بسم الله الرحمن الرحيم

Sudan University of Sciences and Technology

College of Graduate Studies

Assessment of Serum Amino Transferases and Albumin among Hypertensive Patients in ELobied City -North Kordofan State

تقييم إنزيمات ناقلة الأمين وبروتين الألبيومين لدى مرضى ارتفاع ضغط الدم في مدينة الابيض- ولاية شمال كردفان

A dissertation submitted in partial fulfillment for the requirement of M.Sc degree in Clinical chemistry

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الآية

بسم الله الرحمن الرحيم

قال تعالي :

{ الَّذِينَ قَالَ لَهُمُ النَّاسُ إِنَّ النَّاسَ قَدْ جَمَعُوا لَكُمْ فَاخْشَوْهُمْ فَزَادَهُمْ إِيمَاناً وَقَالُوا حَسْبُنَا اللَّهُ وَنِعْمَ الْوَكِيلُ }

صدق الله العظيم

سوره ال عمران الايه(173)

DEDICATION

To all my family members.

To all my teachers elsewhere.

To my dear father Altayb Alhassan Ali,

To the great man my husband Obay Omer Dakeen and his family.

To my dear mother Fatima Ahmed Hussien.

To my special friend Yassmin Mohammed Alam said

To Alqabas International School Administration

To great women and teacher in Alqabas School Mrs. Khulood Taim Mohammed Dirar.

Eitimar

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Firstly, the great praise and thanks to God who gave me the ability to complete this work. I am gratefully acknowledging my supervisor Dr. Seifeldeen Ahmed Mohamed for his patience, motivation, and immense knowledge. His guidance helped me in all the time of research and writing of this research.

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Abstract

Background:

Hypertension is a long-term medical condition in which the blood pressure in the arteries is persistently elevated. Long-term high blood pressure, however, is a major risk factor for coronary artery disease, stroke, heart failure, atrial fibrillation, peripheral vascular disease, vision loss, chronic kidney disease, and dementia

Objectives

This study aims to estimate AST,ALT and albumin in patient with hypertension.

Materials and methods:

This study includes 100 participant, 50 of them have hypertension and the other are control group,5 ml of blood was taken from each participate to prepare serum, the serum prepared was used for the measurement of ALT,AST and albumin using BA400 (BIOCHEMISTRY ANALYZER) and the data obtained were analyzed using SPSS version 20.

Results:

This study included 50 female and male with hypertension and 50 without hypertension age matched، the mean concentration of AST,ALT, albumin were significantly increased among hypertensive patient(35.154±2.3184), (35.858±2.6679), (4.000±.3105) in comparison with control group (23.354±4.5197), (25.478±4.7412), (3.702±.1985) respectively with p value 0.000 , the mean concentration of AST,ALT was significantly increased among male group P value(0.002)(0.037) respectively in comparison with female group p value(0.002), (0.037)respectively. in contracts there is significant increase in mean concentration of albumin in female group in comparison with male group with (P value=0.034).

Person's correlation showed no correlation observed when associated serum AST, ALT, albumin with age of hypertension patient (r 0.013,p value 0.927)(r 0.078 p value 0.550)(r 0.107,p value 0.459) and there is no correlation observed when associate serum AST, ALT with duration of hypertension(r 0.204 p value 0.156)(r 0.239, p value 0.095) , and also serum Albumin not correlated with duration of hypertension patient(r 0.112 p value 0.440).

المستلخص

الخلفية:

ارتفاع ضغط الدم هو حالة طبية طويلة الأجل حيث يتم رفع ضغط الدم في الشرايين باستمرار. ومع ذلك يعد ارتفاع ضغط الدم طويل الأجل أحد عوامل الخطر الرئيسية لمرض الشريان التاجي ، والسكتة الدماغية ، وفشل القلب ، والرجفان الأذيني ، وأمراض الأوعية الدموية الطرفية ، وفقدان البصر ، ومرض الكلى المزمن ، والخرف

الاهدف:

تهدف هذه الدراسة الي تقدير بروتين الالبيومين وانزيم الانين ترانساميناز وانزيم الاسبارتيت ترانساميناز في المرضي الذين يعانون من ارتفاع ضغط الدم0

المواد والأساليب:

