KWAME NKRUMAH OF SCIENCE AND TECHNOLOGY KUMASI

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THE RISK FACTORS OF STROKE AND THE CONTRIBUTION OF METABOLIC SYNDROME

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BY

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DECLARATION

I hereby declare that this submission is my own work towards the award of an MPhil. and that, to the best of my knowledge, it contains no material previously published by another person nor material which has been accepted for the award of any other degree of the University, except where due acknowledgement has been made in the text.

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ABSTRACT

Although stroke cause substantial morbidity and mortality, it is unclear how individuals are affected, or a group of risk factors contribute to stroke outcomes especially in developing countries. This study evaluated the risk factors of stroke and the contribution of metabolic syndrome the condition. This was a cross-sectional study of stroke patients from Komfo Anokye Teaching Hospital, compared to a control of healthy subjects. Adult enrolees who were eligible for inclusion were persons who have had stroke within twenty-four hours of onset without any medication. Questionnaires were used to gather information on medical history, demographic features and lifestyle. The lipid profile, fasting blood sugar and blood pressure were measured, likewise the determination of aminotransferases and gamma-glutamyltransferase. The National Cholesterol Education Program Adult Treatment Panel III and WHO guidelines were used to determine which of the patients had metabolic syndrome. Out of 224 stroke patients, of mean age 65.64(8.75) SD years, used for the study, 56.7% of the patients had hyperglycaemia, whereas 47.2% were known diabetics. Hypertriglyceridaemiawas found in 55.8%, followed by 30.8% of the patients who had a reduced HDL-C and 17.95% of them with increased LDL-C. About 20% of the patients had raised AST, 7.1% raised ALT and 14.7% raised GGT above the normal levels. As high as 63% of stroke patients had high blood pressure. Based on the NCEP criteria, 46.88% of the stroke patients were classified to have metabolic syndrome, while the WHO criteria gave 10.27% of the stroke patients to have metabolic syndrome. None of the 100 healthy controls had the metabolic syndrome. There were a high prevalence of both hypertension and hyperglycaemia among the stroke patients. Stroke patients have all the risk factors of metabolic syndrome, and 46.88% of the patients had the metabolic syndrome, by NCEP guidelines, while none of the control group of healthy subjects had the syndrome. Based on this study, it is

important to stress the need for educating the stroke patients and/or their caregivers, on the aetiology of stroke and the treatment options. The general population should also be educated on primary preventive measures for all age groups and both genders.

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CHAPTER ONE

1.0 INTRODUCTION

The brain is one of the most important organs in the body, regulating all bodily functions and activities and when the flow of oxygen-rich blood to the brain is blocked, or when there' sudden bleeding in the brain then stroke occurs (Donnan *et al*., 2008). Stroke, also considered as a cerebrovascular disorder, is a medical emergency which can cause permanent neurological damage, complications, and death.

Stroke is becoming a common clinical condition even in developing countries. The probability of stroke occurrence rises with the number and severity of vascular risk factors (Algra, 2006). An emerging entity that incorporates risk stratification with the goal of mitigating vascular risk is the metabolic syndrome (McNeill *et al*., 2006). The syndrome is highly prevalent worldwide, and several studies have suggested that individuals with the metabolic syndrome are at high risk for experiencing first and recurrent stroke. The prevalence of the metabolic syndrome is expected to substantially increase in the future, alongside the growing obesity epidemic (Ogden and Algra, 2006), a rise that will likely be associated with an even heavier burden of stroke on the society. It is important to identify persons with risk factors in order to initiate lifestyle modification and the use of drugs treatment to prevent cardiovascular disease and stroke (Grundy *et al*., 2004).

The risk factors that cluster in metabolic syndrome include atherogenic dyslipidaemia, hypertension, insulin resistance, hyperglycaemia, abdominal obesity, physical inactivity, reduced

high density lipoprotein-cholesterol (HDL-C), elevated serum triglycerides, elevated small low-density lipoproteins (Grundy *et al.*, 2005). HDL cholesterol levels are inversely associated with the risk of ischaemic stroke (Sacco and Allen, 2001).

Insulin resistance has only recently emerged as an important risk factor for stroke. Insulin resistance is a state in which defective muscle glycogen synthesis and glucose transport result in a subnormal response to insulin (Grundy *et al*., 2005). Insulin resistance is also commonly seen in elderly individuals, blacks, and in individuals with essential hypertension, obesity, lipoprotein abnormalities, coronary artery disease, carotid artery disease, as well as having a family history of diabetes (Kernam *et al*., 2008).

Results of clinical trials in patients with diabetes mellitus suggest that reducing insulin resistance can prevent carotid atherosclerosis and stroke (Koshiyama *et al*., 2003). Abdominal obesity correlates strongly with insulin resistance (Grundy *et al*., 2005). Individuals with abdominal obesity have an unusually high release of non-esterified fatty acids from adipose tissue, leading to lipid accumulation in sites other than adipose tissue. Ectopic lipid accumulation in muscle and liver predisposes individuals to insulin resistance and dyslipidaemia (Konishi *et al*, 2003). The adipose tissue in obese individuals exhibits abnormalities in producing adipokines that promote insulin resistance (Sprafka *et al*., 1994).

A critique of the metabolic syndrome concept has been that it should not be considered as a separate disease because it may not be clear that the syndrome itself is a vascular risk factor above and beyond its recognized individual risk factors (Alberti and Zimmet, 1998). Several

studies support the relationship between insulin resistance and cardiovascular disease (Isomaa *et al*., 2000).

The progressive increase in obesity, cardiovascular disease and metabolic syndrome prevalence motivated the National Cholesterol Education Program (NCEP), on its third panel, to propose clinical criteria to define metabolic syndrome by the presence of, at least, three altered factors; high blood pressure (BP), hypertriglyceridaemia, low HDL cholesterol, high plasma glucose and abdominal obesity. The presence of metabolic syndrome is associated with a higher risk of developing diabetes mellitus and cardiovascular diseases (Rutler *et al*., 2005).

Due to the paucity of information on risk factors to stroke and the accompanying biochemical changes in Africa, particularly, this study was undertaken to investigate the risk factors present in stroke in-patients, highlighting the contribution of metabolic syndrome. In the study, the prevalence of metabolic syndrome among stroke patients was investigated, using the NCEP and WHO diagnostic criteria.

1.1 AIMS OF THE STUDY

This study was done to evaluate metabolic risk factors present, as well as the associated biochemical changes in stroke patients at the Komfo Anokye Teaching Hospital, Kumasi.

1.2 SPECIFIC OBJECTIVES OF THE STUDY

1. To investigate the demographic features and the medical history of stroke patients, through the use of questionnaire.

2. To measure lipid profile, fasting blood sugar and other biochemical indicators as biomarkers of a potential for stroke.

3. To stratify the patients by their systolic and diastolic blood pressure categories to identify patients and the control who are hypertensive.

4. Use the measured parameters to identify patients who have metabolic syndrome, based on the WHO and NCEP criteria.

1.3 JUSTIFICATION OF STUDY

Though there is increase in the prevalence of non-communicable diseases in Africa, there is currently little information on such diseases, especially stroke. In developed countries, studies have shown the association of stroke with metabolic syndrome. Therefore, this study was performed to investigate: the common risk factors found in stroke in-patients, the associated biochemical changes and the prevalence of metabolic syndrome, using the WHO and NCEP criteria.

Information gathered from the study will shed light on some demographic features, common risk factors and corresponding biochemical changes. These would provide the pathophysiological mechanisms behind the cerebrovascular disorder, based upon which recommendations of appropriate therapeutic measures for the patients, as well as the suggestion of primary preventive measures for the general population could be made. No study of this scope has been carried out in Ghana, and would be among the few in the African setting.

CHAPTER TWO

2.0 LITERATURE REVIEW

2.1 STROKE

The brain is one of the most important organs in the body, coordinating all bodily functions and activities. The five essential parts of the brain are the cerebrum, cerebellum, brain stem, pituitary gland, and hypothalamus (Bamford, 1991). The proper functioning of all regions of the brain is imperative for normal activity (Kidwell *et al*., 2004) and if any of these is affected, stroke may result. A stroke is a medical emergency which can cause permanent neurological damage, complications, and death. It is caused when there is blockage of the flow of oxygen-rich blood to the brain (Donnan *et al*., 2008) and it could also result from a haemorrhagic event in the brain.

A blood clot might originally form in the heart chamber, as a result of an irregular heart rhythm. Such clots may remain attached to the inner lining of the heart, but occasionally they can break off, travel through the bloodstream and form a plug in a brain artery, and cause a stroke (Harbison *et al*.,1999). A plug can also originate in a large artery, for example, the carotid artery and can then travel downstream to clog a small blood vessel within the brain (Biessels *et al*., 2006).

Stroke also occurs when a blood vessel in the brain ruptures and bleeds into the surrounding brain tissue (Johnson *et al*., 2007). Blood is very irritating to the brain and can cause swelling of brain tissue to cause cerebral oedema (Feigin and Johnson, 2005).

The accumulation of blood from a cerebral haemorrhage increases pressure within the skull and causes further damage by squeezing the brain against the bony skull. Within a few minutes of having a stroke, brain cells begin to die and symptoms can show (Shepherd and Saver, 2004). Stroke occurs when blood supply to part of the brain is disrupted, causing some brain cells to die. When blood flow to the brain is impaired, oxygen and glucose cannot be delivered to the brain (Senelick *et al*., 1994). The impairment of the blood supply is caused by narrowing of the small arteries within the brain, causing that tissue to die. Lastly, there could be hardening of the arteries (atherosclerosis) leading to the brain (Brass*et al*, 2005).

There are two major circulation of blood in the body. These are the anterior circulation and the posterior circulation (Beckett *et al*., 2008). The anterior circulation controls most motor activities, sensation, thought, speech, and emotion. This anterior circulation is supplied with blood by the carotid arteries. The posterior circulation supplies the brainstem and the cerebellum and is responsible for controlling the autonomic parts of the brain and coordination. The posterior circulation is supplied with blood by the vertebrobasilar arteries. If these arteries become narrow as a result of atherosclerotic plaque or cholesterol, debris can break off and float downstream and clog blood supply to parts of the brain. As a result, larger parts of the brain would have impaired blood supply, and this may produce more symptoms (Gress *et al*., 2000).

Factors that increase the risk of stroke include history of transient ischaemic attacks (TIAs), atherosclerosis, hypertension, electrocardiogram changes, arrhythmias, rheumatic heart disease, diabetes mellitus, gout, postural hypotension, cardiac or myocardial enlargement, high serum

triglyceride levels, lack of exercise, use of hormonal contraceptives, cigarette smoking, and a family history of stroke (Warburton, 2007).

The symptoms of stroke include dizziness, unsteady walking, loss of balance and coordination, speech problems, numbness, weakness, or paralysis on one side of the body, blurred, blackened, or double vision and a sudden severe headache (Brass *et al*., 2005). People with migraine headache have a very slight increase of occurrence of stroke because of their narrowed brain blood vessels. Migraine headache usually mimics stroke with loss of function of one side of the body or vision or speech problems (Cantu *et al*., 2003).

The blockage of an artery in the brain by a clot (thrombosis) is the most common cause of a stroke (Hart *et al*., 2007). The part of the brain that is supplied by the blocked blood vessel is then deprived of blood and oxygen (Rothwell *et al*., 2004). As a result of blood and oxygen deprivation, that part of the brain dies. Typically, a clot forms in a small blood vessel within the brain that has been previously narrowed due to a variety of risk factors, including: high blood pressure (hypertension), high cholesterol, diabetes, and smoking (Villarosa *et al*., 1993).

The second most common cause of stroke is embolism (Donnan *et al*., 2008). Embolism occurs as a result of an occlusion of a blood vessel, caused by a fragmented clot, a tumour, fat, bacteria, or air. It can occur at any age, especially among patients with a history of rheumatic heart disease, endocarditis, post-traumatic valvular disease, or myocardial fibrillation and other cardiac arrhythmias (Bamford, 1991). The embolus usually develops rapidly in 10 to 20 seconds and without warning. When it reaches the cerebral vasculature, it cuts off circulation by lodging in a narrow portion of an artery (Johnson *et al*., 2007).

2.1.1 Types of stroke

There are two main types of stroke, ischaemic stroke and haemorrhagic stroke.

2.1.1.1 Ischaemic stroke

Ischaemic stroke is a condition in which there is insufficient blood flow to the brain to meet metabolic demand (Sullivan, 2009). This leads to poor oxygen supply, cerebral hypoxia and thus to the death of brain tissue. Ischaemic stroke leads to alterations in brain metabolism, reduction in metabolic rates, and energy crisis (Fairhead *et al*., 2005).

2.1.1.1.1 Types of ischaemic stroke

There are two types of ischaemic stroke; these are focal ischaemic stroke, which is confined to a specific region of the brain; and global ischaemic stroke, which encompasses wide areas of the brain tissue (Smith *et al*., 2008).

2.1.1.1.1.1 Focal brain ischaemic stroke

Focal brain ischaemia occurs when a blood clot has occluded a cerebral vessel (Sullivan, 2009). Focal brain ischaemia reduces blood flow to a specific brain region, increasing the risk of cell death to that particular area (Caplan *et al*., 2008). It can be either caused by thrombosis or embolism.

2.1.1.1.1.2 Global brain ischaemic stroke

Global brain ischaemia occurs when blood flow to the brain is halted or drastically reduced. This is commonly caused by cardiac arrest. If sufficient circulation is restored within a short period of time, symptoms may be transient however, if a significant amount of time passes before restoration, brain damage may be permanent. While reperfusion may be essential to protecting as

much brain tissue as possible, it may also lead to reperfusion injury. Reperfusion injury is classified as the damage that ensues after restoration of blood supply to ischaemic tissue (Sullivan, 2009).

