. the syphilis test should not be used to screen for APS since it has a low sensitivity and specificity.³⁸

**Autoantibodies:**

Antiphospholipid antibodies are a heterogeneous group of autoantibodies of IgG , IgM and IgA classes. These antibodies can be directed to anionic phospholipids, phospholipids protein complexes and cofactors in the absence of phospholipids. Three different autoantibodies to properly diagnose APS or to assess the risk for thrombosis or recurrent fetal loss. These include anti-cardiolipin (acl), anti-Beta₂ Glycoprotein I (B₂GPI), and antiphosphatidylserine (aps).

Anticardiolipin antibodies (acl) are a heterogeneous group of antibodies that react with negatively charged phospholipids. They are found
also in patients with syphilis and other infectious diseases who have no evidence of coagulation disorders.

Beta<sub>2</sub> Glycoprotein I (B<sub>2</sub>GPI) was identified as a necessary cofactor for antiphospholipid antibody binding in immunoassays.

Phosphatidylserine is a more physiologically relevant phospholipid due to its presence in cell membranes of endothelial cells and platelets and its role in the coagulation cascade.

Lupus anticoagulant test should be done first before embarking with these antibodies test. APL may play a role in atherosclerosis. Antibodies to prothrombin are increased risk of myocardial infarction. APL (particularly B<sub>2</sub>GPI and oxidized LDL) but these antibodies do not appear to interfere with coagulation in the sub endothelial space, oxidized and phagocytized by macrophages forming fatty streak, the first step in atherosclerosis. Antibodies to oxidized LDL increased oxidation of LDL, a process that increases macrophage phagocyte formation. 39

**Diagnosis:** -

Definite APS is considered present if at least one of the following clinical criteria and at least one of the following laboratory criteria are satisfied.

**Clinical:**

Either one or more episodes of venous, arterial, or small vessel thrombosis, and/or morbidity with pregnancy.

**Laboratory:**

The presence of either IgG and/or IgM anticardiolipin antibody, and/or lupus anticoagulant activity, the antibodies and/or activity should be found on two or more occasions, at least six weeks apart.
In one study, the prevalence of IgG acl was 6.5 percent on a first test in 522 randomly selected normal blood donors; 4% remained positive nine months later. In another report patients with a first venous thromboembolic event, the incidence of acl was similar to the control population. In comparison, lupus anticoagulant activity was much more common in the patients with venous thromboembolism.

- Lupus anticoagulant activity, which is another wise unexplained prolongation of the activated partial thromboplastin time that is not reversed when the patient’s plasma is diluted 1:1 with normal platelet. Free plasma (this is a procedure that will reverse the clotting abnormality associated with factor deficiencies).
- A false positive serology for syphilis.
- The presence of anticardiolipin antibodies.
- The presence of anti B2 – glycoprotein 1 antibody.

Catastrophic antiphospholipid syndrome: -

It is defined and documented in 1992, is a potentially fatal complication seen in patients with antiphospholipid antibody. It may arise de novo in patients not previously suspected as having an antiphospholipid syndrome, or it may complicate the course of patients currently treated for this syndrome. Precipitating or trigger factors have been identified in 55% of patients; the most common of these factors is infection.

The precipitating factors should be avoided or energetically treated in patients with the antiphospholipid syndrome. in order to prevent this catastrophic course.

The clinical manifestations are those of multi organ failure, and unusual vessels or organs can be involved.
Treatment of the condition with emphasis on effective anticoagulation, intra venous immunoglobulins or plasma exchange, should be aggressive to achieve a satisfactory outcome. Despite all available therapeutics options at this time, the mortality is still high (greater than 50%).  

**Treatment:**

At the moment, antiphospholipid syndrome cannot be cured but the effects can be controlled. Commonly used drugs are antiplatelets and anticoagulants.

People with antiphospholipid antibodies but without a history of clotting:

- Are recommended low-dose Aspirin (75-100mg) daily.
- Some studies suggest that some people go on to develop clots despite taking Aspirin.

- **People with APS who have a history of clotting:** are at risk of recurrence, so they are given long term warfarin therapy with regular INR check.

- **Women with recurrent miscarriages, but without a history of clotting:** the traditional treatment is low dose Aspirin. Heparin is increasingly being used especially for those who have had previous miscarriages in mid to late pregnancy, or other pregnancy complications such as pre-eclampsia.

- **Studies showed that intermediate – to – high intensity warfarin therapy (INR between 2.6 and 3.0) reduced the incidence of thrombotic events by approximately 75 percent, where as low-intensity warfarin or aspirin seemed to be without benefit.**
The advantages of anticoagulation after a first thrombotic events must be weighed against the risk of bleeding with intensive warfarin therapy. In studies, the incidence of bleeding episodes was much lower than the absolute benefit of thrombosis prevention. In addition many patients have major thrombotic recurrences when anticoagulation is stopped.

Some studies have suggested that recurrent venous thromboembolism is prevented by maintaining the INR under three, or even under two.