تشمل هذه الدراسة 100 مشارك 50 منهم مصابون بارتفاع ضغط الدم والآخرون مجموعة ضابطة لمرض ارتفاع ضغط الدم ، تم أخذ 5 مل من الدم من كل مشارك لإعداد المصل ، وتم استخدام المصل المعد لقياس بروتين الالبيومين وانزيم الانين ترانساميناز وانزيم الاسبارتيت ترانساميناز باستخدام جهاز محلل الكيمياء الحيوية 400

النتائج:

شملت هذه الدراسة 50 من الإناث والذكور مع ارتفاع ضغط الدم و 50 دون ارتفاع ضغط الدم مع تطابق الفئات العمرية ،اظهرت الدراسة زيادة في متوسط تركيز انزيم الاسبارتيت ترانساميناز وانزيم الانين ترانساميناز بين المجموعتين، وبروتين الالبيومين (35.154 ± 2.3184) (35.858 ± 2.6679) ، (4.000 ± .10105) على التوالى بشكل كبير بالمقارنة مع الاشخاص المعافين من ارتفاع ضغط الدم ((23.354±4.5197) (25.478±4.7412) (3.702±. 1985)على التوالى.

لوحظ ايضا زيادة متوسط تركيز انزيم الاسبارتيت ترانساميناز وانزيم الانين ترانساميناز بشكل ملحوظ عند مجموعة الذكور قيمة ص (0.002)،(0.037)على التوالى مقارنة بمجموعة الاناث قيمة ص(0.002) (0.037) على التوالى، على عكس بروتين الالبيومين كانت هناك زيادة في متوسط تركيز الالبيومين عند مجموعة الاناث مقارنة بمجموعة الذكور (قيمة ص 0.034)

أظهرت الدراسة عدم وجود علاقة ارتباط ملحوظة عندما يرتبط مصل انزيم الاسبارتيت ترانساميز والانين ترانساميز وبروتين الألبومين مع العمر في مرضى ارتفاع ضغط الدم ، ولوحظ ايضا ان هناك علاقة ارتباط ضعيفة بين سيرم انزيم الاسبارتيت ترانساميناز وانزيم الانين ترانساميناز بالفترة الزمنية لمرض ارتفاع ارتفاع ضغط الدم، اما بروتين الالبيومين لا توجد علاقة ارتباط بينه وبين الفترة الزمنية لمرض ارتفاع ضغط الدم.(قيمة ر 0.112) قيمة ص (0.440)

Chapter one

1. Introduction, Rational and objectives

1.1 Introduction:

Hypertension (HTN or HT), also known as high blood pressure(HBP), is a long-term medical condition in which the blood pressure in the arteries is persistently elevated. High blood pressure typically does not cause symptoms,*(* Hernandorena *et al, 2019).* Long-term high blood pressure, however, is a major risk factor for coronary artery disease, stroke, heart failure,atrial fibrillation, peripheral vascular disease, vision loss, chronic kidney disease, and dementia *(*Lackland *2015).*

The proportion of the world's population with high blood pressure, or uncontrolled hypertension, fell modestly between 1980 and 2008. However, because of population growth and ageing, the number of people with uncontrolled hypertension rose from 600 million in 1980 to nearly 1 billion in 2008. Across the WHO regions, the prevalence of raised blood pressure was highest in Africa, where it was 46% for both sexes combined. Both men and women have high rates of raised blood pressure in the Africa region, with prevalence rates over 40%. The lowest prevalence of raised blood pressure was in the WHO Region of the Americas at 35% for both sexes. Men in this region had higher prevalence than women (39% for men and 32% for women). In all WHO regions, men have slightly higher prevalence of raised blood pressure than women. This difference was only statistically significant in the Americas and Europe *(WHO 2018).*

In sudan the prevalence of hypertension was around 35.7% and the newly diagnosed cases were 22.4% *(* Bushara *et al., 2016).*

The liver, is an organ only found in vertebrates, detoxifies various metabolites, synthesizes proteins and produces biochemicals necessary

for digestion *(*Zakim *et al., 2002).* It is located in the right upper quadrant of the abdomen, below the diaphragm (Corton *et al., 2005).* Its other roles in metabolism include the regulation of glycogenstorage, decomposition of red blood cells and the production of hormones *(*Zakim *et al., 2002).*