2.1.1.1.2 Symptoms of ischaemic stroke

The main symptoms involve impairments in vision, body movement, and speech. Symptoms of brain ischaemia include unconsciousness, blindness, problems with coordination, and weakness in the body. Other effects are cardiorespiratory arrest, and irreversible brain damage. An interruption of blood flow to the brain for more than ten seconds results in the loss of consciousnessand leads to brain ischaemia and consequently results in irreversible brain damage (Raichle *et al*., 1999).

The symptoms of ischaemic stroke reflect the anatomical region undergoing blood and oxygen deprivation. Ischaemia within the arteries branching from the internal carotid artery results in symptoms such as blindness in one eye, weakness in one arm or leg, or weakness in one entire side of the body (Smith *et al*., 2008). Ischaemia within the arteries branching from the vertebral arteries in the back of the brain may result in symptoms such as dizziness, vertigo, double vision, or weakness on both sides of the body (Beers *et al*., 2003). Other symptoms include difficulty speaking, slurred speech, and the loss of coordination (Beers et al., 2003). The symptoms of ischaemic stroke range from mild to severe. The symptoms can last from a few seconds to a few minutes or extended periods of time. If the brain becomes damaged irreversibly and infarction occurs, the symptoms may be permanent (Caplan *et al*., 2008).

Multiple cerebral ischaemic events may lead to subcortical ischaemic depression, also known as vascular depression. This condition is most commonly seen in elderly patients. Late onset depression is increasingly seen as a distinct sub-type of depression, and can be detected with a magnetic resonance imaging (MRI) (Kidwell *et al*., 2004).

2.1.1.1.3 Causes of ischaemic stroke

Ischaemic stroke has been linked to a variety of diseases or abnormalities. Individuals with sickle cell anaemia, compressed blood vessels, ventricular tachycardia, plaque build-up in the arteries, blood clots, extremely low blood pressure, as a result of heart attack, and congenital heart defects have a higher predisposition to brain ischaemia, in comparison with their healthy counterparts (Baldwin, 2003). Sickle cell anaemia causes ischaemic stroke associated with the irregularly shaped red blood cells. Sickle-shaped blood cells clot more easily than normal blood cells, impeding blood flow to the brain (Hill, 2005). Compression of blood vessels also leads to brain ischaemia, by blocking the arteries that carry oxygen to the brain (Kidwell *et al*., 2004).

2.1.1.1.4 Pathophysiology of ischaemic stroke

Ventricular tachycardia represents a series of irregular heartbeats that may cause the heart to completely shut down, resulting in cessation of oxygen flow (Bamford, 1991). Irregular heartbeats may result in formation of blood clots and lead to oxygen deprivation to all organs and ends in ischaemic stroke (Caplan *et al*., 2008).

Blockage of arteries due to plaque build-up may also result in ischaemia. Even a small amount of plaque build-up can result in the narrowing of passageways, causing that area to become more prone to the formation of blood clots. Large blood clots can also cause ischaemia by blocking blood flow.

A heart attack can also cause ischaemic stroke due to the correlation that exists between heart attack and low blood pressure (Chobanian *et al*., 2003). Extremely low blood pressure usually represents the inadequate oxygenation of tissues. Untreated heart attacks may slow blood flow to the extent that blood may start to clot and prevent the flow of blood to the brain or other major organs. Extremely low blood pressure can also result from drug overdose and reactions to drugs (Sloan *et al*., 1991). Therefore, brain ischaemia can result from events other than heart attacks. Congenital heart defects may also cause ischaemic stroke due to the lack of appropriate artery formation and connection. People with congenital heart defects may also be prone to blood clots (Ellis and Tricia, 2003).

Other pathological events that may result in brain ischaemia include cardio- respiratory arrest and severe irreversible brain damage (Feigin and Johnson, 2005).During ischaemic stroke, the brain cannot perform aerobic metabolism due to the loss of oxygen and substrate. The brain is not able to switch to anaerobic metabolism because it does not have any long-term energy stored (Smith *et al*., 2008) The levels of adenosine triphosphate (ATP) drop rapidly. In the absence of biochemical energy, cells begin to lose the ability to maintain electrochemical gradients. There is a massive influx of calcium into the cytosol, a massive release of glutamate from synaptic vesicles, lipolysis, calpain activation, and the arrest of protein synthesis (Hinds, 2009). Additionally, removal of metabolic wastes is slowed. The interruption of blood flow to the brain for ten seconds results in the immediate loss of consciousness. The interruption of blood flow for twenty seconds results in the stopping of electrical activity (Raichle *et al*., 1999).

2.1.1.2 Haemorrhagic stroke

A haemorrhagic stroke is caused by a sudden bleeding, or haemorrhage, into or next to the brain. This problem accounts for about 20 percent of all people admitted to hospitals for strokes (Yadav *et al*., 2007). A sudden, severe headache like a thunderclap is a very serious neurological sign of haemorrhagic stroke. Headache which is accompanied by nausea, vomiting, a stiff neck, or loss of mental or physical functions requires immediate medical attention. Also, any possible stroke is an emergency, and swift diagnosis and treatment are essential.

Haemorrhage affecting the brain or its adjacent spaces is a very serious condition and depending on the location and may even be life- threatening (Furie *et al*., 2005). Many haemorrhages in or close to the brain stop spontaneously within the first hour. Bleeding can continue until the accumulated fluid disrupts vital brain structures. The brain functions become impaired but the severity depends mainly on the size and location of the bleeding. A haemorrhage involving the deep structures of one brain hemisphere results in weakness on the other side of the body and numbness and visual problems on the same side (Villarosa *et al*., 1993). Haemorrhage occurring in a person's brain stem causes immediate plunge and finally results in coma, with weakness in both arms and legs and impaired movements of the eyeball (Goldstein *et al*., 2006)

2.1.1.2.1 Types of haemorragic stroke

There are two main types of haemorrhagic strokes: intracerebral haemorrhage and subarachnoid haemorrhage (Leah *et al*., 2009). Haemorrhagic strokes involving bleeding within the brain is called intracerebral haemorrhage and bleeding between the inner and outer layers of the tissue covering the brain is called subarachnoid haemorrhage.

2.1.1.2.1.1 Intracerebral haemorrhage

Intracerebral haemorrhage is a type of stroke that occurs within the brain tissue itself and can be caused by brain trauma, or it can occur spontaneously in haemorrhagic stroke. Non-traumatic intracerebral haemorrhage is a spontaneous bleeding into the brain tissue (Stam *et al*., 2005). Intracerebral haemorrhages can happen in any of the cerebral lobes or the cerebellum, but they are most likely to occur in the deeper brain structures such as the basal ganglia, thalamus, and brain stem. The problem arises at weak spots in the walls of small arteries inside the brain, which have been caused by disease and these tiny blood vessels start to leak. Because the actual source of the bleeding is often small, it can take time for the lost blood to build, up; this will cause the symptoms to increase with time (Shepherd and Saver, 2004).

2.1.1.2.1.1.1 Symptoms of Intracerebral Haemorrhage

The symptoms of intracerebral haemorrhage include sudden weakness or numbness in one part of the body, difficulties speaking or understanding language, abrupt confusion, and problems seeing in one eye or in half the visual field. Intracerebral haemorrhage is more likely to cause a steady worsening of the initial symptoms, as blood continues to accumulate (Vinas and Pilitsis, 2006).Other symptoms include headache, feeling nauseous, or vomiting in the minutes after onset. In intracerebral haemorrhage involving the cerebellum, symptoms usually begin abruptly with vomiting and such severe loss of coordination that a person cannot stand or walk. These signs are occasionally accompanied by slurred speech and double vision (Goldstein *et al*., 2006). The growing mass of blood does not change the symptoms until it starts to compress the adjacent brain stem, which ends in a coma. And at this point it would be too late for surgeons to drain the haematoma and reverse the damage (Sacco and Allen, 2008).

That small margin of time between an alert state and an irreversible coma makes it imperative for people with stroke symptoms to get medical help quickly, and for clinicians to consider the possibility of a stroke in all people showing sudden vomiting and incoordination (Furie *et al*., 2005). Symptoms suggesting brain dysfunction develop and steadily worsen as the haemorrhage expands. Some symptoms such as weakness, paralysis, loss of sensation, and numbness, often affect only one side of the body (Hill, 2005). People may be unable to speak, or become confused, vision may be impaired or lost, the eyes may point in different directions or become paralyzed, and the pupils may become abnormally large or small.

2.1.1.2.1.1.2 Causes of Intracerebral Haemorrhage

Intracerebral haemorrhage most often results when chronic high blood pressure weakens a small artery, causing it to burst (McCaffery, 2001). Using cocaine or amphetamines can cause temporary but very high blood pressure and haemorrhage (Donnan *et al*., 2005). In some older people, an abnormal protein called amyloid accumulates in arteries of the brain. This condition which is called amyloid angiopathy weakens the arteries and can cause haemorrhage (Vinas and Pilitsis, 2006). Less common causes include blood vessel abnormalities present at birth, injuries, and tumours, inflammation of blood vessels, bleeding disorders, and use of anticoagulants in doses that are too high (Ezekowitz *et al*., 2003). Bleeding disorders and use of anticoagulants increase the risk of dying from an intracerebral haemorrhage. Intracerebral haemorrhage begins abruptly, in about half of the people, it begins with a severe headache, often during activity but in older people, the headache may be mild or absent (Ezekowitz *et al*., 2003).

2.1.1.2.1.2 Subarachnoid Haemorrhage

A subarachnoid haemorrhage is bleeding into the space between the inner layer and middle layer of the tissue covering the brain (Donnan *et al*., 2008). It is a life-threatening disorder that can rapidly result in serious, permanent disabilities. It is the only type of stroke which is more common among women than men (Feigin and Johnson, 2005). The most common cause is rupture of a bulge in an artery. The rupture of an artery causes a sudden and severe headache, followed by a brief loss of consciousness. Computed tomography, sometimes a spinal tap, and angiography are done to confirm the diagnosis (Warach *et al*., 2003). Drugs are used to relieve the headache and to control blood pressure, and surgery is done to stop the bleeding (Beckett *et al*., 2008). Subarachnoid haemorrhage usually results from head injuries. However, haemorrhage due to a head injury causes different symptoms and is not considered a stroke.

Subarachnoid haemorrhage is considered a stroke only when it occurs spontaneously; that is, when the haemorrhage does not result from external forces, such as an accident or a fall. A spontaneous haemorrhage usually results from the sudden rupture of an aneurysm in a cerebral artery (Stam *et al*., 2005). Aneurysms are bulges in a weakened area of an artery's wall and typically occur where an artery branches. Aneurysms may be congenital, be present at birth or they may develop later, after years of high blood pressure which weakens the walls of arteries (Bamford *et al*., 1991). Most subarachnoid haemorrhages result from congenital aneurysms (Stam *et al*., 2005). It can also result from rupture of an abnormal connection between arteries and veins in or around the brain and is termed as arteriovenous malformation (Adams *et al*., 1993). An arteriovenous malformation may be present at birth, but it is usually identified only if symptoms develop. A blood clot can form on an infected heart valve and travels to an artery that

supplies the brain, which will cause the artery to become inflamed; as a result the artery will then weaken and rupture. Before rupturing, an aneurysm usually causes no symptoms unless it presses on a nerve or leaks small amounts of blood, usually before a large rupture and causes headache (Bamford *et al*., 1991).

2.1.1.2.1.2.1Symptoms of Subarachnoid Haemorrhage

The headache may be unusually sudden and severe, called a thunderclap headache (Furie *et al*., 2005). Other symptoms include facial or eye pain, double vision and loss of peripheral vision (Beers *et al*., 2003). These symptoms can occur minutes to weeks before the rupture. A rupture usually causes a sudden, severe headache that peaks within seconds. It is often followed by a feeling of restlessness, a brief loss of consciousness and patient may remain in a coma, and sometimes, death. People may become sleepy and confused, unresponsive, and difficult to arouse (Cantu *et al*., 2003).

Blood and cerebrospinal fluid around the brain irritate the layers of tissue covering the brain, causing a stiff neck, as well as continuing headaches, often with vomiting, dizziness, and low back pain within 24 hours of the symptoms (Allen *et al*., 2005). Frequent fluctuations in the heart rate and in the breathing rate often occur, sometimes accompanied by seizures. About 25% of people have symptoms that indicate damage to a specific part of the brain; such symptoms include weakness or paralysis, loss of sensation on one side of the body, difficulty understanding and using language (aphasia). Severe impairments may develop and become permanent within minutes or hours. Fever is common during the first 5 to 10 days (Allen *et al*., 2005).

The severity of haemorrhagic stroke will lead to conditions such as hydrocephalus, vasospasm and a second rupture.

Within 24 hours hydrocephalus occurs, the blood from a subarachnoid haemorrhage may clot (Harbison *et al*., 1999). The clotted blood will prevent the fluid surrounding the brain (cerebrospinal fluid) from draining as it normally does. As a result, fluid accumulates within the brain, increasing pressure within the skull. Hydrocephalus may contribute to symptoms such as headaches, sleepiness, confusion, nausea, and vomiting and may increase the risk of coma and death (Kothari *et al*., 1999).

Vasospasm results after about 3 to 10 days after the haemorrhage, arteries in the brain may contract, limiting blood flow to the brain (Reynolds *et al*., 2003). As a result, brain tissues will not get enough oxygen and may die. Vasospasm may cause symptoms similar to those of ischaemic stroke, such as weakness or loss of sensation on one side of the body, difficulty using or understanding language, vertigo, and impaired coordination (Gorelick, 1998).