Some experts feels that anticoagulation can be discontinued if the APL become negative or titers significantly decrease (40%) upon retesting.42

**Prophylaxis in patients without thrombi:**

The incidence of thrombotic episodes in asymptomatic patients has been reported to range from 10 percent to as high as 75 percent when antibody titers are very high. One prospective three year study of 90 patients with SLE found 34 who had at least one positive test for acl; however, the presence of acl did not predict an APS thromboembolic event. Thus, prophylactic therapy for asymptomatic individuals with anticardiolipin antibodies is not generally recommended. However, women should be advised to avoid oral contraceptives.43

**Management of antiphospholipid syndrome during pregnancy:**

Because of the higher risks for stroke, pregnancy loss, and other complications with apl, mothers need close monitoring of the disease. If the women has antiphospholipid antibodies and is pregnant for the first time, or has had normal pregnancies in the past, no treatment may be advised. However, if she has had miscarriages in the past, she should be given aspirine, prednislone, and/or sub cutaneous heparine.44
OBJECTIVES

1) To determine the incidence of APLAs among adults Sudanese IBD patients.

2) To find out any special features characteristic to this special group of patients.
MATERIAL AND METHODS

Patients and materials:

This is a cross-sectional, case-controlled study, which has been conducted in Elshaab and Khartoum teaching hospitals during the period from July 2003 till January 2005.

Inclusion criteria.

Patients were selected randomly, after taking their verbal consent from those who fulfilled the inclusion criteria which were; 1) Adults, 2) Documented brain infarcts either by CT or MRI.

There were two control groups, the first group were patients within the same age group who have other conditions other than vascular disorders (such as infectious diseases). The second group were adult individuals who were completely healthy.

Sample size:

89 cases of ischaemic brain diseases were selected randomly. 35 patients who suffered from conditions like infections or connective tissue disorders and another 36 adults who were completely healthy were included in the study.

Data collection:

Data were collected using a simple direct questionnaire filled by the investigator himself (app. 1).

The questionnaire included five main divisions; patients identification, presenting complaints, relevant past history, full physical examination then the last section which includes investigations requested such as blood counts, ECG, Doppler U/S of the carotids, lipid profile and serology.
The lipid profile and antiphospholipid antibodies testing were performed by a recognized chemical pathology laboratory, done by an accredited pathologist.

**Technical data:**

- Sample material: serum.
- Required sample size: 10 microliter of sample to be diluted 1:100 with sample buffer.
- Total incubation time: 60 minutes at room temperature (20-28°C).
- Sensitivity: IgG and IgM: 0.5 u/ml.
- Specificity: the antiphospholipid screen test kit is specific for autoantibodies directed against phospholipids or the complex of negatively charged phospholipids and beta-2 glycoprotein I.
  
  No cross-reactivity was observed to anti-DNA antibodies and those types of antibodies occurring in syphilis.

**Principles of the procedure:**

Antiphospholipid screen (IgG/IgM) is an indirect solid phase enzyme immunometric assay (ELISA). It is designed for the quantitative measurement of IgG/IgM class autoantibodies directed against phospholipids. The microplate is coated with highly purified negatively charged phospholipids: cardiolipin phosphatidyl serine, phosphatidyl instol, and phosphatidic acid. Antiphospholipid autoantibodies require beta 2 glycoprotein I as a co-factor for binding. The microplate is therefore saturated with human beta 2 glycoprotein I.
The binding of present autoantibodies, formation of the sandwich complexes and enzymatic colour reaction take place during three different reaction phases.

**Normal values:**

Antiphospholipid antibodies

<table>
<thead>
<tr>
<th></th>
<th>IgG (GPL u/ml)</th>
<th>IgM (MPL u/ml)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Normal</td>
<td>less than 10</td>
<td>less than 10</td>
</tr>
<tr>
<td>Elevated</td>
<td>more than or equal to 10</td>
<td>more than or equal to 10</td>
</tr>
</tbody>
</table>

The serum was considered APLAS +ve if either IgG or IgM or both antibodies were detected in high concentration.

**Analysis:**

After that data were entered into a computer to be analyzed using SPSS system.

Results were obtained, represented statically and then discussed.

Lastly recommendations are derived in view of improving the management and subsequently the outcome of patients suffering from ischaemic brain diseases.
RESULTS

This study included 89 patients with ischemic brain disease (41 males, 48 females), 35 diseased control and 36 healthy individuals. The groups were matched for sex. [Fig.1]

The study showed that while 34.8% of patients suffering from ischemic brain disease (IBD) were found to have positive APLA, 31.4% of the diseased control group and 16.7% of the healthy individuals were found to be positive for the test [Table 1]. The percentage of +ve APLAS is significantly higher in the IBD group, compared to the other two group (P= 0.05).