The liver is responsible for the breakdown and excretion of many waste products. It plays a key role in breaking down or modifying toxic substances (e.g., methylation) and most medicinal products in a process called drug metabolism. This sometimes results in toxication, when the metabolite is more toxic than its precursor *(*Pocock. *2006).* Essential hypertension is known to be associated with the metabolic syndrome, which is characterized by insulin resistance, and strongly linked to the development of fatty liver (hepatic steatosis). Fatty liver is a common problem and there are a number of causes, including alcohol ingestion and hepatitis C infection.*(*Yu AS, Keeffe Rev Gastroenterol Disord *2002)* Because of association between Essential hypertension and the metabolic syndrome *;(* Ferrannini *et al., 1987)* hyperinsulinaemia being seen in up to 50% of non-obese patients with hypertension.*(*Pollare *et al., 1990)* Abdominal obesity, which is a major risk factor for the development of hypertension, (Freedman *et al., 2002), (*Thompson *et al., 1999)* is also associated with insulin resistance and the metabolic syndrome. (Meigs *2003)* The presence of insulin resistance also seems to be involved in the pathogenesis of complications related to hypertension,*(*Steinberg Tarshoby *et al., 1997),* (Laakso *et al., 1990.)*

An association between abnormal liver function tests and hypertension was identified by Ramsay in 1977,*(* Ramsay lancet *1977)* who found that up to 15% of all male hypertensive patients had abnormal liver function tests.(van Barneveld *et a1.,989).*

1.2 Rationale:

Hypertension affects at least 50% of persons over the age of 60 and is an important cause of morbidity and mortality from cardiovascular and cerebrovascular disease and liver disease, Few study puplish in sudan about liver enzymes.

This study aimed to determine the possible effect of Hypertension on the liver function by measuring the Inflammation and Synthetic function of liver through assessment of enzyme levels and serum albumin among cases and controls.

1.3 Objectives

General objective:

To assess some biochemical markers of liver functions among Sudanese patient with hypertension.

Specific objective:

1. To measure and compare the liver enzymes and Albumin among cases and controls.
2. To compare level of AST, ALT and albumin in hypertensive patient according to gender.
3. To correlate between AST, ALT, and albumin with study variable(age and duration) in case group.

Chapter Two

2. Literature review

2.1 Hypertension (HTN or HT):

Hypertension also known as high blood pressure (HBP), is a long-term medical condition in which the blood pressure in the arteries is persistently elevated *(* Naish *2014)* High blood pressure typically does not cause symptoms.*(High Blood Pressure Fact Sheet". 2015)* Long-term high blood pressure, however, is a major risk factor for coronary artery disease, stroke, heart failure, atrial fibrillation, peripheral arterial disease, vision loss, chronic kidney disease, and dementia. *(* Lackland *et al., 2015) (*Mendis *et al., 2011) (*Hernandorena *et al., 2017)* (Lau *et al., 2017).*

Hypertension is classified as either primary (essential) high blood pressure or secondary high blood pressure.(Poulter *et al., 2015).* About 90–95% of cases are primary, defined as high blood pressure due to nonspecific lifestyle and genetic factors. *(*Poulter *et al., 2015) (* Carretero *2000). ("Essential hypertension. Part I: definition and etiology". Circulation)* Lifestyle factors that increase the risk include excess salt in the diet, excess body weight, smoking, and alcohol use. *("High Blood Pressure Fact Sheet from the original on 2016) (*Poulter *et al 2015)* The remaining 5–10% of cases are categorized as secondary high blood pressure, defined as high blood pressure due to an identifiable cause, such as chronic kidney disease, narrowing of the kidney arteries, an endocrine disorder, or the use of birth control pills. (Poulter *et al., 2015).*

Blood pressure is expressed by two measurements, the systolic and diastolic pressures, which are the maximum and minimum pressures, respectively. *(High Blood Pressure Fact Sheet, from the original on 2016).* For most

adults, normal blood pressure at rest is within the range of 100–130 millimeters mercury (mmHg) systolic and 60–80 mmHg diastolic. *(* Whelton *et al., 2018). (*Mancia *et al., 2013)* . ESH/ESC guidelines for the management of arterial hypertension: the Task Force for the Management of Arterial Hypertension of the European Society of Hypertension (ESH) and of the European Society of Cardiology (ESC)". European Heart Journal For most adults, high blood pressure is present if the resting blood pressure is persistently at or above 130/80 or 140/90 mm Hg. *(*Poulter *et al,m 2015). (*Whelton *2018)* Different numbers apply to children. (James *2014)* Ambulatory blood pressure monitoring over a 24-hour period appears more accurate than office-based blood pressure measurement.*(* Poulter *et al 2015). (*Naish *2014).*