Sometimes a second rupture occurs, usually within a week (Yerman, 2007). Intraventricular haemorrhage occurs when the source of the bleeding is located close to or within the wall surrounding one of the brain ventricles. In these cases, the blood drains into the fluid-filled ventricular system, often sparing healthy brain tissue (Gorelick, 1998).

When the walls of the pouch grow too weak to hold the blood inside, it ruptures. The leaking blood may drain not only into the small space surrounding the brain but occasionally directly into brain tissue. The mass of the growing haematoma may also displace or compress vital brain structures. As the brain itself is not sensitive to pain, headaches from haemorrhagic strokes are believed to be due to either the stretching of the arterial wall when an aneurysm ruptures, the

sudden increase of pressure within the skull, or the stretching of the membranes surrounding the brain (Gueyffier *et al*., 1997).

Haemorrhagic strokes that stop shortly after they begin may not cause the steady progression of symptoms that helps clinicians distinguish them from ischaemic stroke (Beckett *et al*., 2008). However, it is very important to identify which type of stroke a person has had. Treatment to declog an artery may cause or contribute to another haemorrhage. Distinguishing haemorrhage from brain ischaemia requires emergency brain imaging.

An abrupt displacement or compression of vital brain structures may lead to sleepiness, loss of consciousness, and coma (Westover *et al*., 2007). Weakness or numbness in one side of the body and impaired vision, speech, or awareness of the disorder also tends to be bad signs; they indicate that important brain tissue is being disrupted. Any stroke symptom requires immediate attention in a hospital.

2.1.1.2.1.2 .3 Diagnosis of haemorrhagic stroke

The diagnosis of a haemorrhagic stroke is based on the person's history, a neurological examination, and brain imaging (Sloan *et al*., 1991). A computed tomography (CT) scan shows fresh blood in the skull as a white spot on the film (Kidwell *et al*., 2004). Sometimes, a person's symptoms and clinical examination point to a subarachnoid haemorrhage, but the CT scan cannot confirm the diagnosis because there is only a small amount of blood in the space between the brain and the surrounding membranes. In this case, the physician usually undertakes a lumbar puncture, or spinal tap, in order to detect any fresh blood cells in the cerebrospinal fluid(Yadav *et al*., 2007).

Magnetic resonance imaging (MRI) also detects fresh bleeding in the brain, but it is even more useful in the search for possible underlying causes. It also detects vascular malformations, tumours, evidence for congophilic amyloid angiopathy, and aneurysms (Ezekowitz *et al*., 2003).

A specialized type of ultrasound called transcranial doppler ultrasonography is another useful tool for spotting larger malformations of blood vessels; it is often used for follow-up evaluations of people who have had a haemorrhagic stroke (Shuaib and Hachinski, 1991).

The most reliable technique to confirm or rule out the presence of aneurysms and other malformations of the blood vessels is a cerebral angiogram; physicians inject contrast dye into the blood system to make arteries stand out on X-ray films (Kidwell *et al*., 2004).

People having a haemorrhagic stroke should usually be kept under close observation in the acute phase of the disease and may even require the support of an intensive care unit. Balancing conservative treatment (administering pain and comfort medication, stabilizing vital signs, lowering the pressure inside the head, and so on) against the need for invasive treatment options such as surgery, is influenced by a complex variety of factors (Feigin and Johnson, 2005). Some cases of intracerebral haemorrhage may require removing the blood in order to relieve otherwise healthy brain areas from pressure. In some instances of intraventricular haemorrhage, surgeons may relieve pressure by inserting a small tube into the ventricles to drain the system (Beckett *et al*., 2008).

Whether an aneurysm that caused haemorrhage is treated immediately, after the acute phase, depends on the individual's condition and on the treatment chosen. Options include "clipping" the aneurysm surgically or blocking it with metal coils inserted through a very small tube

(catheter) during the angiogram (Sloan *et al.*, 1991). Haemorrhagic strokes tend to be more deadly than ischaemic strokes. Subarachnoid haemorrhage is the most life-threatening, with an average mortality of 40 percent within the first month after the bleeding (Kothari *et al*., 1999). Overall, a person's prognosis tends to be worse if there is more blood around the brain. But an individual's chances also depend on the exact location of the haematoma and on how severely he or she has been affected. These types of strokes may also cause secondary complications for people after the initial bleeding (Ezekowitz *et al*., 2003).

One third of people with such strokes have epileptic seizures, which are usually managed with medication (Becket *et al*., 2008). Other direct effects of the haemorrhage on the brain include irregular heartbeat, fluid in the lungs, impaired electrolyte balance, and fever (Shuaib and Hachinski, 1991). The most feared acute complication is more bleeding from the original haemorrhage source and up to 20 percent of people with ruptured aneurysms have this trouble (Adams *et al*., 1993).

Vasospasm usually occurs between the third and fifth day after the haemorrhage (Grundy *et al*., 2005). When these arteries narrow, there is a risk of an additional, ischaemic stroke. People who survive a haemorrhagic stroke and the critical period that immediately follows often make a remarkable recovery. As the mass of the haematoma slowly decreases, the actual disruption of brain tissue can turn out to be smaller than what clinicians or family members had feared (Shuaib and Hachinski, 1991).

2.2 TRANSIENT ISCHAEMIC ATTACK (TIA)

A transient ischaemic attack (TIA) is a disorder that is caused by changes in the blood supply to a particular area of the brain, resulting in brief neurologic dysfunction that persists for less than 24 hours. If symptoms persist longer, then it is categorized as a stroke (Beers *et al.,* 2003). Symptoms can include numbness or weakness in the face, arm, or leg, especially on one side of the body; confusion or difficulty in talking or understanding speech; trouble seeing in one or both eyes; and difficulty with walking, dizziness, or loss of balance and coordination (Lipton, 1999).

TIA is a warning to stroke or it is said to be mini-stroke as it produces stroke-like symptoms but no lasting damage. Recognizing and treating TIAs can reduce the risk of a major stroke. Most strokes are not preceded by TIAs; however, of the people who have had one or more TIAs, more than a third will later have a stroke (Baldwin, 2003). A person who has had one or more TIAs is more likely to have a stroke than someone of the same age and sex who has never experienced this condition (Xiong *et al*., 2006). TIAs are important in predicting if a stroke will occur rather than when one will happen. They can occur days, weeks or even months before a major stroke (Warburton, 2007). In about half the cases, the stroke occurs within one year of the TIA (Sacco and Allen, 2008).

2.2.1 Causes of transient ischaemic attack

The most common cause of a TIA is an embolus that occludes an artery in the brain (Donnan *et al*., 2005). This most frequently arises from a dislodged atherosclerotic plaque in one of the carotid arteries (i.e. a number of major arteries in the head and neck) or from a thrombus (i.e. a blood clot) in the heart due to atrial fibrillation (irregular beating of the heart) (Fuster *et al*.,

2006). Other reasons include excessive narrowing of large vessels due to an atherosclerotic plaque and increased blood viscosity due to some blood diseases (Raichle *et al*., 1999).

TIA is related with medical conditions like hypertension, heart disease, atrial fibrillation, migraine, cigarette smoking, hypercholesterolaemia, and diabetes mellitus (Krieger *et al*., 2001). Medical help is available to reduce and eliminate these factors. Lifestyle changes such as eating a balanced diet, maintaining healthy weight, exercising, and enrolling in smoking and alcohol cessation programmes can also reduce these factors (Xiong *et al*., 2006).

Unlike stroke, when a TIA is over, there is no injury to the brain. Because there is no way to tell whether symptoms are from a TIA or an acute stroke, patients should assume that all stroke-like symptoms signal an emergency.

A prompt evaluation is necessary to identify the cause of the TIA and determine appropriate therapy. Depending on a patient's medical history and the results of a medical examination, the doctor may recommend drug therapy or surgery to reduce the risk of stroke in people who have had a TIA (Graham *et al*., 2000). The use of antiplatelet agents, particularly aspirin, is a standard treatment for patients at risk of stroke. People with atrial fibrillation may be prescribed anticoagulants (Algra, 2006).

2.3 METABOLIC SYNDROME

Metabolic syndrome is a combination of metabolic disorders that increase the risk of developing cardiovascular disease and type2 diabeties (Ford *et al*., 2002).The metabolic disorders are high triglyceride, high blood pressure, obesity, low HDL-cholesterol, high LDL-cholesterol and genetic factors (Raichle *et al*., 1999). These risk factors together, increase the likelihood of heart disease, stroke, peripheral vascular disease, and type 2 diabetes (Xiong *et al*., 2006). The metabolic syndrome is a cluster of vascular riskfactors that share insulin resistance as a common

underlyingpathophysiologic mechanism (Ferranini *et al*., 1997). The metabolic syndrome has been shown to be associated with an increased riskfor cardiovascular disease and ischaemic stroke (Biessels *et al*., 2006). Recent epidemiologicstudies have highlighted its increasing prevalence worldwide,which is as high as 40% in people aged >20 years, with more than approximately 47million people affected in the United States alone (Allen *et al*., 2005).

Many features of metabolic syndrome are associated with insulin resistance. This means that the body does not use insulin efficiently to lower glucose in the blood. Insulin resistance is a combination of genetic and lifestyle factors which include diet, physical activity and perhaps, interrupted sleep patterns (Allen *et al*., 2005). Consistently high levels of insulin and glucose are linked to many harmful changes to the body, which usually damage the lining of coronary and other arteries. Insulin resistance is a key step toward the development of heart disease and stroke. Insulin resistance also results in an increase in triglyceride levels, which can block arteries and cause heart attacks and strokes (Xiong *et al*., 2006).

Metabolic syndrome is characterized by defective endogenous fibrinolysis withan enhancement of fibrinolysis inhibitors and will contribute to the increased risk of ischaemic stroke (Grundy *et al*., 2005).The impact of metabolic syndrome on global cardiovascular risk, ischaemic stroke risk, development of carotid atheromatosis, and other vascularеffects seem to be higher in women than in men (Yaffe *et al*., 2009). There are numerous risk factors, some modifiable but others are unmodifiable. Some risk factors which are controllable and modifiable are the components of the metabolic syndrome. Most of these components can be treated and managed with lifestyle modifications, and the earlier people addressed the risk factors and altered their behaviours, the earlier they could reduce the risk of developing any number of serious medical complications. Women with metabolic syndrome are also at an increased risk for dementia and

cognitive dysfunction (Iglseder *et al*., 2005). Some of the unmodifiable risk factors are age and family history or genetic predisposition.

2.3.1 BLOOD PRESSURE

Blood pressure is the force of blood pushing against the walls of the arteries as the heart pumps blood out of the arteries. It is also a pressure exerted by circulating blood on the walls of blood vessels (Booth, 1999). If this pressure rises and stays high over time (high blood pressure), it can damage the body in many ways.High blood pressure is a serious condition that can lead to coronary heart disease, heart failure, stroke, metabolic syndrome, kidney failure (Klabunde, 2005).

2.3.1.1 Systolic and diastolic blood pressure

There are two types of blood pressure which are systolic and diastolic blood pressure. Systolic blood pressure is the pressure which is exerted when the heart beats, while blood is being pumped. Diastolic blood pressure is the pressure which is exerted when the heart is at rest and between heart beats (Deakin and Low, 2000).

The mean blood pressure decreases as the circulating blood moves away from the heart through the arteries, has its greatest decrease in the small arteries and arterioles, and continues to decrease as the blood moves through the capillaries and back to the heart through veins (Klabunde, 2005).

There are many physical factors that influence arterial pressure; each of these may in turn, be influenced by factors such as diet, exercise, disease, drugs or alcohol, stress, and obesity (Yadav *et al*., 2007). The volume of blood flow from the heart is called the cardiac output which is the heart rate multiplied by the stroke volume (Grundy *et al*., 2005). Stroke volume is the amount of

blood pumped out from the heart with each contraction. The higher the heart rate then, the higher the arterial pressure (Rosenson *et al*., 2004). The more blood present in the body, the higher the rates of blood return to the heart and the resulting cardiac output (Guyton *et al*., 2000).

There is some relationship between dietary salt intake and increased blood volume, potentially resulting in higher arterial pressure, though this varies with the individual and is highly dependent on autonomic nervous system response and the renin-angiotensin system (Pesola *et al*., 2001).

The higher the resistance of circulation, the higher the arterial pressure upstream from the resistance to blood flow. Resistance is related to vessel radius vessel length, as well as the smoothness of the blood vessel walls. The larger the radius the lower the resistance and the longer the vessel the higher the resistance (Niiranen *et al*., 2006). Smoothness is reduced by the build-up of fatty deposits on the arterial walls, causing a high blood pressure (Struijk *et al*., 2008).

Vasoconstrictors reduce the size of blood vessels, thereby increasing blood pressure. Vasodilators, such as nitroglycerin increase the size of blood vessels, thereby decreasing arterial pressure (Mitchell, 2006).

Certain medical conditions can change the viscosity of the blood. Low red blood cell concentration, reducesviscosity, whereas increased red blood cell concentration increases viscosity(Yadav *et al*., 2007). Viscosity also increases with blood sugar concentration. Aspirin and related blood thinner drugs decrease the viscosity of blood, but studies have found that they act by reducing the tendency of the blood to clot, instead (Rosenson *et al*., 2004).

Each individual's autonomic nervous system responds to and regulates all these interacting factors so that although the above issues are important, the actual arterial pressure response of a

given individual varies widely because of both split-second and slow-moving responses of the nervous system and end organs (Struijk *et al*., 2008). These responses are very effective in changing the variables and resulting blood pressure from moment to moment.