Out of 41 males with IBD, 12 were found +ve for APLAS (29%). This is compared to 19 APLAS +ve females out of 58 with IBD (40 %). On the other hand 36% of males and 23% of females in the diseased control group were positive. 23% of males & 12% of females of the healthy individuals were positive for the test as well. [Table 2]

The highest percentage (71%) of the positive APLA was found among the age group 20-29, the lowest (24%) in those between 40-49 in those with IBD. In the diseased control group, the highest percentage (67%) was in those aged (40-49) and the lowest (10%) was above 60 years. In the healthy control group the highest percentage (50%) was among those aged 50-59 and the lowest 0%, in those aged more than 60 years. This difference is statistically significant (p.0.01). [Table 3a, b & c]

At presentation, stroke patients who were APLA positive complained of, motor weakness (in 87%) headache (48%), seizures (35%), speech disturbance (29%), disturbed consciousness (13%) and vomiting
While patients who were APLA negative presented with motor weakness (93%), speech disturbance (53%), disturbed consciousness (33%), headache (28%), seizures (8.6%), vomiting (6.8%). [Fig. 2]

In patients with IBD who were APLA positive past history of diabetes mellitus was encountered in 23%, systemic hypertension in 26%, cardiac disorders in 9.7%, TIA in 6.5%, DVT in 13%, abortion in 23% migraine in 9.7%. [Fig. 3]

In APLA negative with IBD past history of diabetes was encountered in 16% of patients, hypertension in 28%, cardiac disorders in 10%, TIA in 8.6%, DVT in 2%, abortion in 5%, migraine in 3%. [Fig. 3]

History of diabetes mellitus was encountered in 3.8% of positive patients compared to 56.3% of the negative group. Hypertension in 33.3% of APLA positive patients and 66.7% of the negative group. [Fig. 3]

Cardiac disorders were demonstrated in 33.3% of APLA positive group compared to 66.7% of the negative patients. TIA preceded the stroke in 28.6% positive and 71.4% negative ones. DVT in 80% positive patients compared to 20% of the negative group. Abortion was found in 70% of the positive patients and 30% of the negative ones. Migraine was encountered in about 60% of APLA positive patients and in about 40% of the negative group. This was statistically not significant [P. 0.23]. [Fig. 3]

Full consciousness was found in 35.6% of APLA positive patients compared to 64.4% of the negative individuals, while 60.7% of APLA positive patients present with normal speech, 39.3% of the negative group had had normal speech as well, normal cranial nerve examination was found in about 3.2% of the positive and in 61.8% of the negative group. Normal power was detected in 33.8% of the positive and in 66.2% of the negative patients. This difference was statistically non significant [P. 0.08] [Fig.4].
Disturbed level of consciousness was found in 10 patients who were positive for the test compared to 20 who were negative for the test. Speech disturbance in 14 positive and 47 negative patients. CN affection in 18 positive patients & 37 of the negative group motor weakness in 7 who were positive and 11 who were negative for the test. This is statistically non significant [P= 0.4]. [Fig. 4]

Motor weakness of grade 0/5 was found in 24.0% of positive APLA compared to 23.6% of the negative ones. The highest percentage of the grades of motor weakness in APLA positive patients was found in power grade 2/5 and 3/5. This is statistically non significant [P= 0.43]. [Table 4]

Abnormal blood counts (increased ESR, decreased platelets) were found in about 61.3% of APLA positive patients compared to 41.4% of the negative group. Normal blood counts was observed in 58.6% of APLA negative patients compared to 38.7% of the positive group. This is statistically significant [P= 0.005] [Table 5].

Abnormal lipid profile was seen in 44.8 % of APLAS -ve , 12.9% of the positive patients . It was normal in 55.2 % of the -ve group and 87.1% of the +ve individuals . This difference is statistically non significant.( P= 3.6 ); [Table 6]

Echocardiography was done in eight cases, three of them had had MS, and were APLAS -ve. One had hypertension, one had had MS,AS,one had had MS,MR and all were -ve for the test. One had had IHD and was +ve for the test. This difference is statistically non significant ( p. 0.15 ) . [Table 7].

Doppler’s U/S of the carotids was performed in six patients, only four of them had had carotid arteries abnormalities but were –ve for the test , the remaining two patients had had carotid abnormalities associated with positive test. This difference is statistically significant ( p.0. 002 ) [Table 8].
VDRL was done in 14 patients, eight were APLAS positive and six were negative. The test was positive in five of the APLAS +ve and –ve in three of them. It was –ve in all the six patients who were APLAS –ve . this difference was statistically significant ( p. 0.02 ) [Table 9].

AntidsDNA was done in 18 patients, 12 were APLAS +ve and six were –ve it was found positive in only one APLAS +ve patient and –ve in all the remaining 17 patients. Statistically significant (P 0.03) [Table 10].

ANF was done in 24 patients, 14 were APLAS +ve and 10 were -ve . the test was found to be positive in four APLAS +ve patients, one APLAS -ve patient. And it was -ve in the remaining 19 patients . [Table 11]

PTT was done n 16 patients and it was found to be abnormal in five patients who were APLA negative, it was normal in seven patients with positive APLA and in two who were negative for the test .This is statistical non significant (P= 0.08) [Table 12].