Lifestyle changes and medications can lower blood pressure and decrease the risk of health complications. *(* National Heart, Lung, and Blood Institute. from the original on *2016)* Lifestyle changes include weight loss, physical exercise, decreased salt intake, reducing alcohol intake, and a healthy diet. *(* Poulter *et al 2015)* If lifestyle changes are not sufficient then blood pressure medications are used.*(* National Heart, Lung, and Blood Institute from the original on 6 April *2016)* Up to three medications can control blood pressure in 90% of people.*(* Poulter *et al 2015)* The treatment of moderately high arterial blood pressure (defined as >160/100 mmHg) with medications is associated with an improved life expectancy.*(* Musini *et al., 2019)* The effect of treatment of blood pressure between 130/80 mmHg and 160/100 mmHg is less clear, with some reviews finding benefit *(* Whelton *et al., 2018) (* Sundström *et al., 2015). (Effects of blood pressure reduction in mild hypertension: a systematic review and meta-analysis". Annals of Internal Medicine)* (Xie *et al., 2016)* and others finding unclear benefit.(

Diao *2012). (Pharmacotherapy for mild hypertension". The Cochrane Database of Systematic Reviews.) (*Garrison *et al 2017) (Blood pressure targets for hypertension in older adults)*. The Cochrane Database of Systematic Reviews *(*Musini *et al 2017)* High blood pressure affects between 16 and 37% of the population globally.*(* Poulter *2015)* In 2010 hypertension was believed to have been a factor in 18% of all deaths (9.4 million globally).(Campbell *et al 2015).*

2.1.1 A etiology of Hypertension (HTN or HT):

Low blood pressure can be caused by low blood volume, hormonal changes, widening of blood vessels, medicine side effects, anemia, heart problems or endocrine problems.

Reduced blood volume, hypovolemia, is the most common cause of hypotension. This can result from hemorrhage; insufficient fluid intake, as in starvation; or excessive fluid losses from diarrhea or vomiting. Hypovolemia is often induced by excessive use of diuretics. Low blood pressure may also be attributed to heat stroke. The body may have enough fluid but does not retain electrolytes. Absence of perspiration, light headedness and dark coloured urine are also indicators.

Other medications can produce hypotension by different mechanisms. Chronic use of alpha blockers or beta blockers can lead to hypotension. Beta blockers can cause hypotension both by slowing the heart rate and by decreasing the pumping ability of the heart muscle.

Decreased cardiac output despite normal blood volume, due to severe congestive heart failure, large myocardial infarction, heart valve problems, or extremely low heart rate (bradycardia), often produces hypotension and can rapidly progress to cardiogenic shock. Arrhythmias often result in hypotension by this mechanism.

Some heart conditions can lead to low blood pressure, including extremely low heart rate (bradycardia), heart valve problems, heart attack and heart failure. These conditions may cause low blood pressure because they prevent the body from being able to circulate enough blood.

Excessive vasodilation, or insufficient constriction of the resistance blood vessels (mostly arterioles), causes hypotension. This can be due to decreased sympathetic nervous system output or to increased parasympathetic activity occurring as a consequence of injury to the brain or spinal cord or of dysautonomia, an intrinsic abnormality in autonomic system functioning. Excessive vasodilation can also result from sepsis, acidosis, or medications, such as nitrate preparations, calcium channel blockers, or AT1 receptor antagonists (Angiotensin II acts on AT1 receptors). Many anesthetic agents and techniques, including spinal anesthesia and most inhalational agents, produce significant vasodilation.

Meditation, yoga, or other mental-physiological disciplines may reduce hypotensive effects. *(* Joel *et al., 2005)*

Lower blood pressure is a side effect of certain herbal medicines, *(*Tabassum *et al., 2011)* which can also interact with hypotensive medications. An example is the theobromine in Theobroma cacao, which lowers blood pressure *(* Mitchell *et al., 2011)* through its actions as both a vasodilator and a diuretic, *(* William *2014)* and has been used to treat high blood pressure. (Kelly *2013).*