2.3.2 High Arterial Pressure

Arterial hypertension can be an indicator of other problems and may have long-term adverse effects. Sometimes, it can be an acute problem, for example, hypertensive emergency. All levels of arterial pressure put mechanical stress on the arterial walls (Laurent, 2003). Higher pressures increase heart workload and progression of unhealthy tissue growth (atheroma) which develops within the walls of the arteries (Guyton *et al*., 2000).

The higher the pressure, the more unhealthy tissue would grow and tends to progress and the heart muscle tends to thicken, enlarge and become weaker over time(Yadav *et al*., 2007). Persistent hypertension is one of the risk factors for strokes, heart attacks, heart failure and arterial aneurysms, and is the leading cause of chronic renal failure(Pesola *et al*.,2001). Even moderate elevation of arterial pressure leads to shortened life expectancy (Laurent, 2003). At severely high pressures, mean arterial pressures 50% or more above average, a person is expected to live no more than a few years, unless appropriately treated (Guyton *et al*., 2000).

2.3.3 Low arterial pressure

Low blood pressure is also known as hypotension. Hypotension is a medical concern only if it causes signs or symptoms, such as dizziness, fainting, or in extreme cases, shock (National Heart Lung and Blood Institute, 2008). When arterial pressure and blood flow decrease beyond a certain point, the perfusion of the brain becomes critically decreased; that is, the blood supply is

not sufficient, causing light-headedness, dizziness, weakness or fainting. Sometimes, the arterial pressure drops significantly when a patient stands up from sitting. This is known as orthostatic hypotension or postural hypotension (Dugdale *et al*., 2009). Gravity also reduces the rate of blood return from the body veins below the heart and back to the heart, thus reducing stroke volume and cardiac output (Ausielle *et al*., 2007). In healthy conditions, the veins below the heart quickly constrict and the heart rate increases to minimize and compensate for the gravity effect (Pesola *et al*., 2001). This is carried out involuntarily by the autonomic nervous system. The system usually requires a few seconds to fully adjust and if the compensations are too slow or inadequate, the individual will suffer a reduced blood flow to the brain and this will result in dizziness and potential blackout (Struijk *et al*., 2008). Repositioning the body perpendicular to gravity largely eliminates the problem (Yadav *et al*., 2007). Other causes of low arterial pressure include haemorrhage, toxins including toxic doses of blood pressure medicine, hormonal abnormalities, such as Addison's disease (Gorelick and Mazzone, 2009).

Shock is a complex condition which leads to critically decreased perfusion. The usual mechanisms are loss of blood volume, pooling of blood within the veins, reducing adequate return to the heart and a low effective heart pumping. Low arterial pressure, especially low pulse pressure, is a sign of shock and contributes to and reflects decreased perfusion (Ausielle *et al*., 2007).

2.5 LIPID PROFILE

Lipid profile is a collective term given to the estimation of typically, total cholesterol, high density lipoprotein-cholesterol, low density lipoprotein-cholesterol, and triglycerides, used to assess risk of metabolic syndrome and coronary heart disease. It is recommended that healthy adults with no other risk factors for heart disease be tested for a fasting lipid profile once every

five years (Futterman and Lemberg, 1999). Individuals may also be screened using only a cholesterol test and not a full lipid profile.

Screening for a lipid profile is recommended for children and youth who are at an increased risk of developing heart disease in adulthood (Iso *et al*., 2004). Some of the risk factors are similar to those in adults and include a family history of heart disease or health problems such as diabetes, high blood pressure, or being overweight. A lipid profile may also be ordered at regular intervals to evaluate the success of lipid-lowering lifestyle changes, such as diet and exercise or to determine the effectiveness of drug therapy, such as statins (Hachinski *et al*., 1996)

2.5.1 Low-density lipoprotein (LDL)

Low-density lipoprotein is one of the five major groups of lipoproteins, which in order of size, largest to smallest, are chylomicrons, VLDL, LDL, IDL and HDL, that enable lipids like cholesterol and triglycerides to be transported within the water-based bloodstream. Blood tests typically report LDL-C, the amount of cholesterol contained in LDL. LDL particles can also transport cholesterol into the artery wall, retained there by arterial proteoglycans and attract macrophages which engulf the LDL particles and start the formation of plaques (Durrington and Guyton, 2003). Increased levels are associated with atherosclerosis (Hachinski *et al*., 1996).

Over time, vulnerable plaques rupture, activate blood clotting and produce arterial stenosis, which if severe enough, results in heart attack, stroke, and peripheral vascular disease symptoms and major debilitating events (Rosenson *et al*.,2004). LDL-C is commonly used to estimate how much low density lipoproteins are driving progressions of atherosclerosis (John *et al*., 2007). High levels of LDL particles cause health problems and cardiovascular disease (Segrest *et al*., 2001).

There is correlation between higher triglyceride levels and higher levels of smaller, denser LDL particles and alternately, lower triglyceride levels and higher levels of the larger, less dense LDL (John *et al*., 2007).The concentration and size of the LDL particles more powerfully relate to the degree of atherosclerosis progression than the concentration of cholesterol contained within all the LDL particles (Gary and Raeven, 2007). The healthiest pattern, though relatively rare, is to have small numbers of large LDL particles and no small particles. Small LDL particles, though common, is an unhealthy pattern; high concentrations of small LDL particles (even though potentially carrying the same total cholesterol content as a low concentration of large particles) correlates with much faster growth of atheroma, progression of atherosclerosis and earlier and more severe cardiovascular disease events and death (Durrington .and Guyton 2003). LDL particles, formed as VLDL lipoproteins, lose triglyceride through the action of lipoprotein lipase (LPL) and they become smaller and denser (i.e. fewer fat molecules with same protein transport shell), containing a higher proportion of cholesterol esters (Warnick, 1999).

LDL particles pose a risk for cardiovascular disease when they invade the endothelium and become oxidized, since the oxidized forms are more easily retained by the proteoglycans (Despres, 2007). A complex set of biochemical reactions regulate the oxidation of LDL particles, chiefly stimulated by presence of necrotic cell debris (Otvos, 1999) and free radicals in the endothelium.

2.5.2 Cholesterol

Cholesterol is a waxy steroid found in the cell membranes and transported in the blood plasma of all animals (Leah *et al*., 2009). It is an essential structural component of mammalian cell membranes, and is used to establish proper membrane permeability and fluidity. In addition, cholesterol is an important component for the manufacture of bile acids, steroid hormones, and

fat-soluble vitamins, including Vitamins A, D, E, and K (Pawlina and Michael, 2006). Cholesterol is the principal sterol synthesized by animals, but small quantities are synthesized in other eukaryotes, such as plants and fungi. It is almost completely absent among prokaryotes, which include bacteria (Pearson *et al*., 2010). Although cholesterol is an important and necessary molecule for animals, a high level of serum cholesterol is an indicator for diseases such as heart disease.

Since cholesterol is essential for all animal life, it is primarily synthesized from simpler substances within the body. However, high levels in blood circulation, depending on how it is transported within lipoproteins, are strongly associated with progression of atherosclerosis. It is excreted by the liver via the bile into the digestive tract. Typically about 50% of the excreted cholesterol is reabsorbed by the small bowel back into the bloodstream (Pawlina and Michael, 2006). Phytosterols can complete cholesterol re-absorption in intestinal tract back into the intestinal lumen for elimination (John *et al*., 2007).

Cholesterol is required to build and maintain membranes; it modulates membrane fluidity over the range of physiological temperatures (Benfante*et al*., 2004). The hydroxyl group on cholesterol interacts with the polar head groups of the membranephospholipids and sphingolipids, while the bulky steroid and the hydrocarbon chain are embedded in the membrane, alongside the non polarfatty acid chain of the other lipids. In this structural role, cholesterol reduces the permeability of the plasma membrane to protons and sodium ions (Haines and Guyton, 2007).

Within the cell membrane, cholesterol also functions in intracellular transport, cell signaling and nerve conduction. Cholesterol is essential for the structure and function of invaginated caveolae and clathrin-coated pits, including caveola-dependent and clathrin-dependent endocytosis

(Shuaib and Hachinski, 1991). The role of cholesterol in such endocytosis can be investigated by using methyl beta cyclodextrin (MβCD) to remove cholesterol from the plasma membrane (Benfante *et al*., 2004). Recently, cholesterol has also been implicated in cell signaling processes, assisting in the formation of lipid rafts in the plasma membrane (Di Mascio *et al*., 2005)

Within cells, cholesterol is the precursor molecule in several biochemical pathways. In the liver, cholesterol is converted to bile, which is then stored in the gallbladder. Bile contains bile salts, which solubilize fats in the digestive tract and aid in the intestinal absorption of fat molecules.

2.5.3 Triglyceride

A triglyceride is an ester derived from glycerol and three fatty acids. It is the main constituent of vegetable oil and animal fats (Nelson and Cox, 2000). The enzyme pancreatic lipase acts at the ester bond, hydrolysing the bond and releasing the fatty acids. Lipids cannot be absorbed by the duodenumas triglyceride.

Triglycerides, as major components of very-low-density lipoprotein (VLDL) and chylomicrons, play an important role in metabolism as energy sources and transporters of dietary fat. They contain more than twice as much energy (9 kcal/g or 38 kJ/) as carbohydrates and proteins (Parks, 2002). In the intestine, triglycerides are split into monoacylglycerol and free fatty acids in a process called lipolysis, with the secretion of lipases and bile, which are subsequently moved to absorptive enterocytes, cells lining the intestines. The triglycerides are rebuilt in the enterocytes from their fragments and packaged together with cholesterol and proteins to form chylomicrons. These are excreted from the cells and collected by the lymph system and transported to the large vessels near the heart before being mixed into the blood (Parks, 2002). Various tissues can capture the chylomicrons, releasing the triglycerides to be used as a source of energy. Fat and liver cells can synthesize and store triglycerides. When the body requires fatty acids as an energy

source, the hormone glucagon signals the breakdown of the triglycerides by hormone-sensitive lipase to release free fatty acids. As the brain cannot utilize fatty acids as an energy source (unless converted to ketone bodies), the glycerol component of triglycerides can be converted into glucose, via gluconeogenesis by conversion into dihydroxyacetone phosphate and consequently into glyceraldehyde 3-phosphate, for brain fuel when it is broken down.

Triglycerides cannot pass through cell membranes freely. Special enzymes on the walls of blood vessels called lipoprotein lipases must break down triglycerides into free fatty acids and glycerol. However, the relatively negative impact of raised levels of triglycerides, compared to that of LDL: HDL ratios is as yet unknown. The risk can be partly accounted for by a strong inverse relationship between triglyceride level and HDL-cholesterol level. Persons with a body mass index (BMI) equal to or greater than 28 kg/m^2 experienced a 30% increase in TAG concentration, while those with BMI less than $28kg/m^2$, experienced no change (Daley *et al*., 2004). These data demonstrate that certain characteristics (e.g. BMI) can make some individuals more sensitive with respect to lipid and lipoprotein changes when dietary carbohydrate is increased. Such characteristics that have been identified from previous work in this field, include BMI, insulin sensitivity (Coulsto and Cutler, 2009), concentration of TAG before the dietary change is made (Parks, 2002), hormone replacement therapy (Kasim *et al*., 2000), and genetic factors (Dreon and Booth, 2007).

2.5.4 High Density Lipoprotein

High-density lipoprotein (HDL) is one of the five major groups of lipoproteins. In healthy individuals, about thirty percent of blood cholesterol is carried by HDL (Gorelick, 1998). HDL particles are able to remove cholesterol from atheroma within arteries and transport it back to the

liver for excretion or re-utilization (Olson, 2008). Those with higher levels of HDL-C seem to have fewer problems with cardiovascular diseases.

HDL transports cholesterol mostly to the liver or steroidogenic organs, like adrenals, ovary, and testes by direct and indirect pathways. HDL is removed by HDL receptors, which mediate the selective uptake of cholesterol from HDL (Kwiterovich, 2000). In humans, probably the most relevant pathway is the indirect one, which is mediated by cholesteryl ester transfer protein (Barter *et al*., 2007). This protein exchanges triglycerides of VLDL against cholesteryl esters of HDL. As a result, VLDLs are processed to LDL, which are removed from the circulation by the LDL receptor pathway. The triglycerides are not stable in HDL, but get degraded by hepatic lipase so that finally, small HDL particles are left, which restart the uptake of cholesterol from cells (Kwiterovich, 2000).

The cholesterol delivered to the liver is excreted into the bile and, hence, intestine, either directly or indirectly after conversion into bile acids. Delivery of HDL cholesterol to adrenals, ovaries, and testes is important for the synthesis of steroid hormones (Daley *et al*., 2004). Several steps in the metabolism of HDL can contribute to the transport of cholesterol from lipid-laden macrophages of atherosclerotic arteries, termed foam cells, to the liver for secretion into the bile. This pathway has been termed reverse cholesterol transport and is considered as the classical protective function of HDL toward atherosclerosis (Barter *et al*., 2007).

HDL however, carries many lipid and protein species, several of which have very low concentrations but are biologically very active. For example, HDL and their protein and lipid constituents help to inhibit oxidation, inflammation, activation of the endothelium, coagulation,

and platelet aggregation (Kwiterovich, 2000). All these properties may contribute to the ability of HDL to protect from atherosclerosis, and it is not yet known which are the most important.

In the stress response, serum amyloid A, which is one of the acute-phase proteins and an apolipoprotein, is under the stimulation of cytokines (IL-1, IL-6), and cortisol produced in the adrenal cortex and carried to the damaged tissue incorporated into HDL particles. At the inflammation site, it attracts and activates leukocytes. It has been postulated that the concentration of large HDL particles more accurately reflects protective action, as opposed to the concentration of total HDL particles (Kwiterovich, 2000).