89 of our patients with IBD were examined by CT scan. It showed a single cerebral infarct in 26 patients with APLA (86.7%)and multi infarct brain disease in 4(13.3%).In 58 patients with a negative APLA ,53 had single cerebral infarcts (91.4%) and 5 had multiple infarcts (8.6%) this difference was not significant (P=0.4). CT brain documented cerebral infarction in about 32.9%of APLA positive patients and showed multi infarct brain disease in about 32.9% of APLA positive group. This is statistically non significant (P= 0.4) [Table 13].

86.5% of patients with IBD stayed in hospital for more than two weeks. [Fig. 5]

Different regimens were provided to patients with IBD .Anti platelets alone were given in 55.1%, anti coagulants in 5.6% and anti platelets plus neuroprotecvies in 20.2%. [Fig. 6]
On reassessing patients with IBD, a month following their stroke, 41.9% of APLA positive patients were unable to walk compared to 58.1% who were negative for the test. 16.1 % of APLA positive patients were able to walk with support and 41.9% of them were able to walk unsupported. This is statistically non significant.(P= 0.1). [Table 14]

Follow up CT scan brain was done in 4 APLA positive patients and it was found to be normal in only one patient. [Fig. 7]

Table [15] demonstrated the co relation between different system affection and APLA in the diseased control group. The highest percentage of positive APLAs was found in diseases affecting the respiratory system (38.5%), 36.4% GIT and 28.6% affecting other systems. This is statistically non significant (P= 0.6).
Table (1):

Showing percentage of APLAS among the study population

<table>
<thead>
<tr>
<th>Antiphospholipid antibodies</th>
<th>Group</th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>IBD</td>
<td>Diseased control</td>
<td>Healthy control</td>
</tr>
<tr>
<td>Normal -ve</td>
<td>58 (65.2%)</td>
<td>24 (68.6%)</td>
<td>30 (83.3%)</td>
</tr>
<tr>
<td>Abnormal +ve</td>
<td>31 (34.8%)</td>
<td>11 (31.4%)</td>
<td>6 (16.7%)</td>
</tr>
<tr>
<td>Total</td>
<td>89 (100%)</td>
<td>35 (100%)</td>
<td>36 (100%)</td>
</tr>
</tbody>
</table>
Table (2):

Showing sex distribution in the study population and APLA status

<table>
<thead>
<tr>
<th>Group</th>
<th>Antiphospholipid antibodies</th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>-ve</td>
<td>+ve</td>
</tr>
<tr>
<td><strong>IBD</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>* Male</td>
<td>29 (71%)</td>
<td>12 (29%)</td>
<td></td>
</tr>
<tr>
<td>* Female</td>
<td>29 (60%)</td>
<td>19 (40%)</td>
<td></td>
</tr>
<tr>
<td><strong>Disease control</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>* Male</td>
<td>14 (64%)</td>
<td>8 (36%)</td>
<td></td>
</tr>
<tr>
<td>* Female</td>
<td>10 (77%)</td>
<td>3 (23%)</td>
<td></td>
</tr>
<tr>
<td><strong>Healthy control</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>* Male</td>
<td>14 (77%)</td>
<td>4 (23%)</td>
<td></td>
</tr>
<tr>
<td>* Female</td>
<td>16 (88%)</td>
<td>2 (12%)</td>
<td></td>
</tr>
</tbody>
</table>
Table (3a):

Showing age distribution among patients presenting with IBD and APLA status

<table>
<thead>
<tr>
<th>IBD</th>
<th>Antiphospholipid antibodies</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>-ve</td>
</tr>
<tr>
<td>20 – 29</td>
<td>4 (29%)</td>
</tr>
<tr>
<td>30 – 39</td>
<td>5 (62%)</td>
</tr>
<tr>
<td>40 – 49</td>
<td>13 (76%)</td>
</tr>
<tr>
<td>50 – 59</td>
<td>11 (69%)</td>
</tr>
<tr>
<td>&gt;60</td>
<td>25 (74%)</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td><strong>58 (100%)</strong></td>
</tr>
</tbody>
</table>
Table (3b):

Showing age distribution among the disease control group and APLA status

<table>
<thead>
<tr>
<th>Disease control</th>
<th>Antiphospholipid antibodies</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>-ve</td>
</tr>
<tr>
<td>20 – 29</td>
<td>5 (63%)</td>
</tr>
<tr>
<td>30 – 39</td>
<td>5 (71%)</td>
</tr>
<tr>
<td>40 – 49</td>
<td>1 (33%)</td>
</tr>
<tr>
<td>50 – 59</td>
<td>4 (57%)</td>
</tr>
<tr>
<td>&gt;60</td>
<td>9 (90%)</td>
</tr>
<tr>
<td>Total</td>
<td>24 (100%)</td>
</tr>
</tbody>
</table>
Table (3c):