2.1.2 Pathophysiology:

In most people with established essential hypertension, increased resistance to blood flow (total peripheral resistance) accounts for the high pressure while cardiac output remains normal.*(*Conway*2005)* There is evidence that some younger people with prehypertension or 'borderline hypertension' have

high cardiac output, an elevated heart rate and normal peripheral resistance, termed hyperkinetic borderline hypertension. *(*Palatini *2009)* These individuals develop the typical features of established essential hypertension in later life as their cardiac output falls and peripheral resistance rises with age. (Palatini *2009)* Whether this pattern is typical of all people who ultimately develop hypertension is disputed. *(*Andersson *et al., 2004)* The increased peripheral resistance in established hypertension is mainly attributable to structural narrowing of small arteries and arterioles, *(*Folkow *2008)* although a reduction in the number or density of capillaries may also contribute. *(*Struijker Boudier *2010).*

It is not clear whether or not vasoconstriction of arteriolar blood vessels plays a role in hypertension. *(*Schiffrin *2016),* Hypertension is also associated with decreased peripheral venous compliance *(*Safar *2013)* which may increase venous return, increase cardiac preload and, ultimately, cause diastolic dysfunction.

Pulse pressure (the difference between systolic and diastolic blood pressure) is frequently increased in older people with hypertension. This can mean that systolic pressure is abnormally high, but diastolic pressure may be normal or low, a condition termed isolated systolic hypertension.(Chobanian *2007)* The high pulse pressure in elderly people with hypertension or isolated systolic hypertension is explained by increased arterial stiffness, which typically accompanies aging and may be exacerbated by high blood pressure. *(*Zieman *et al 2005)*

Many mechanisms have been proposed to account for the rise in peripheral resistance in hypertension. Most evidence implicates either disturbances in the kidneys' salt and water handling (particularly abnormalities in the intrarenal renin–angiotensin system) *(*Navar *2010)* or abnormalities of the

sympathetic nervous system. *(*Esler *et al 2010)* These mechanisms are not mutually exclusive and it is likely that both contribute to some extent in most cases of essential hypertension. It has also been suggested that endothelial dysfunction and vascular inflammation may also contribute to increased peripheral resistance and vascular damage in hypertension.*(*Versari *et al., 2009) (*Marchesi *et al., 2008)* Interleukin 17 has garnered interest for its role in increasing the production of several other immune system chemical signals thought to be involved in hypertension such as tumor necrosis factor alpha, interleukin 1, interleukin 6, and interleukin 8. (Gooch *2014).*

Consumption of excessive sodium and/or insufficient potassium leads to excessive intracellular sodium, which contracts vascular smooth muscle, restricting blood flow and so increases blood pressure.*(* Adrogué *2007)* (Perez *2014).*

2.1.3 Sign and Symptoms:

Hypertension is rarely accompanied by symptoms, and its identification is usually through screening, or when seeking healthcare for an unrelated problem. Some people with high blood pressure report headaches (particularly at the back of the head and in the morning), as well as lightheadedness, vertigo, tinnitus (buzzing or hissing in the ears), altered vision or fainting episodes. *(*Fisher *2005)* These symptoms, however, might be related to associated anxiety rather than the high blood pressure itself, *(*Marshall *2012).*

On physical examination, hypertension may be associated with the presence of changes in the optic fundus seen by ophthalmoscopy. (Wong *2007)* The severity of the changes typical of hypertensive retinopathy is graded from I to IV; grades I and II may be difficult to differentiate. (Wong *2007)* The

severity of the retinopathy correlates roughly with the duration or the severity of the hypertension. (Fisher *2005).*

2.1.4 Classification of hypertension:

2.1.4.1 Primary hypertension:

Hypertension results from a complex interaction of genes and environmental factors. Numerous common genetic variants with small effects on blood pressure have been identified (Ehret *et al 2011)* as well as some rare genetic variants with large effects on blood pressure. (Lifton *et al., 2001)* Also, genome-wide association studies (GWAS) have identified 35 genetic loci related to blood pressure; 12 of these genetic loci influencing blood pressure were newly found.(Kato *et al., 2015)* Sentinel SNP for each new genetic locus identified has shown an association with DNA methylation at multiple nearby CpG sites. These sentinel SNP are located within genes related to vascular smooth muscle and renal function. DNA methylation might affect in some way linking common genetic variation to multiple phenotypes even though mechanisms underlying these associations are not understood. Single variant test performed in this study for the 35 sentinel SNP (known and new) showed that genetic variants singly or in aggregate contribute to risk of clinical phenotypes related to high blood pressure(Kato *et al., 2015).*