2.6 BLOOD SUGAR

Blood sugar concentration, or glucose level, refers to the amount of glucose present in the blood of a human or animal. Normally, in mammals the blood glucose level is maintained at a reference range between about 3.6 and 5.8 mM (mmol/l) (Ronald *et al*., 2001). It is tightly regulated as a part of metabolic homeostasis.

Mean normal blood glucose levels in humans are about 90 mg/dl, equivalent to 5mM (mmol/l) (Ronald *et al*., 2001). The total amount of glucose normally in circulating human blood is therefore, about 3.3 to 7g (assuming an ordinary adult blood volume of 5 litres, for an average adult male) (John *et al*., 2007). Glucose levels rise after meals for an hour or two by a few grams and are usually lowest in the morning, before the first meal of the day. Transported via the bloodstream from the intestines or liver to body cells, glucose is the primary source of energy for body's cells, fats and oils (ie, lipids) being primarily a compact energy store.

Failure to maintain blood glucose in the normal range leads to conditions of persistently high (hyperglycaemia) or low (hypoglycaemia) blood sugar. Diabetes mellitus, characterized by persistent hyperglycaemia from any of several causes, is the most prominent disease related to carbohydrate metabolism. The fasting blood glucose (FBG) level is the most commonly used indication of overall glucose homeostasis, largely because perturbing events such as food intake are avoided. Abnormalities in these test results are due to problems in the multiple control mechanisms of glucose regulation.

The metabolic response to a carbohydrate challenge is conveniently assessed by a postprandial glucose level, drawn two hours after a meal or a glucose load. The glucose tolerance test, consisting of several timed measurements, after a standardized amount of oral glucose intake, is used to aid in the diagnosis of diabetes. It is regarded as the gold standard of clinical tests of the insulin glucose control system, but is difficult to administer, requiring much time and repeated blood tests (Shuaib and Hachinski, 1991). Note that food commonly includes carbohydrates which do not participate in the metabolic control system; an example being simple sugars, such as fructose, many of the disaccarhides (which either contain simple sugars other than glucose but cannot be digested by humans) and the more complex carbohydrate which also cannot be digested by humans. There are some carbohydrates which are not digested even with the assistance of gut bacteria; examples being several of the fibres (soluble or insoluble). Food also commonly contains components which affect glucose (and other sugars') digestion. Fat, for example slows down digestive processing, even for such easily handled food constituents as starch (Ronald *et al*., 2001). Avoiding the effects of food on blood glucose measurement is important for reliable results since those effects are so variable.

Finally, there are several influences on blood glucose level aside from food intake. Infection, for instance, tends to change blood glucose levels, as does stress, either physical or psychological (Ronald *et al*., 2001). Exercise, especially if prolonged or long after the most recent meal, will have an effect, as well (Graham and Gennareli, 2000). In the normal person, maintenance of blood glucose at near constant levels will nevertheless be quite effective.

2.7 LIVER FUNCTION TEST

Liver function tests refer to clinical biochemistry laboratory blood assays, designed to give information about the state of a patient's liver (Lee, 2004). The parameters measured include albumin, bilirubin (direct and indirect) and others. Liver transaminases; aspartate aminotransferase/alanine aminotransferase (AST/ALT) are biomarkers of liver injury in a patient with some degree of disturbed liver function (McClatchey and Kenneth, 2002). Most liver diseases cause only mild symptoms initially, but it is vital that these diseases be detected early. Hepatic involvement in some diseases can be of crucial importance.

2.7.1 Alanine aminotransferase (ALT)

Significantly elevated levels of ALT often suggest the existence of medical problems, such as viral hepatitis, diabetes, congestive heart failure, liver damage by other causes, bile duct problems, infectious mononucleosis (Goldberg and Kirschm 1996). Elevated ALT may also be caused by dietary choline deficiency (Kochhar and Christen, 2002). However, elevated levels of ALT do not automatically mean that medical problems exist. Fluctuation of ALT levels is normal over the course of the day, and ALT levels can also increase in response to strenuous physical exercise (Lee, 2004).

When elevated ALT levels are found in the blood, the possible underlying causes can be further narrowed down by measuring other enzymes. For example, elevated ALT levels due to liver cell

damage can be distinguished from biliary duct problems by measuring alkaline phosphatase (Goldberg and Kirschm, 1996). Also, myopathy-related ALT increases can be ruled out by measuring creatine kinase enzymes (Lee, 2004). Many drugs may elevate ALT levels, including Zileuton, anti-inflammatory drugs, antibiotics, cholesterol medications, and anti-convulsants (Goldberg and Kirschm, 1996).

2.7.2 Aspartate aminotransferase (AST)

AST is similar to alanine transaminase (ALT) in that both enzymes are associated with liver parenchymal cells (Perry *et al.,* 1998). The difference is that ALT is found predominantly in the liver, with clinically negligible quantities found in the kidneys, heart, and skeletal muscle, while AST is found in the liver, heart (cardiac muscle), skeletal muscle, kidneys, brain, and red blood cells (Hayashi *et al*., 2003). ALT is a more specific indicator of liver inflammation than AST, as AST may be also elevated in diseases affecting other organs, such as myocardial infarction, acute pancreatitis, acute haemolytic anaemia, severe burns, acute renal disease, musculoskeletal diseases, and trauma (Goldberg and Kirschm, 1996). AST was defined as a biochemical marker for the diagnosis of acute myocardial infarction in 1954 (Perry *et al.,* 1998) however, the use of AST for such a diagnosis is now redundant and has been superseded by the cardiac troponins (Kochhar and Christen 2002).

2.7.3 Gamma-glutamyltransferase (GGT)

γ-Glutamyltransferase is an enzyme that transfers gamma-glutamyl group (Yokoyama, 2007). It is found in many tissues, most notably the liver and has significance in medicine as a diagnostic marker (Rosalki *et al*., 1998). GGT is present in the cell membranes of many tissues, including the kidneys, bile duct, pancreas, liver, spleen, heart, brain and seminal vesicles (Goldberg and Thompson,1999). It is involved in the transfer of amino acids across the cellular membrane

(Meister, 2004) and also participates in leukotriene metabolism (Raulf *et al*., 2006). Its involvement in glutathionemetabolism allows the transfer of the glutamylmoiety to a variety of acceptor molecules, including water, certain L-amino acids, and peptides, leaving the cysteine product to preserve intracellularhomeostasis of oxidant status (Schulman *et al*.,1999, Yokoyama, 2007).

2.7.3.1 Diagnostic Significance of GGT

γ-Glutamyltransferase has several uses as a diagnostic marker in medicine. Elevated serum GGT activity can be found in diseases of the liver, biliary system, and pancreas (Schulman *et al*., 1999). In this respect, it is similar to alkaline phosphatase (ALP) in detecting disease of the biliary tract. The two markers correlate well, though there is conflicting data about whether GGT has better sensitivity (Betro *et al*., 2002; Lumet and Gambino, 2003).

ALP is still the first test for biliary disease. The main value of GGT over ALP is in verifying that ALP elevations are due to biliary disease; ALP can also be increased in certain bone diseases, but GGT is not (Lumet and Gambino, 2003). GGT is elevated by large quantities of alcohol ingestion (Lamy *et al*., 2005). Isolated elevation or disproportionate elevation, compared to other liver enzymes such as ALP or ALT indicates alcohol abuse or alcoholic liver disease (Kaplan *et al*., 1995). It also indicates excess alcohol consumption up to 3 or 4 weeks prior to the test. Alcohol increases GGT production by inducing hepatic microsomal enzyme production and it causes the leakage of GGT from hepatocytes (Barouki *et al*., 2004).Numerous drugs raise GGT levels, including barbiturates and phenytoin (Rosalki *et al*., 1998). Elevated levels of GGT may also be due to congestive heart failure.

CHAPTER THREE

3.0 METHODOLOGY

3.1 SELECTION OF PATIENTS

Stroke in-patients were selected from the Komfo Anokye Teaching Hospital (KATH) in Kumasi, from specific wards for male and female stroke patients. There were 117 males and 107 females within an age range of 25-120 years.

The inclusion criteria for the selection were patients who have had a stroke in less than twenty-four hours without any medication. The patients were those admitted with sudden onset of characteristic neurological deficit and having distinctive neurological signs. Patients with loss of consciousness due to head injury, coma, trauma, tumour, poisoning or epilepsy were not included. This was a cross-sectional study. A questionnaire was administrated to each patient's caregiver in order to obtain the following information; demographic features (age, sex), socio-economic status (education and employment), medical history with specific attention to hypertension and diabetes and lifestyle (smoking and drinking). The study started from October 2009 and ended in January 2011. The control subjects (100) within an age range of 28-80 years were recruited from the Clinical Analysis Laboratory at KNUST.

The Committee for Human Research Publications and Ethics of the Komfo Anokye Teaching Hospital gave the approval for the study.

3.2 LABORATORY TESTS

The following laboratory tests were carried out:

1. Lipid profile

2. Liver function tests, including determination of AST, ALT and GGT

3. Fasting blood sugar

4. Blood pressure

3.2.1 Specimen collection and processing

About 5 ml of venous blood specimens were collected into non- anticoagulated tubes and were labeled with patients identifications. Another 5 ml of their blood were also collected into ethylenediaminetetra acetic acid (EDTA) tubes. The blood specimens in both tubes were centrifuged to obtain serum and plasma, respectively. The samples were centrifuged in a speed of 12000-13000 rpm at 5 minutes.

3.2.2 Fasting blood sugar

The test was done with Biotechnical Instrument (BT-3000 PLUS; made in Vila do Conde, Portugal) an automated analyzer (Fig 3.1).Taylor and Taylor reagents (Taylor and Taylor Company Limited in England) were used and the analyser read the results between 400-800 nm. The patients' plasma was put into sample tubes with their identifications. These were loaded onto a sample plate of the analyzer. Command "run" was issued and the results were read after 30 minutes.

3.2.2.1. Glucose Oxidase Method

Glucose oxidase catalyses the oxidation of glucose to gluconic acid and hydrogen peroxide. The H_2O_2 is broken down to water and oxygen by a peroxidase in the presence of an oxygen acceptor which in turn, is converted to a coloured compound, the amount of which can be measured colorimetrically (Hawk, 2006).

3.2.3 Lipid profile

Fifty microlitres (50 µl) of serum samples were put into sample tubes which were labeled with the patients' identifications. The samples were uploaded onto the sample plate of the analyzer. A command "run" was issued and results were printed out after 30 minutes.

3.2.3.1 Principle for triglyceride

The serum lipids are extracted by isopropanol, which also precipitates serum proteins. The interfering phospholipids, containing glycerol as integral part, are removed by adsorption on alumina. Filtrate is used for saponification and glycerol is separated from triglycerides. Action of metaperiodate converts glycerol into glyceraldehyde, which forms a yellow coloured complex with acetyl acetone. The intensity of the coloured complex is measured at 410nm (Hawk, 2006).

3.2.3.2 Principle for cholesterol

Cholesterol esters are hydrolysed by cholesterol ester hydrolase to free cholesterol and fatty acids. The free cholesterol produced and pre-existing molecules are oxidised by cholesterol oxidase to Cholesten-4-en-3-one and hydrogen peroxide. Peroxidase acts on hydrogen peroxide and liberates oxygen which reacts with the chromogen (4-amino phenazone/phenol) to form a red coloured compound which is read at 510 nm (Hawk, 2006).

3.2.3.3 Principle for HDL-C

In the presence of phosphotungstic acid and magnesium chloride, LDL, VLDL and chylomicrons are precipitated. Centrifugation leaves only the HDL in the supernatant. Cholesterol in the HDL fraction was measured per the assay principle given for cholesterol, and absorbance measured at 510nm (Hawk, 2006).

3.2.3.4 Principle for LDL-C

LDL-C reacts with sulphuric acid, phosphoric acid and vanillin to form pink colour complex. (Hawk, 2006).

3.2.4 Liver function tests

Fifty microlitres (50 µl) of serum samples were put into sample tubes which were labeled with the patients identifications. The samples were uploaded onto the sample plate of the analyzer. A command "run" was issued and results were printed out after 30 minutes.

3.2.4.1 Estimation of Aminotransferases

The amount of oxaloacetate or pyruvate produced by transamination is reacted with 2,4-dinitrophenyl hydrazine (DNPH) to form a brown-coloured hydrazone, the colour intensity of which is measured in alkaline solution at 520 nm (Hawk, 2006).

3.2.4.2 GGT

The quantitative method to measure GGT involved a reaction for the formation of a dye that is the chromophore, the change to L-γ-glutamyl-*p* –nitroanilide. Due to the poor solubility and stability of L-γ-glutamyl-*p* –nitroanilide, this product was modified by use of substrate, L-γ-glutamyl-3-carboxy-4-nitroanilide. The addition of a sample containing gamma-

glutamlytransferase to the substrate, L-γ-glutamyl-3-carboxy-4-nitroanilide and glycylglycine, leads to the formation of L-γ-glutamyl- glycylglycine and 3-carboxy-4-nitroanilide. The absorbance of the chromophore is measured at a wavelength of 405 nm. The production of 3-carboxy-4-nitroanilide is proportional to the activity of GGT in the sample (Hawk, 2006).

3.3 BLOOD PRESSURE

Blood pressure was taken using a mercury sphygmomanometer and stethoscope. Measurements were taken from the left upper arm after patients had been sitting for 5 minute in accordance with recommendation of American Heart Association (Booth, 1999).The stroke patients were in a wheel chair for the measurement. Duplicate measurements were taken with a 5 minute rest interval between measurements and the mean value was recorded to the nearest 2.0mmHg.

3.4 QUALITY CONTROL MEASURES

Care was taken to ensure that the assay methods produced reliable results. Assays (Assay raegents for the individual reagents from Taylor and Taylor Company from England) reagents for manufacturer's quality control samples were performed every day before the test specimens were performed to give assurance that the method was performing satisfactorily.