Showing age distribution among healthy control and APLA status

<table>
<thead>
<tr>
<th>Healthy control</th>
<th>Antiphospholipid antibodies</th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>-ve</td>
<td>+ve</td>
<td></td>
</tr>
<tr>
<td>20 – 29</td>
<td>14 (87%)</td>
<td>2 (13%)</td>
<td></td>
</tr>
<tr>
<td>30 – 39</td>
<td>12 (86%)</td>
<td>2 (14%)</td>
<td></td>
</tr>
<tr>
<td>40 – 49</td>
<td>2 (67%)</td>
<td>1 (33%)</td>
<td></td>
</tr>
<tr>
<td>50 – 59</td>
<td>1 (50%)</td>
<td>1 (50%)</td>
<td></td>
</tr>
<tr>
<td>&gt;60</td>
<td>1 (50%)</td>
<td>0</td>
<td></td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td><strong>30 (100%)</strong></td>
<td><strong>6 (100%)</strong></td>
<td></td>
</tr>
</tbody>
</table>
Table (4):

Showing the grades of motor weakness among patients with IBD and anti PLA status

<table>
<thead>
<tr>
<th>The grades of motor weakness</th>
<th>Antiphospholipid antibodies</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>-ve</td>
</tr>
<tr>
<td>0/5</td>
<td>13 (23.6%)</td>
</tr>
<tr>
<td>1/5</td>
<td>1 (1.8%)</td>
</tr>
<tr>
<td>2/5</td>
<td>10 (18.2%)</td>
</tr>
<tr>
<td>3/5</td>
<td>27 (49.1%)</td>
</tr>
<tr>
<td>4/5</td>
<td>3 (5.5%)</td>
</tr>
<tr>
<td>5/5</td>
<td>1 (1.8%)</td>
</tr>
<tr>
<td>Total</td>
<td>55 (100%)</td>
</tr>
</tbody>
</table>
Table (5):

Showing FBC distribution among patients with IBD and APLAS status

<table>
<thead>
<tr>
<th>FBC</th>
<th>Antiphospholipid antibodies</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Normal -ve</td>
</tr>
<tr>
<td>Normal</td>
<td>34 (58.6%)</td>
</tr>
<tr>
<td>Abnormal</td>
<td>24 (41.4%)</td>
</tr>
<tr>
<td>Total</td>
<td>58 (100%)</td>
</tr>
</tbody>
</table>
Table (6):

Showing lipid profile distribution among patients presenting with IBD and APLAS status

<table>
<thead>
<tr>
<th>Lipid profile</th>
<th>Antiphospholipid antibodies</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Normal -ve</td>
</tr>
<tr>
<td>Normal</td>
<td>32 (55.2%)</td>
</tr>
<tr>
<td>Abnormal</td>
<td>26 (44.8%)</td>
</tr>
<tr>
<td>Total</td>
<td>58 (100%)</td>
</tr>
</tbody>
</table>
Table (7):

Showing Echocardiographic findings in patients with IBD and APLAS status

<table>
<thead>
<tr>
<th>Echocardiographic Findings</th>
<th>Antiphospholipid antibodies</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Normal -ve</td>
</tr>
<tr>
<td>MS</td>
<td>3 (50.0%)</td>
</tr>
<tr>
<td>AS, MR</td>
<td>0</td>
</tr>
<tr>
<td>HTN</td>
<td>1 (16.7%)</td>
</tr>
<tr>
<td>MS, AS</td>
<td>1 (16.7%)</td>
</tr>
<tr>
<td>MS, MR</td>
<td>1 (16.7%)</td>
</tr>
<tr>
<td>IHD</td>
<td>0</td>
</tr>
<tr>
<td>Total</td>
<td>6 (100%)</td>
</tr>
</tbody>
</table>
Table (8):

Showing distribution of Doppler’s carotid findings among patients with IBD and APLAS status

<table>
<thead>
<tr>
<th>Doppler carotids abnormality</th>
<th>Antiphospholipid antibodies</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Normal -ve</td>
</tr>
<tr>
<td>Bilateral atheroma</td>
<td>1 (25.0%)</td>
</tr>
<tr>
<td>ICA Throm</td>
<td>1 (25.0%)</td>
</tr>
<tr>
<td>Stenosis mimial</td>
<td>1 (25.0%)</td>
</tr>
<tr>
<td>Proxim ICA stenosis</td>
<td>1 (25.0%)</td>
</tr>
<tr>
<td>Total</td>
<td>4 (100%)</td>
</tr>
</tbody>
</table>
Table (9):

Showing distribution of VDRL test among patients with IBD and APLAS status

<table>
<thead>
<tr>
<th>VDRL</th>
<th>Antiphospholipid antibodies</th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>-ve</td>
<td>+ve</td>
<td></td>
</tr>
<tr>
<td>Normal</td>
<td>6 (100%)</td>
<td>3 (37.5%)</td>
<td></td>
</tr>
<tr>
<td>Abnormal</td>
<td>0</td>
<td>5 (62.5%)</td>
<td></td>
</tr>
<tr>
<td>Total</td>
<td>6 (100%)</td>
<td>8 (100%)</td>
<td></td>
</tr>
</tbody>
</table>
Table (10):

Showing distribution of antidsDNA results among patients presenting with IBD and APLAS status