Blood pressure rises with aging and the risk of becoming hypertensive in later life is considerable. (Vasan *et al., 2002)* Several environmental factors influence blood pressure. High salt intake raises the blood pressure in salt sensitive individuals; lack of exercise, central obesity can play a role in individual cases. The possible roles of other factors such as caffeine consumption, (Mesas *et al., 2011)* and vitamin D deficiency (Vaidya *2010)* are less clear. Insulin resistance, which is common in obesity and is a

component of syndrome X (or the metabolic syndrome), is also thought to contribute to hypertension. (Sorof *2002)* One review suggests that sugar may play an important role in hypertension and salt is just an innocent bystander. *(*DiNicolantonio *et al., 2017).*

Events in early life, such as low birth weight, maternal smoking, and lack of breastfeeding may be risk factors for adult essential hypertension, although the mechanisms linking these exposures to adult hypertension remain unclear. *(*Lawlor *2005),* An increased rate of high blood urea has been found in untreated people with hypertension in comparison with people with normal blood pressure, although it is uncertain whether the former plays a causal role or is subsidiary to poor kidney function. *(*Gois *2017)* Average blood pressure may be higher in the winter than in the summer. *(*Fares *2013)* Periodontal disease is also associated with high blood pressure *(*Martin- *et al., 2016).*

2.1.4.2 Secondary hypertension:

Hypertension with certain specific additional signs and symptoms may suggest secondary hypertension, i.e. hypertension due to an identifiable cause. For example, Cushing's syndrome frequently causes truncal obesity, glucose intolerance, moon face, a hump of fat behind the neck/shoulder (referred to as a buffalo hump), and purple abdominal stretch marks. (O'Brien *2007)* Hyperthyroidism frequently causes weight loss with increased appetite, fast heart rate, bulging eyes, and tremor. Renal artery stenosis (RAS) may be associated with a localized abdominal bruit to the left or right of the midline (unilateral RAS), or in both locations (bilateral RAS). Coarctation of the aorta frequently causes a decreased blood pressure in the lower extremities relative to the arms, or delayed or absent femoral arterial pulses. Pheochromocytoma may cause abrupt ("paroxysmal") episodes of

hypertension accompanied by headache, palpitations, pale appearance, and excessive sweating.*(*O'Brien *2007).*

2.1.4.3 Hypertensive crisis:

Severely elevated blood pressure (equal to or greater than a systolic 180 or diastolic of 110) is referred to as a hypertensive crisis. Hypertensive crisis is categorized as either hypertensive urgency or hypertensive emergency, according to the absence or presence of end organ damage, respectively. *(*Rodriguez *2010)*

In hypertensive urgency, there is no evidence of end organ damage resulting from the elevated blood pressure. In these cases, oral medications are used to lower the BP gradually over 24 to 48 hours. *(*Marik *2007).*

In hypertensive emergency, there is evidence of direct damage to one or more organs. *(*Chobanian *2003) (* Perez *2008)* The most affected organs include the brain, kidney, heart and lungs, producing symptoms which may include confusion, drowsiness, chest pain and breathlessness. *(*Marik *2007)*

In hypertensive emergency, the blood pressure must be reduced more rapidly to stop ongoing organ damage, *(*Marik *2007)* however, there is a lack of randomized controlled trial evidence for this Pregnancy(Gestational hypertension and Pre-eclampsia).

Hypertension occurs in approximately 8–10% of pregnancies.*(*O'Brien *2007)* Two blood pressure measurements six hours apart of greater than 140/90 mm Hg are diagnostic of hypertension in pregnancy.(Harrison's principles of internal medicine *2011)* High blood pressure in pregnancy can be classified as pre-existing hypertension, gestational hypertension, or pre-eclampsia.(the original on *2016).*

Pre-eclampsia is a serious condition of the second half of pregnancy and following delivery characterised by increased blood pressure and the

presence of protein in the urine, It occurs in about 5% of pregnancies and is responsible for approximately 16% of all maternal deaths globally, Pre-eclampsia also doubles the risk of death of the baby around the time of birth,Usually there are no symptoms in pre-eclampsia and it is detected by routine screening. When symptoms of pre-eclampsia occur the most common are headache, visual disturbance (often "flashing lights"), vomiting, pain over the stomach, and swelling. Pre-eclampsia can occasionally progress to a life-threatening condition called eclampsia, which is a hypertensive emergency and has several serious complications including vision loss, brain swelling, seizures, kidney failure, pulmonary edema, and disseminated intravascular coagulation (a blood clotting disorder), (O'Brien E *2007)(*Gibson P *2009).*