The sample tubes were placed carefully on the sampler. The required quantity of reagent was dispensed by a reagent probe, in the reaction cups. The specimen containers were labelled appropriately before the specimen collection. It was ensured that the patients were in fasting state before blood samples were taken, for the lipid profile and blood glucose determinations.

Figure 3.1 BT 3000 PLUS

3.5 DEFINITION OF THE METABOLIC SYNDROME

NCEP-ATP CRITERIA

The US National Cholesterol Education Program Adult Treatment Panel III (2001) requires at least, three of the following:

Central obesity: waist circumference ≥ 102 cm or 40 inches (male), ≥ 88 cm or 36 inches 54 (female)

Triglyceride ≥ 1.7 mmol/L,

HDL-C < 1.03mmol,L (male), < 1.29mmol/L(female)

Blood pressure ≥ 130/85 mmHg,

Fasting plasma glucose ≥ 6.1 mmol/L (110 mg/dl)

WHO CRITERIA

The prevalence of the metabolic syndrome was also defined by WHO criteria. A participant had WHO-defined metabolic syndrome if he or she had diabetes, impaired glucose tolerance, impaired fasting glucose or insulin resistance, plus two or more of the following abnormalities:

Blood pressure: ≥ 140/90 mmHg

Dyslipidaemia:

Triglycerides (TG): ≥ 1.695 mmol/L and high density lipoprotein-cholesterol

(HDL-C) ≤ 0.9 mmol/L (male), ≤ 1.0 mmol/L (female).

Central obesity: waist:hip ratio > 0.90 (male); > 0.85 (female), or body mass index > 30 kg/m²

Microalbuminuria: urinary albumin excretion ratio ≥ 20 μg/min or albumin:creatinine ratio ≥ 30 mg/g.

3.6 STATISTICAL ANALYSIS

Statistical analysis was conducted by calculating simple means and standard error of mean for continuous variables, and frequency counts and percentages for categorical variables. Fischer's, test, Pearson's correlation and student's t-test analyses were carried out on variables. Significance was set at $p<0.05$. All analyses were performed with the SPSS 16.0 for Windows 2000 software. The laboratory parameters determined were fasting blood sugar, lipid profile, blood pressure, AST, ALT and GGT.

CHAPTER FOUR

4.0 RESULTS

4.1 CHARACTERISTICS OF STROKE PATIENTS

From Table 1, the mean age of all the stroke patients was 65.64(8.75) SD years. The mean systolic and diastolic blood pressures for the patients were 179.80 and 107.80 mmHg respectively. Whereas about 15% of the patients smoked cigarette, about 30% of the patients consumed alcoholic beverages. Over half of the patients were known hypertensive patients (i.e. 51.3%), about 32%, known diabetics. Seven of the stroke patients died, which constitute 3% of the stroke patients during the course of the study.

The mean age, as well as the mean systolic and diastolic blood pressure of the female participants was similar to that of their male counterparts. The proportions of the male participants who smoked cigarettes (26.5%) and consumed alcoholic beverages (47.0%) were significantly higher, as compared to the females who smoked (1.9%) and consumed alcoholic beverages (12.1%) as shown in Table 1.

Except for the mean triglyceride level that was significantly ($p = 0.0426$) higher among the male participants (2.83) as compared to the female subjects (2.25), all the other lipid profile parameters were similar in both genders. The mean levels of the markers of liver dysfunction were also similar in both genders. Fasting blood glucose level was significantly higher ($p = 0.0454$) in the male subjects (8.79 [1]), as compared to their female counterparts (7.58) as shown in

Table 1.

Variable	Total (n=224)	Female (n=107)	Male (n=117)	P value
Socio-demographic data				
Age (years)	65.64(8.75)	67.51(14.30)	63.92 (10.47)	0.0965
SBP (mmHg)	179.80(46.53)	180.60 (66.25)	179.10 (65.71)	0.8293
DBP (mmHg)	107.80(24.19)	107.30 (31.49)	108.20 (36.51)	0.8454
Smoking	33(14.7%)	2(1.9%)	31(26.5%)	< 0.0001
Alcohol	68(30.4%)	13(12.1%)	55(47.0%)	< 0.0001
Lipid profile				
LDL-C (mmol/l)	3.10(0.44)	3.17 (0.46)	3.02 (0.73)	0.7665
HDL-C (mmol/l)	1.77(0.17)	1.92 (0.32)	1.64 (0.18)	0.2875
TG (mmol/l)	2.52(0.22)	2.25 (0.26)	2.83 (0.39)	0.0426
TC (mmol/l)	3.81(0.35)	3.54 (0.49)	4.06 (0.50)	0.1523
Liver function test				
AST (U/L)	30.02(5.42)	29.34 (7.20)	31.08 (8.08)	0.3778
ALT (U/L)	26.85(5.39)	24.82 (5.13)	27.52 (6.82)	0.1113
GGT (U/L)	35.54(8.88)	34.13 (9.99)	35.14 (10.14)	0.6782
FBS (mmol/l)	8.21(0.86)	7.58 (1.10)	8.79 (1.33)	0.0454
Medical History				
Known hypertensive	115(51.3%)	50(46.7%)	65(55.6%)	0.2285
Known diabetes	71(31.7%)	30(28.0%)	41(35.0%)	0.3145
Death	7(3.1%)	6(5.6%)	1(0.9%)	0.0562

Table 1: General characteristics of the study population stratified by gender

Continuous data are presented as mean (standard deviation) and categorical data presented as proportion. The continuous data were compared using unpaired t-test whilst categorical data were compared using Fischer's exact test.

Meanings of abbreviations;Gamma-glutamyltransferase (GGT), Aspartate aminotransferase (AST),Alanine aminotransferase (ALT),Systolic Blood Pressure (SBP), Diastolic Blood Pressure

(DBP), Total Cholesterol (TC), Triglyceride (TG),High Density Lipoprotien-cholesterol (HDL-C),Low Density Lipoprotien-cholesterol (LDL-C),Fasting Blood Sugar (FBS).

The highest prevalence of lipid disorder was seen in hypertriglyceridaemia (55.8%), followed by reduced HDL-cholesterol (30.8%), hypercholesterolaemia (23.2%) and increased LDL cholesterol level (17.9%) as shown in Table 2. When the studied population was stratified based on gender, there was no significant difference in the percentages of the various dyslipidaemia parameters, and the orders of dyslipidaemia were similar to that of the total studied population.

Using the blood pressure grading system (World Health Organisation/ International Society of Hypertension, 1999), about 63% of the patients met the severe hypertension criterion, followed by mild, moderate and high normal blood pressure. When the classification was done by gender, there were no significant differences in the level of the various grading (Table 2).

Whereas about 20% of the entire patients' population had their AST level raised, 7.1% had their ALT level raised and 14.7% had their GGT level raised above the normal level (Table 2).

More than half of the patients had hyperglycaemia (56.7%), impaired fasting glucose was seen in about 10% and diabetes was found in about 47% of the patients. Significant proportion of the male subjects had hyperglycaemia (65.0%) and diabetes (53.8%) as compared to their female counterparts, in whom 47.7% were hyperglycaemia and 40.2% were diabetic.

Table 2: Prevalence of dyslipidaemia, hypertension, and abnormal liver function test and glycaemic control disorders

Variables	Cut off or ranges		Total n=224	Female n=107	Male n=117	P value
Dyslipidaemia						
Hypercholesterolaemia	TC (>5.2 mmol L^{-1})		52/224(23.2%)	21/107(19.6%)	31/117(26.5%)	0.2681
Hypertriglyceridaemia	TG (>1.8 mmol L^{-1})		125/224(55.8%)	58/107(54.2%)	67/117(57.3%)	0.6872
Reduced HDL cholesterol	HDL-C (<1.0 mmol L^{-1})		69/224(30.8%)	32/107(29.9%)	37/117(31.6%)	0.8849
Increased LDL cholesterol	LDL-C (>4.1 mmol L^{-1})		40/224(17.9%)	22/107(20.6%)	18/117(15.4%)	0.3830
Blood pressure disorder						
Blood pressure category	Systolic	Diastolic				
Optimal	<120mmHg	<80mmHg	13/18(72.2%)	5/7(71.4%)	8/11(72.7%)	1.0000
Normal	120-129	80-84	3/12(25.0%)	1/7(14.3%)	2/5(40.0%)	0.5227
High normal	130-139	85-89	1/21(4.8%)	1/12(8.3%)	0/9(0.0%)	1.0000
Mild	140-159	90-99	16/29(55.2%)	7/14(50.0%)	9/15(60.0%)	0.7152
Moderate	160-179	100-109	10/43(23.3%)	2/16(12.5%)	8/27(29.6%)	0.2757
Severe	≥180	≥110	64/101(63.4%)	32/51(62.7%)	32/50(64.0%)	1.0000
Liver dysfunction						
AST (U L^{-1})	> 40		44/224(19.6%)	17/107(15.9%)	27/117(23.1%)	0.1835
ALT (U L^{-1})	> 40		16/224(7.1%)	11/107(10.3%)	15/117(12.8%)	0.6772
GGT (U L^{-1})	> 50		33/224(14.7%)	15/107(14.0%)	18/117(15.4%)	0.8513
Glycaemic control disorders						
Hyperglycaemia	FBS ≥ 6.1 mmol L^{-1}		127/224(56.7%)	51/107(47.7%)	76/117(65.0%)	0.0105
Impaired Fasting Glucose	FBS 6.1 to 6.9 mmol L^{-1}		21/224(9.4%)	8/107(7.5%)	13/117(11.1%)	0.3706
Diabetes	FBS ≥ 7.0 mmol L^{-1}		106/224(47.3%)	43/107(40.2%)	63/117(53.8%)	0.0453

The proportions of the various blood pressure classifications (World Health Organisation/ International Society of Hypertension, 1999), calculated out of the total male and female studied population is as shown in Figure 4.1. Optimal, normal, high normal, mild, moderate and severe blood pressure were similar in both genders (i.e. 4.7% *vs.* 6.8%, 0.9% *vs.* 1.7%, 0.9% *vs.* 0.0%, 6.5% *vs.* 7.7, 1.9% *vs.* 6.8%, 29.9% *vs.* 27.4% and 5.65 *vs.* 12.0% for Optimal, normal, high normal, mild, moderate and severe blood pressure respectively).

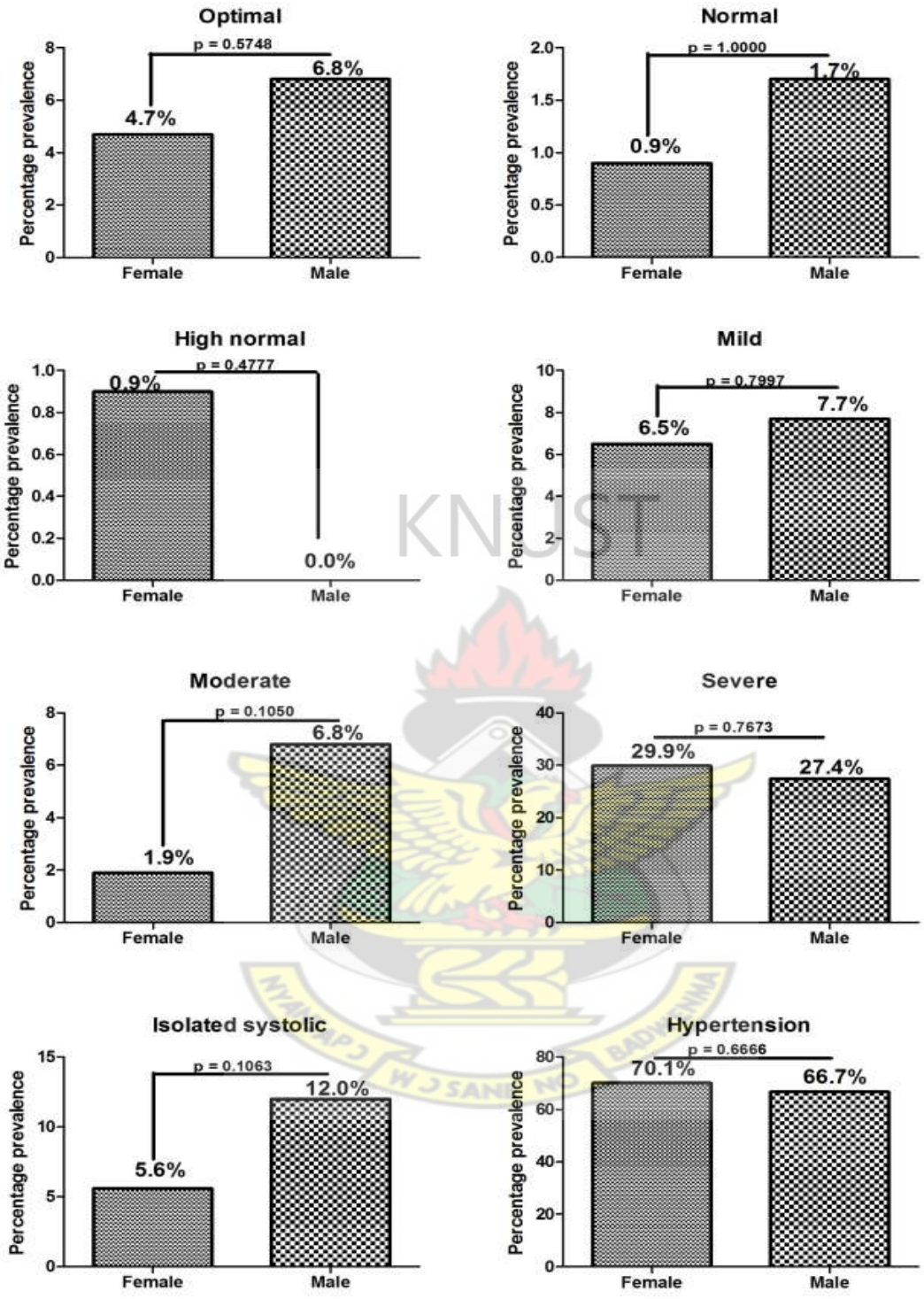

Figure 4.1: Proportions of the various blood pressure grading for female and male subjects

LDL-cholesterol correlates less positively with HDL-cholesterol ($r = 0.21$; $p < 0.05$),but more positively with triglyceride ($r = 0.48$; $p < 0.001$) and total cholesterol ($r = 0.44$; $p < 0.001$). Triglyceride correlates less positively with HDL-cholesterol ($r = 0.28$; $p< 0.05$) but more positively with total cholesterol ($r = 0.58$; $p < 0.001$) as shown in Table 3.