<table>
<thead>
<tr>
<th>AntidsDNA</th>
<th>Antiphospholipid antibodies</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>-ve</td>
<td>+ve</td>
</tr>
<tr>
<td>Normal</td>
<td>6 (100%)</td>
<td>11 (91.7%)</td>
</tr>
<tr>
<td>Abnormal</td>
<td>0</td>
<td>1 (8.3%)</td>
</tr>
<tr>
<td>Total</td>
<td>6 (100%)</td>
<td>12 (100%)</td>
</tr>
</tbody>
</table>
Table (11):

Showing distribution of ANF results among patients with IBD and APLAS status

<table>
<thead>
<tr>
<th>ANF</th>
<th>Antiphospholipid antibodies</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>-ve</td>
</tr>
<tr>
<td>Normal</td>
<td>9 (90.0%)</td>
</tr>
<tr>
<td>Abnormal</td>
<td>1 (10.0%)</td>
</tr>
<tr>
<td>Total</td>
<td>10 (100%)</td>
</tr>
</tbody>
</table>
Table (12):

Showing distribution of PTT results among patients presenting with IBD and APLAS status

<table>
<thead>
<tr>
<th>PTT</th>
<th>Antiphospholipid antibodies</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>-ve</td>
</tr>
<tr>
<td>Normal</td>
<td>2 (50.0%)</td>
</tr>
<tr>
<td>Abnormal</td>
<td>2 (50.0%)</td>
</tr>
<tr>
<td>Total</td>
<td>4 (100%)</td>
</tr>
</tbody>
</table>
Table (13):

Showing distribution of the final diagnosis in patients presenting with IBD and APLAS status

<table>
<thead>
<tr>
<th>Final diagnosis</th>
<th>Antiphospholipid antibodies</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Normal</td>
<td>Abnormal</td>
</tr>
<tr>
<td>Cerebral infarct</td>
<td>53 (91.4%)</td>
<td>26 (86.7%)</td>
</tr>
<tr>
<td>Multi-infract brain disease</td>
<td>5 (8.6%)</td>
<td>4 (13.3%)</td>
</tr>
<tr>
<td>Total</td>
<td>58 (100%)</td>
<td>30 (100%)</td>
</tr>
</tbody>
</table>
Table (14):

Showing the distribution of the degree of disability after a month in patients with IBD and APLA status

<table>
<thead>
<tr>
<th>Motor weakness</th>
<th>Antiphospholipid antibodies</th>
<th>Normal -ve</th>
<th>Abnormal +ve</th>
</tr>
</thead>
<tbody>
<tr>
<td>Unable to walk</td>
<td></td>
<td>18 (31.0%)</td>
<td>13 (41.9%)</td>
</tr>
<tr>
<td>Walk with support</td>
<td></td>
<td>20 (34.5%)</td>
<td>5 (16.1%)</td>
</tr>
<tr>
<td>Walk without support</td>
<td></td>
<td>20 (34.5%)</td>
<td>13 (41.9%)</td>
</tr>
<tr>
<td>Total</td>
<td></td>
<td>58 (100%)</td>
<td>31 (100%)</td>
</tr>
</tbody>
</table>
Table (15):

Showing the distribution of system affection in the disease control group

<table>
<thead>
<tr>
<th>Disease</th>
<th>Antiphospholipid antibodies</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>-ve</td>
</tr>
<tr>
<td><strong>Chest</strong></td>
<td></td>
</tr>
<tr>
<td>* Pulm. Koch</td>
<td>3</td>
</tr>
<tr>
<td>* Pneumonia</td>
<td>5</td>
</tr>
<tr>
<td><strong>GIT</strong></td>
<td></td>
</tr>
<tr>
<td>* Hepatitis</td>
<td>5</td>
</tr>
<tr>
<td>* HCC</td>
<td>0</td>
</tr>
<tr>
<td>* Abd. T.B</td>
<td>1</td>
</tr>
<tr>
<td>* Belharsias</td>
<td>1</td>
</tr>
<tr>
<td>* Brucellosis</td>
<td>1</td>
</tr>
<tr>
<td><strong>GUS</strong></td>
<td></td>
</tr>
<tr>
<td>* UTI</td>
<td>1</td>
</tr>
<tr>
<td>* CRF</td>
<td>2</td>
</tr>
<tr>
<td><strong>CTD</strong></td>
<td></td>
</tr>
<tr>
<td>* Scleroderma</td>
<td>1</td>
</tr>
<tr>
<td>* Overlap syn</td>
<td>1</td>
</tr>
<tr>
<td><strong>NS</strong></td>
<td></td>
</tr>
<tr>
<td>* GBS</td>
<td>1</td>
</tr>
<tr>
<td>* MS</td>
<td>1</td>
</tr>
<tr>
<td>* Malaria</td>
<td>0</td>
</tr>
<tr>
<td>* HIV</td>
<td>1</td>
</tr>
</tbody>
</table>
DISCUSSION