In contrast, gestational hypertension is defined as new-onset hypertension during pregnancy without protein in the urine *(* the original on *2016) (*Perez *2008).*

2.1.4.4 Hypertension in Children:

Failure to thrive, seizures, irritability, lack of energy, and difficulty in breathing,(Rodriguez-Cruz *et al., 2010)* can be associated with hypertension in newborns and young infants. In older infants and children, hypertension can cause headache, unexplained irritability, fatigue, failure to thrive, blurred vision, nosebleeds, and facial paralysis, (Rodriguez-Cruz *et al., 2010)* (Dionne *et al., 2012)*

2.1.5 Diagnosis of Hypertension:

Hypertension is diagnosed on the basis of a persistently high resting blood pressure. The American Heart Association recommends at least three resting measurements on at least two separate health care visits. (ronow *et al., 2011).* (ACCF/AHA 2011 expert consensus document on hypertension in

the elderly) a report of the American College of Cardiology Foundation Task Force on Clinical Expert Consensus Documents developed in collaboration with the American Academy of Neurology, American Geriatrics Society, American Society for Preventive Cardiology, American Society of Hypertension, American Society of Nephrology, Association of Black Cardiologists, and European Society of Hypertension The UK National Institute for Health and Care Excellence recommends ambulatory blood pressure monitoring to confirm the diagnosis of hypertension if a clinic blood pressure is 140/90 mmHg or higher.*(the original on 2018).*

2.1.6 Complication of Hypertension (HTN):

Are clinical outcomes that result from persistent elevation of blood pressure. *(*White *2009),* Hypertension is a risk factor for all clinical manifestations of atherosclerosis since it is a risk factor for atherosclerosis itself, *(*Insull *2009) (*Liapis *et al 2009) (*Riccioni *2009)(* Safar *2009) (*Werner *2008)*. It is an independent predisposing factor for heart failure, *(*Gaddam Verma , *2009) (*Reisin *2009)* coronary artery disease, *(*Agabiti-Rosei *2008)(Murphy BP et al 2009)* stroke,(White *2009)* kidney disease, *(*Tylicki *2003) (*Truong *et al 2009)* (Tracy *2002)* and peripheral arterial disease. *(*Aronow *2008)* (Gardner , Afaq *2008)* It is the most important risk factor for cardiovascular morbidity and mortality, in industrialized countries. *(*Novo *et al 2009).*

2.1.6 .1 Complications affecting the heart:

2.1.6.2 Left ventricular hypertrophy

Hypertensive heart disease is the result of structural and functional adaptations *(Steinmetz M 2009)* leading to left ventricular hypertrophy,*(*Motz *2004)* diastolic dysfunction, *(*Hennersdorf *et al 2007)* CHF, abnormalities of blood flow due to atherosclerotic coronary artery disease,*(* Steinmetz ,

Nickenig *2009)* and microvascular disease, (Agabiti - Rosei *2008) (*Hennersdorf , Strauer *2006)* and cardiac arrhythmias, Individuals with left ventricular hypertrophy are at increased risk for, stroke, *CHF* and sudden death. (Wachtell *et al 2008)* Aggressive control of hypertension can regress or reverse left ventricular hypertrophy and reduce the risk of cardiovascular disease.*(*Petrović *2008) (*Cuspidi *2007) (* Simko *2007)* (Wachtell *2007)* left ventricular hypertrophy are seen in 25% of the hypertensive patients and can easily be diagnosed by using echocardiography. *(*Herpin *2002)* Underlying mechanisms of hypertensive left ventricular hypertrophy are of 2 types: mechanical, mainly leading to myocyte hypertrophy; neuro-hormonal, mainly resulting in a fibroblastic proliferation. *(*Herpin *2002).*

Abnormalities of diastolic function, ranging from asymptomatic heart disease, *(* Parekh *et al 2009) (*Biria *et al 2008)* (Caserta *et al. 2007)* to overt heart failure, *(* Verma *2009)(*Ellis *et al 2007)* are common in hypertensive patients. Patients with diastolic heart failure have a preserved ejection fraction, which is a measure of systolic function. *(*Okoshi *et al 2007) (*Fukuta *2007)* Diastolic dysfunction is an early consequence of hypertension-related heart disease and is exacerbated by left ventricular hypertrophy (Fukuta , Little *2007)* and ischemia.