Among the male subjects, age increases with fasting blood glucose ($r = 0.25$; $p < 0.01$). Triglyceride is directly associated with LDL-cholesterol, HDL-cholesterol, total cholesterol and fasting blood glucose level (Table 3). LDL-cholesterol and total cholesterol had direct relationship from this study ($r = 0.41$; $p <0.001$). Indicators of blood pressure as well as markers of liver dysfunction correlate positively with each other (Table 3).

Table 3: Table 3: Pearson Product Moment Correlation Coefficient of serum biochemical parameters and anthropometric data for female (upper right-hand side) and male (lower left-hand side)

	AGE	**LDL**	**HDL**	**TG**	**TC**	**SBP**	**DBP**	**AST**	**ALT**	**GGT**	**FBS**
AGE		-0.10	-0.02	-0.02	-0.17	0.05	0.00	-0.17	**-0.19***	**-0.33*****	0.12
LDL	0.11		**0.21***	**0.48*****	**0.44*****	-0.16	-0.12	-0.06	-0.01	-0.03	-0.03
HDL	-0.04	-0.01		**0.28****	0.05	-0.07	-0.08	-0.01	0.00	0.02	-0.17
TG	0.05	**0.41*****	**0.22***		**0.58*****	**-0.24***	**-0.20***	0.04	0.10	-0.03	0.03
TC	-0.09	**0.41*****	0.16	**0.74*****		-0.18	-0.06	0.02	0.01	-0.01	-0.02
SBP	0.12	-0.13	-0.10	-0.16	**-0.30*****		**0.73*****	-0.09	-0.04	0.03	-0.03
DBP	0.10	-0.13	-0.05	-0.11	**-0.27****	**0.77*****		-0.05	-0.07	0.02	0.08
AST	-0.09	-0.01	0.07	0.00	-0.04	0.01	0.07		**0.65*****	**0.43*****	0.00
ALT	-0.11	0.00	0.07	0.01	-0.03	-0.01	0.04	**0.98*****		**0.49*****	-0.11
GGT	-0.07	-0.06	0.10	-0.06	-0.11	0.09	0.15	**0.75*****	**0.67*****		-0.11
FBS	**0.25****	0.06	-0.01	**0.27****	0.14	-0.11	-0.04	-0.07	-0.05	-0.10	

***Correlation is significant at the 0.05 level (2-tailed), **Correlation is significant at the 0.01 level (2-tailed), ***Correlation is significant at the 0.001 level (2-tailed).**

4.2 CHARACTERISTICS OF CONTROL SUBJECTS

Table 4: General characteristics of the control population stratified by gender

Parameters	Males n=48	Female n=52	p – value
AGE (Years)	65.72(8.43)	64.31(11.88)	0.856
FBS (mmol/L)	5.01(0.36)	5.09(0.45)	0.767
Diastolic BP (mmHg)	70.98(11.71)	71.44(11.92)	0.816
Systolic BP (mmHg)	133.20(24.81)	136.30(23.70)	0.376
Total –C(mmol/L)	3.40(0.37)	3.20(0.38)	0.498
Triglyceride(mmol/L)	0.94(1.02)	0.83(0.95)	0.076
LDL-C (mmol/L)	2.93(0.22)	2.97(0.21)	0.820
HDL-C (mmol/L)	1.55(0.14)	1.67(0.09)	0.542

Continuous data are presented as mean (Standard deviation) and categorical data presented as proportion. The continuous data were compared using unpaired t-test whilst categorical data were compared using Fischer's exact test.

From Table 4, the mean age of the control male subjects was 65.72 and that of females was 64.31 years. The mean age, as well as the mean systolic and diastolic blood pressure of the female participants was similar to that of their male counterparts. All the other lipid profile parameters were similar in both genders. Fasting blood sugar level was similar (p = 0.767) in the female subjects (5.09mmol l^{-1}) and their male counterparts (5.026mmol l^{-1}).

4.3 USE OF NCEP FOR IDENTIFYING SUBJECTS WITH METABOLIC SYNDROME.

The US National Cholesterol Education Program Adult Treatment Panel III (2001) requires at least, three of the following:

Central obesity: waist circumference ≥ 102 cm or 40 inches (male), ≥ 88 cm or 36 inches 54 (female)

TG ≥ 1.7 mmol/L

HDL-C < 1.03mmol,L (male), < 1.29mmol/L(female)

Blood pressure ≥ 130/85 mmHg

Fasting plasma glucose ≥ 6.1 mmol/L (110 mg/dl)

Table 5: Proportions of stroke patients with dyslipidaemia, hyperglycaemia and elevated blood pressure according to NCEP criteria

M.S Components	Female n=107	Male n=117	Total N=224
Triglycerides (≥1.7mmol/L)	64(28.57)	74(33.04)	138(61.61)
HDL – C (<1.03mmol/L for male, <1.29mmol/L for female)	52(23.21)	40(17.86)	92(41.07)
Fasting Blood Sugar (≥ 6.1mmol/L)	51(22.77)	76(33.93)	127(56.70)
Blood Pressure (≥ 130/85 mmHg)	85(37.95)	89(39.73)	174(77.68)

Where, n=frequency and the corresponding percentage in parentheses

The proportions of patients with dyslipidaemia, according to NCEP criteria were determined, based on the sex of the stroke patients. The percentages of patients with elevated triglyceride, elevated sugar and high blood pressure were higher in males than in the females while reduced HDL-C was higher in the females than males.

Table 6: Proportion of stroke patients by age having components of metabolic syndrome according to NCEP criteria

M.S Components	Age (years)						
	25 - 40	41 - 56	57 - 72	73 - 88	89 - 104	105 - 120	TOTAL
Blood Pressure (≥130/85 mmHg)	6(2.68)	38(16.96)	86(38.39)	36(16.07)	5(2.23)	3(1.34)	174(77.68)
Triglycerides (≥1.7 mmol/L)	4(1.79)	20(8.92)	68(30.34)	36(16.07)	7(3.12)	3(1.34)	138(61.61)
HDL – C (<1.03 mmol/L for male, <1.29 mmol/L for female)	5(2.23)	19(8.48)	41(18.30)	22(9.82)	3(1.34)	2(0.89)	92(41.07)
Fasting Blood Sugar (≥ 6.1mmol/L)	2(0.89)	17(7.58)	60(26.79)	44(19.64)	4(1.79)	0(0.00)	127(56.70)

Where, n=frequency and the corresponding percentage in parentheses

The proportions of patients with various metabolic risk factors were stratified by their ages, according to NCEP criteria. From Table 6, the ages between 57-72 had the highest frequencies for all the components. The risk factor of highest prevalence was seen in blood pressure which had a total of 174(77.68%). This was followed by triglyceride for which 138(61.61%) of the subjects had elevated values. The HDL-C posed the lowest risk.

Table 7: Prevalence of metabolic syndrome components according to NCEP Criteria for stroke patients

Sex	M.S Components				
	0	1	2	3	Total
Female	4(3.74)	18(16.82)	35(32.71)	50(46.73)	107(100)
Male	5(4.27)	18(15.38)	39(33.33)	55(47.01)	117(100)
Total	9(4.02)	36(16.07)	74(33.04)	105(46.88)	224(100)

Where, n = frequency and the corresponding percentage in parentheses

The prevalence of metabolic syndrome components according to NCEP criteria was determined for stroke patients according to the subjects who had the designated risk factors. According to Table 7, it was only nine of the patients (4.02% of the overall population) who did not have any of the risk factors or components of metabolic syndrome. On the other hand, the patients who had metabolic syndrome; that is, those who had three of the risk factors were 105, constituting 46.88% of the overall population. The percentages of the patients with metabolic syndrome in both sexes were almost the same; 47.01% were males, compared to 46.73% of females.

4.4 USE OF WHO CRITERIA FOR DETERMINING PRESENCE OF METABOLIC SYNDROME

The World Health Organization criteria (1999) require presence of one of diabetes mellitus, impaired glucose tolerance, impaired fasting glucose or insulin resistance, and two of the following:

Blood pressure: ≥ 140/90 mmHg

Dyslipidaemia: triglycerides (TG): ≥ 1.695 mmol/L and high density lipoprotein-cholesterol (HDL-C) ≤ 0.9 mmol/L (male), ≤ 1.0 mmol/L (female)

Central obesity: waist:hip ratio > 0.90 (male); > 0.85 (female), or body mass index > 30 kg/m²

Microalbuminuria: urinary albumin excretion ratio ≥ 20 μg/min or albumin:creatinine ratio ≥ 30 mg/g

Table 8: Proportions of stroke patients with dyslipidaemia, hyperglycaemia and elevated blood pressure according to WHO criteria

M.S Components	Female	Male	Total
Triglycerides (≥1.6957mmol/L)	63(28.13)	75(33.48)	138(61.61)
HDL – C (≤0.9mmol/L for male, ≤ 1.0mmol/L for female)	34(15.18)	39(17.41)	73(32.58)
Fasting Blood Sugar (≥ 6.1mmol/L)	51(22.77)	76(33.93)	127(56.69)
Blood Pressure (≥ 140/90 mmHg)	86(38.39)	96(42.86)	174(81.25)

Where, n = frequency and the corresponding percentage in parentheses

The proportions of patients with dyslipidaemia, according to WHO criteria were determined, according to the sex of the stroke patients. The percentage of patients with elevated triglyceride, elevated sugar and high blood pressure were higher in males than in the females while reduced HDL-C was higher in the females than males.

Table 9: Proportion of stroke patients by age, having components of metabolic syndrome according to WHO criteria

M.S Components	Age (years)						
	25 - 40	41 - 56	57 – 72	73 - 88	89 - 104	105 - 120	TOTAL
Blood Pressure (≥140/90mmHg)	6(2.68)	38(16.96)	86(38.39)	36(16.07)	5(2.23)	3(1.34)	174(77.68)
Triglycerides (≥1.695 mmol/L)	4(1.78)	20(8.92)	68(30.34)	36(16.07)	7(3.12)	3(1.34)	138(61.61)
HDL – C (<0.9 mmol/L for male, <1.0 mmol/L for female)	5(2.23)	10(4.46)	31(13.83)	22(9.82)	3(1.34)	2(0.89)	73(32.58)
Fasting Blood Sugar (≥ 6.1mmol/L)	2(0.89)	17(7.58)	60(26.79)	44(19.64)	4(1.778)	0(0.00)	127(56.69)

Where, n=frequency and the corresponding percentage in parentheses

The prevalence of metabolic syndrome components by WHO criteria were determined according to ages. From Table 9, the ages between 57-72 had the highest frequencies for all the components. The highest prevalence of risk factors was seen in blood pressure which had a total of 174(77.68%). This was followed by triglyceride for which 138(61.61%) of the subjects had elevated values. The HDL-C posed the lowest risk.

Table 10: Prevalence of metabolic syndrome components according to WHO criteria for the Stroke Patients

Sex	M.S Components				
	0	1	2	3	Total
Male	14(11.97)	44(37.61)	44(37.61)	15(12.82)	117(100)
Female	16(14.95)	43(40.19)	40(37.38)	8(7.48)	107(100)
Total	30(13.39)	87(38.84)	84(37.50)	23(10.27)	224(100)

Where, n=frequency and the corresponding percentage in parentheses

The prevalence of metabolic syndrome components, according to WHO criteria was determined for stroke patients, using the designated risk factors. The males had a metabolic syndrome prevalence of 12.82% while the females had 7.48%. The females who had none of the risk factors were more than the males; 14.95% as against 11.97%.

Table11: Comparison of various risk factors among the control according to WHO and NCEP criteria

Risk factor control	Criteria	**N**	**Mean**	**P -value**
FBS mmol/L	WHO NCEP	3 12	9.10(3.92) 7.03(1.22)	0.0825
SBP mmHg	WHO NCEP	13 26	160.50(53.84) 146.30(42.82)	0.0199
DBP mmHg	WHO NCEP	2 9	89.50(4.73) 86.89(6.43)	0.1264
TRIG mmol/L	WHO NCEP	3 3	2.00(0.08) 2.00(0.08)	1.00
HDL-C mmol/L	WHO NCEP	5 16	0.84(0.04) 0.99(0.04)	0.0325

Continuous data are presented as mean (standard deviation) and categorical data presented as proportions. The continuous data were compared using unpaired t-test whilst categorical data were compared using Fischer's exact test.

Meanings of abbreviations; Systolic Blood Pressure (SBP), Diastolic Blood Pressure (DBP), Triglyceride (TG),High Density Lipoprotien-cholesterol (HDL-C), Fasting Blood Sugar (FBS),World Health Organization (WHO) and National Cholesterol Education Program (NCEP).

From Table 11, there is significant difference for systolic and HDL-C when the metabolic syndrome components were compared in the controls for WHO and NCEP criteria.