Our study showed that 34.8% of patients suffering from IBD, 31.4% of the disease control and 16.7% of the healthy individuals were found to be APLA positive. The incidence of APLAS in patients with IBD and those with other diseases are comparable. This may reflect a similar pathogenesis of APLAS in both groups. The incidence of APLAS in patients with IBD is double that in healthy individuals. This may reflect a possible causal relationship between IBD and APLAS. In many studies APLAS is associated with increased risk for incidence and recurrence of cerebral ischemia, myocardial infarction and venous thrombosis. This incidence of positive APLA in our study group with IBD is very high compared to previous studies. The Barcelona study in 1991, reported an incidence of only 6.8% in 146 patients with IBD. Another study in Milan, Italy in 1998 reported an 18% incidence in 55 patients with IBD. Both these studies are old, done 14 and seven years ago and both were done in Caucasians. Our result may represent a high incidence of APLA in IBD in Africans. No other African study is available for comparison. The higher incidence might partially reflect the recent availability of more sensitive assays for APLAs. Malaria is known to be associated with false +ve APLAS tests and the local high endemicity of malaria might also be contributory. The 16.7% incidence of +ve APLA in healthy individuals is relatively high in our study compared to the previous reports of five percent. Similar high percentages have been reported in other studies. A study conducted in normal blood donors showed high prevalence of positive test among this group. Also APLA were noted with certain infections and with the administration of certain drugs.
Our results demonstrated a higher percentage of +ve APLA in IBD patients among females (40%) compared to males (29%). This is closely matched with a study done in New York which showed a female to male ratio of 2:1. Another study in Italy showed a significant increased frequency in females. A third study conducted in San Antonio stated that APLA are an independent risk factor in stroke in young women. This does not match with the Barcelona study which showed males predominance in APL +ve patients.

We studied 160 individuals, half of them males and the other half were females. 24 of the males were APLA +ve and 25 females were +ve. This gives an overall F:M of +ve APLA of about 1:1.

Among IBD patients females who were +ve for APLAs outnumber males with a ratio of 2:1.5. This is in sharp contrast to the ratio in other diseases and in healthy individuals, where males take the lead reversing the ratio to 2:3 and 1:2 respectively. Taking into account the high incidence of APLAs in stroke patients who were in the third decade (71% in our study) the above ratios reflect that young females who are APL +ve are at a special high risk to develop stroke.

In this study, the highest percentage of positive APLAs in stroke patients was found in the age group (20-29) that is (32.3%). This was well matched with a study done in San Carlo which demonstrated high prevalence of APLA in young adults with cerebral ischemia of undetermined cause. Also this matches with the results of another study done in Italy with the same conclusion. Regarding the disease control group in our study the highest percentage of APLAs was found among those aged 40 – 49 (67%) and in the healthy control, the highest percentage was found between 50 – 59 (50%). The results points to the strong association of APLA with
stroke in young age. In other diseases and in healthy individuals, the incidence of APLA increases with age. The same observation was reported previously. A group of Canadian workers reported 25% incidence of APLAs in patients with stroke under 45 years of age in 1998.23

Motor weakness was the commonest presenting symptom in our patients with IBD regardless of the APLA status. Headache and fits were more common in APLA +ve patients. The incidence in the APLA positive group were 48% and 35% compared to 28% and 8.6% in APLA –ve patients. This difference between the two groups was statistically significant (P= .004,.0001). On the other hand disturbance of speech and consciousness were lower in the APLA +ve group. The incidence was 29% and 13% compared to 53% and 33% in the APLA -ve group. This difference was also statistically significant (P= 0.3 , 0.001).

History of DVT, abortion and migraine was observed in higher percentage in APLA +ve patients (Fig.4). This matches with the literature, which stated that APLA can be detected in approximately 10% of all patients with venous thrombosis. APLA also occurs with increased frequency (5—10%) in women with greater than three spontaneous recurrent abortion. A study in Austria22 showed great association between migraine and APS.

Nervous system examination in our study showed cranial nerves affection in 18 patients, speech disturbance in 14 patient, disturbed level of consciousness in 10 patients, motor weakness in seven patients, sensory and cerebellar sings were detected in three patients, optic neuritis and internuclear ophthalmoplegia in only one patient. This relative incidence of neurological deficit is in keeping with the work reported in Iran31. Although stroke patient who were APLA +ve tend to have less motor
weakness than those who were negative, our study showed that APLA status did not affect the degree of motor weakness following stroke. Patients who were APLA +ve had comparable incidences of different degrees of muscle power to those who were APLA –ve.

Our study showed an elevated ESR & low platelets in 61.3% of APLAS +ve patients, compared to 41.4% of the –ve group. This was matched with the Iran study which demonstrated an elevated ESR and thrombocytopenia in a similar percentage of their patients. It was also in keeping with two other studies conducted in Boston and Douglas. Both concluded an association between high ESR, low platelets and APS. High ESR and low platelets can be taken as pointers to a possible +ve APLA test in stroke patients.

Elevated lipid profile was found in 12.9% of APLAS +ve patients compared to 44.8% of the -ve group. It can thus be concluded that hyperlipidaemia plays a little role in APLAS +ve patients, although it is a major risk factor for stroke in general.

Echocardiography was done in eight patients, only one patient with APLAS was found to have valvular lesions. This was compairable to study conducted in San carlo which demonstrated normal echocardiographic findings in patients with +ve APLAS. But our findings stand in sharp contrast with another study published in SMJ which showed an association between valvular lesions on echocardiography and APS.

Atrial fibrillation was detected in four of our patients, conforming with a study published in American heart association. It stated that, cerebral infarction in patients with atrial fibrillation is presumed to result from embolization of intracardiac thrombi, commonly from the left atrium.
Dopplers u/s of the carotid arteries was done in six patients of the study population, two patients who were APLAS +ve had had carotid stenosis as well. This was matched with a study done in San Carlo, that demonstrated significant carotid stenosis associated with positive APLAS.

VDRL Test for syphilis was done in 14 patients and found to be positive in five patients with positive APLAS. This was supported by a study published by persons in Scotland which showed an association between positive APLAS & false positive VDRL.

AntidsDNA was done in a total of 18 of our patients. It was found to be positive in one patient out of 12 who were APLAS +ve. This is a 8.3%. In contrast ANF was done in 24 patients, and was found to be positive in four out of 14 patients who were APLAS +ve at a percentage of 28.6%. This was in keeping with the literature which stated a significant association between the presence of ANF, AntidsDNA, and antiphospholipid antibodies. The patient who was APLAS +ve and had AntidsDNA antibodies probably has SLE. But most of our patient has primary APS, not associated with SLE.

Partial Thromboplastin Time (PTT) was done in 16 patients with IBD and was found to be prolonged in five out of eight patients who were APLA +ve. This is matching with the literature, which showed significant association between a prolonged PTT and the presence of APLAs in the serum.

Both cerebral infarcts and multi-infarct brain disease is demonstrated in our study population with ischemic brain disease. This comparable with the literature which stated that both are known to occur in APS.

In our study, IBD patients stayed in hospital for more than 2 weeks in 86.5% of the cases, this is a considerable long hospital stay. Most of these patients were managed in general medical ward, a unified management
scheme is lacking and a staff specially trained in stroke management is not available.

Modalities of treatment provided to IBD patient was found to be as follows in our patients: antiplatlets alone in 55.1% anticoagulant in 16.9%, antiplatlets + anticoagulants in 5.6%, and antiplatlets + neuroprotectives in 20.2%. This shows that only 22.5% of our IBD patients received anticoagulation. This was against the recommendation worldwide, that APLA +ve patients should all receive anticoagulation. The above-mentioned treatment modalities depended mainly on the preference of the treating physicians. These patients were not admitted in a specialized stroke unit.

Follow up CT brain 6 weeks following stroke was performed in 4 patients who were APLA +ve and was found to become normal in three of them but still abnormal in only one patient. Although this number is small for any sound deductions, this may indicate that APLAS imparts a special good prognosis to the long-term morbidity in stroke patients.

In the diseased control group in our study, APLAS were found to be positive in five patients with pulmonary koch, two with bilharsiasis, one with hepatitis, one with hepatocellular carcinoma, one with urinary tract infection and one with malaria. This was in keeping with the literature in which APLAS were reported to be associated with similar conditions.
CONCLUSIONS

- We demonstrated a higher incidence of APLA in Sudanese patients than reported worldwide.
- The female to male ratio of the APLA was 1.5 : 1 in IBD while it was 1 : 2 in healthy controls.
- APLAs tend to occur with higher incidence in young female stroke patients in keeping with the reports from other countries.
- Stroke patients who are APLA +ve tend to have more headaches and fits at presentation, but they tend to have less disturbance of consciousness and speech, and motor weakness.
- Follow up CT done in a small number of our APLA +ve stroke patients, suggests a possible long-term good prognosis in this group.
- Strokes in APLA +ve patients tend to be associated with history of DVT, abortion, and migraine, comparable with reports from other parts of the world.
- In keeping with studies from other countries, APLAs in our patients tend to be associated with high ESR, Low platelets count, prolonged PTT, and carotid stenosis demonstrated by doppler U/S scanning.
- APLAs showed strong association with +ve VDRL & ANF.
- Modalities of treatments applied in IBD Patients lacked a unified treatment regimens for APLAs +ve patients with stroke.
RECOMMENDATIONS

• More research is needed into the APLA status in the general population in Sudan, because of the local endemicity of many infections known to be associated with a positive test. Our study suggested the local incidence to be double that reported in Europe in healthy individuals.

• Healthy controls who were +ve for APLAs needs to be followed-up further.

• There is a need for a more refined sensitive and specific test for APLA.

• Because of the high incidence of +ve APLA in IBD patients, this test should be included among the routine investigations of stroke patients, specially young females without evident other risk factors.

• IBD patients who present with headache and fits, specially if they report migraine, DVT, or abortion in the past history, need to be investigated for APLA.

• A high ESR and low platelet count can be taken as pointers to a possible +ve APLA test.

• Anti phospholipid syndrome should be suspected in any patient with the disease who has a +ve VDRL, ANF test or prolonged PTT.

• It is time to establish a specialized stroke units and set a unified regimen of treatments for those patients. In order to improve the outcome and prognosis.
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