Table 12: Comparison of the various risk factors among the stroke patients and the control

Socio-demographic data	Stroke (n=224)	Control (n-100)	P-Value
AGE(Years)	65.64(8.74)	66.01(9.34)	0.818
Fasting Blood Sugar mmol/L	8.208(0.870)	5.03(0.29)	<0.0001
Blood pressure diastolic: mmHg	107.8(24.21)	81.74(14.38)	<0.0001
Blood pressure systolic: mmHg	179.8(46.45)	134.39(27.64)	<0.0001
Total cholesterol mmol/L	3.813(0.35)	3.29(0.34)	0.0629
Triglyceride mmol/L	2.517(0.23)	0.89(0.05)	<0.0001
LDL-C mmol/L	3.095(0.44)	1.55(0.06)	<0.0001
HDL-C mmol/L	1.77(0.17)	1.375(0.06)	0.2588

Continuous data are presented as mean (standard deviation) and categorical data presented as proportion. The continuous data were compared using unpaired t-test whilst categorical data were compared using Fischer's exact test.

According to Table 12, there is significant difference in the lipid profile values except that of the HDL-C in which the mean level of the stroke patients was higher (p-value 0.259) than the control subjects. There are significant differences for both mean systolic and diastolic blood pressure and also mean fasting blood glucose and ages when the stroke were compared with the control.

CHAPTER FIVE

5.0 DISCUSSION

This study provid a unique opportunity to look at various characteristics of stroke patients admitted at Komfo Anokye Teaching Hospital in Kumasi. Though the prevalence of stroke among Africans is getting high, due to what has been described as 'epidemiological transition' (Xiong *et al*., 2006), not much work has been done on this condition.

Stroke is notoriously difficult to treat and the ability to forecast stroke is critical but has been challenging, making the detailed study of predisposing factors essential. There is good evidence that modification of risk factors will reduce the risk of stroke. This study involving 224 stroke patients, compared to 100 apparently healthy persons, suggests that while there could be differences in some stroke risk factors, between women and men, there are other factors that show no gender differences.

On lifestyle, information gathered on the patients are in Table 1, which shows men reported higher rates of cigarette smoking, similar to a study by Husten *et al. (2004)* and higher alcohol use than women, which is similar to a study by Ofili *et al*. (1993), which reported that African American men reported higher alcohol and cigarette use than women. In both the Framingham Study and the Nurses' Health Study (Fustinoni and Biller, 2000) cessation of smoking led to a prompt reduction in stroke risk, within 2 to 4 years. This reduction in risk occurred throughout all the age ranges of these studies, and in heavy, as well as moderate smokers.

The study also shows a high prevalence of diabetes; 35.0% in males and 28.0% in females. For the overall population of stroke patients, the prevalence of diabetes was found to be 31.7%,

which was similar to a study by Hier *et al*., (1991) who found the prevalence of diabetes to be 33% in patients with stroke. Baker and Katsuki (1999), found the presence of diabetes in 30% of Japanese stroke cases. Diabetes is known to predispose to the development of stroke by its contribution to the atherogenesis in the cerebral vessels by the multiple lipid disorders associated with it (Adams *et al*., 1993).

Persons with diabetes have an increased susceptibility to stroke, because of the presence of notably, hypertension, obesity, and abnormal blood lipids (Otvos, 1999). Table 6, shows that stroke risk factors like hypertension, diabetes, hyperlipidaemia tend to increase with age in both genders between the ages of 41 to 88. Such findings had actually been reported in another study by Chobanian (2003). Therefore, it is very important to address the issue of prevention early in life because the precursors of the disease are present long before clinically significant levels of hypertension are recognized (Srinivasan *et al*., 2003). In this present study, the percentages of hypertension and diabetes between men and women did not differ significantly (p= 0.22) (Table1). Hypertension is the single most important modifiable risk factor for stroke. From Table 1, 51.3% of the studied populations were known hypertensives, which are similar to a study by McDowell *et al*., (2001) which also reported 51% of hypertensives. It is clear from the present study that hypertension is similarly associated with both male and female stroke cases.

The proportion of the various blood pressure classifications, calculated out of the total male and female studied population is as shown in Figure 4.1. Optimal, normal, high normal, mild, moderate and severe blood pressures were similar in both genders. It was the severe group which predominated, made up of 64% males and 62.7% females. These allude to the major contributory

role hypertension plays in the aetiology of stroke. It has been shown that blood pressure was strongly and directly associated with the risk of stroke throughout middle and old age, but the association was weakened in the older age group, from Table 6. This is similar to a study by Woo *et al*., (2002). At some age threshold, patients with very high pressure would have died, or the morbidities of patients with such high pressures are so high that their relatives do not see the need for taking them to the hospital.

Hypertension can accelerate atherogenesis in the cerebral vessels, it can mechanically damage these vessels and it can indirectly, through the development of cardiac insufficiency, lead to reduced perfusion in previously narrowed cerebral vessels (Dodu, 1998). It seems that hypertension is indeed one of the main characteristics of the stroke-prone individual. It should be detected early, treated, and controlled.

Though the prevalence of diabetes did not show any gender-bias, as pointed out earlier, quite a different pattern emerges when the patients are looked at, based on the disorders of glycaemic control, dependent on some glucose cut-off levels (Table 2). Per the glucose levels, 53.8% of the males were diabetic, as against 40.2% of females; the males with hyperglycaemia were as high as 65.0%, as against 47.7% females. However, the prevalence of impaired fasting glucose showed no difference between males and females.

Whether there will be normal glycaemic control, impaired glucose tolerance, or diabetes, would be determined by various aspects of glucose metabolism that may contribute to risk factors for stroke, including insulin sensitivity, hyperinsulinaemia and increased insulin resistance (the relative inability of insulin to enhance glucose disposal). Hyperinsulinaemia and increased

insulin resistance have been shown to be risk factors for stroke among subjects with normal glucose status (Allan *et al.*, (2007).

Another significant finding in this study is that dyslipidaemia, particularly hypertriglyceridaemia, is the most common disorder among the lipid profile test, using the NCEP and WHO criteria as shown in Tables 5 and 9 respectively. This finding is similar to those of a national estimate from China (Gu *et al*., 2005). The rapid nutrition transition in Ghanaians, characterized by a more sedentary lifestyle and an energy-dense higher fat diet may, at least in part, account for the higher prevalence of hypertriglyceridaemia in this Ghanaian study population. This element of nutrition transition is a central contributor of hyperlipidaemia (Yuan *et al*., 2007).

Among all the dyslipidaemia, the men had the higher percentages except that of increased LDL-C, as shown in Table 2. This is similar to a study by Konishi *et al.* (2003), who found an increased LDL-C in women. Among the stroke patients, elevated level of serum triglycerides had the highest prevalence of 55.8%, representing more than half of the stroke patients (Table 2). The study shows a highly significant difference between triglyceride levels of stroke patients, as compared to control group, as shown in Table 13. This present study also found a positive correlation of serum triglyceride levels with total cholesterol for both men and women (r=0.58 for women and r= 0.74 for the men) in the stroke patients, as shown in Table 3. This finding is similar to a study by Khan and Rehman, (2005).

Diabetes, because of its common association with dyslipidaemia is a common cause of stroke. Dyslipidaemia is also one of the major risk factors noted in patients of stroke without diabetes.

Benfante *et al*. (2004), likewise Di Mascio *et al*. (2005), found a positive association between serum cholesterol and risk of stroke similar to that of this study. Diabetes frequently exists as a concurrent disease in cerebrovascular accidents and is also considered as a risk factor in the development of stroke, though less potent than hypertension (Hill, 2005).

This study also looked at the assessment of risk factors contributing to metabolic syndrome in stroke patients. The WHO and NCEP criteria were used to determining the prevalence of metabolic syndrome.

NCEP criteria, gave a higher prevalence of metabolic syndrome of 46.88%, as compared to the WHO standard, which gave 10.27% (Tables 7 and 10 respectively). Similar to the findings of this study, Lee *et al.*, 2004 and Xavier *et al.* (2009) found higher prevalence of metabolic syndrome among Singaporeans and Japanese, respectively, using NCEP and WHO criteria. This is also similar to a study by Turpin *et al* (2008) which had the prevalence of metabolic syndrome to be 10% (for WHO) and 62% (for NCEP) in 200 preeclampsia pregnant women. Metabolic syndrome is a known cardiovascular disease risk factor and has been associated with high risk of stroke in many studies. Ding *et al*. (2010), as well as Liu *et al.,* (2011) have suggested a dose-response correlation between metabolic syndrome components and risk of cardiovascular disease and incidence of stroke.

From this study, it has been observed that elevated blood pressure and elevated fasting glucose are common among stroke patients; this is seen in Table 1, and is similar to a work by McNeill *et al.* (2006). Considering the different components of the metabolic syndrome, elevated blood

pressure (hypertension) was the most prevalent component in both NCEP and WHO criteria, as shown in Tables 5 and 9 respectively. This finding is similar to what Magid *et al*. (2004) observed in a study on stroke patients in Saudi Arabia, where hypertension was seen as a major risk factor for stroke. The association between blood pressure and stroke is strong and direct, and the absolute risk of stroke associated with high blood pressure increases with age between 57-72 but decreases in older ages from Table 6.

Therefore, in many of the patients, the stroke could have resulted not only from hypertension alone, but from a combination of hypertension and diabetes, since subjects with hypertension are more likely to develop type 2 diabetes. A study by Gress *et al*. (2000) had assessed the joint effect of hypertension and type 2 diabetes on stroke risk in the general population. It was found that the risk of stroke attributable to a history of both diabetes and hypertension was substantially greater than for either condition alone, and this has been corroborated by the present study.

The association between metabolic syndrome and stroke has been confirmed in this study population, except that other aetiological factors could be contributory, as some of the patients did not have the metabolic syndrome factors.

It was observed that the prevalence of metabolic syndrome components increased with age but was reduced in the oldest age group (Tables 6 and 9). Such an observation was also made by Tan *et al*. (2004), likewise Lee *et al* (2004), whose studies showed the prevalence of metabolic syndrome increased with age but was reduced in the oldest age group. The rise in metabolic syndrome and stroke has been reported to be highest in adults above their menopausal and androposal stages (Alexander *et al.,* 2003). This contradicts results shown elsewhere (Tan *et al*.,

2004; Lee, 2004).This is seen in the ages between 57-72 years for all the metabolic syndrome components in both NCEP and WHO criteria; this can be seen in Tables 6 and 9 respectively.

The prevalence of the metabolic syndrome is thus dependent on which definition is used. Since both NCEP and WHO definitions use many of the same variables, including central or abdominal obesity, dyslipidaemia, hypertension, and hyperglycaemia, moderate agreement between the two definitions in diverse populations was expected (Ford *et al*., 2003). However, substantial differences exist. Only fasting plasma glucose was used to assess glycaemic status in the NCEP which misdiagnosed some subjects.

Aminotransferase levels are highly correlated with the γ-glutamyltransferase level, according to Table 3.This is similar to a study by Perry *et al*. (2008). Several studies proposed that γ-glutamyltransferase is a marker of oxidative stress, as it is involved in the generation of reactive oxygen species Lee *et al* (2004). Overall, the serum aminotransferase level is likely to be a marker of liver dysfunction rather than a causal factor of stroke. Actually, the serum aminotransferase level is a sensitive marker of liver damage, but it does not provide information on the underlying causes of liver damage. Although the causal relation between aminotransferase level and stroke risk is still unclear, serum aminotransferase levels can be used as a predictor of stroke. The role of serum aminotransferase levels in the development of stroke needs to be further studied.

The proportions of the patients with increased aminotransferases (Table 2) were similar to a study by Perry *et al*., (2008), in which 23.1% and 12.8% of the males had elevated AST and

ALT respectively while 15.9% and 10.3% of the females had elevated AST and ALT, respectively. Alcohol intake is a main cause of aminotransferase elevation in men but not in women, the relation between aminotransferase and stroke risk can be different by sex (Woo et al., 2002). From Table 3, it can be observed that all the liver enzymes correlate with each other. ALT correlates positively with AST (r=0.98 for males and 0.65 for the females), as well as GGT which also correlates positively with the aminotransferase.

CHAPTER SIX

6.0 CONCLUSIONS AND RECOMMENDATIONS

6.1 CONCLUSIONS

This study identified several risk factors of stroke. There was a high prevalence of both hypertension and hyperglycaemia among the stroke patients. The risk factors identified in the stroke patients were as follows: 63% had high blood pressure, known hypertensives were 51.3%, hyperglycaemia 56.7%, diabetes 47.3%, alcoholism 30.4%, hypertriglyceridaemia 55.8% when the various risk factors were considered.

The highest predominant risk factor observed was hypertension, followed by diabetics and hypertriglyceridaemia.Stroke patients have all the risk factors of metabolic syndrome, while none of the control group of healthy subjects had the syndrome.

From this present study, it has also been found that 46.88% and 10.27% stroke patients had metabolic syndrome, using NCEP and WHO guidelines, respectively. The NCEP resulted in a high percentage of the stroke patients with metabolic syndrome which is similar to a study by Anil *et al*. (2010), in which they identified 75% and 24% patients with metabolic syndrome using NCEP and WHO criteria, respectively.

This study has shown that the metabolic syndrome is prevalent in some of the stroke patients. Since the factors responsible for metabolic syndrome are modifiable, careful consideration should be given to the risk factors of metabolic syndrome in developing countries and

appropriate community-based prevention strategies aimed at reducing the frequency of this syndrome should be advocated.

6.2 RECOMMENDATIONS

Further study should be carried out to attain a larger sample size for both stroke patients and controls. It is also recommended that additional indices like uric acid and C - reactive protein should be measured.

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