2.1.6.3Complications affecting the brain:(Hypertensive encephalopathy and Cerebrovascular accident):

Hypertension is an important risk factor for brain infarction and hemorrhage, (White *2009) (*Agabiti-Rosei *2008) (*Schrader *2009)* (Zeng *et al 2009) (*Varon *2007)* (Sare *2009)(*Palm *2009) (*Tanahashi *2009)* Approximately 85% of strokes are due to infarction and the remainder are due to hemorrhage, either intracerebral hemorrhage or subarachnoid hemorrhage, The incidence of stroke rises progressively with increasing blood pressure

levels, particularly systolic blood pressure in >65 years. Treatment of hypertension convincingly decreases the incidence of individuals both ischemic and hemorrhagic strokes, *(*Loscalzo*, 2008).*

Hypertension is also associated with impaired cognition in an aging population, *(*Iadecola *et al., 2009)* (Erkinjuntti *2009) (*Birns *2009) (*Moretti *et al.,2008)* Hypertension-related cognitive impairment and dementia may be a consequence of a single infarct due to occlusion of a (strategic) larger vessel or multiple lacunar infarcts due to occlusive small vessel disease resulting in subcortical white matter ischemia,*(* Erkinjuntti *2009) (*Moretti *et al 2008) (*Pantoni *2009) (*Pantoni Poggesi *, et al 2009) (*Pantoni Poggesi *2009)* Several clinical trials suggest that antihypertensive therapy has a beneficial effect on cognitive function, although this remains an active area of investigation,*(*Zekry *2009)(*Viswanathan *et al., 2009) (*Sorrentino *et al.,2008).*

Cerebral blood flow remains unchanged over a wide range of arterial pressures (mean arterial pressure of 50–150 mmHg) through a process termed autoregulation of blood flow. *(* Hall, John *et al 2006)* Signs and symptoms of hypertensive encephalopathy may include severe headache, nausea and vomiting (often of a projectile nature), focal neurologic signs, and alterations in mental status. Untreated, hypertensive encephalopathy may progress to stupor, coma, seizures, and death within hours, (Müller-Wiefel *2007)* (Isles *2009) (*Refai *et al 2008) (*O'Hara McCoy *2008)* It is important to distinguish hypertensive encephalopathy from other neurologic syndromes that may be associated with hypertension, e.g., cerebral ischemia, hemorrhagic or thrombotic stroke, seizure disorder, mass lesions, pseudotumor cerebri, delirium tremens, meningitis, acute intermittent

porphyria, traumatic or chemical injury to the brain, and uremic encephalopathy, (Loscalzo *et al., 2008).*

Complications affecting the eye (Hypertensive retinopathy):

Hypertensive retinopathy with AV nicking and mild vascular tortuosity, hypertensive retinopathy is a condition characterized by a spectrum of retinal vascular signs in people with elevated blood pressure, *(*Walsh *2003)* It was first described by Liebreich in 1859. *(Liebreich R. Ophthalmoskopischer Befund bei Morbus Brightii. Albrecht von Graefes Arch Ophthalmol 1859)*, The retinal circulation undergoes a series of pathophysiological changes in response to elevated blood pressure, (Tso *2005)* In the initial, vasoconstrictive stage, there is vasospasm and an increase in retinal arteriolar tone owing to local autoregulatory mechanisms. This stage is seen clinically as a generalized narrowing of the retinal arterioles. Persistently elevated blood pressure leads to intimal thickening, hyperplasia of the media wall, and hyaline degeneration in the subsequent, sclerotic, stage. this stage corresponds to more severe generalized and focal areas of arteriolar narrowing, changes in the arteriolar and venular junctions, and alterations in the arteriolar light reflex (i.e., widening and accentuation of the central light reflex, or "copper wiring), *(*Wong *2004).*

This is followed by an exudative stage, in which there is disruption of the blood–retina barrier, necrosis of the smooth muscles and endothelial cells, exudation of blood and lipids, and retinal ischemia. These changes are manifested in the retina as microaneurysms, hemorrhages, hard exudates, and cotton-wool spots. Swelling of the optic disk may occur at this time and usually indicates severely elevated blood pressure (i.e., malignant hypertension). Because better methods for the control of blood pressure are now available in the general population, malignant hypertension is rarely

seen. In contrast, other retinal vascular complications of hypertension, such as macroaneurysms and branch-vein occlusions, are not uncommon in patients with chronically elevated blood pressure. These stages of hypertensive retinopathy however, may not be sequential. (Tso *2005)* (Pache *et al., 2002)* For example, signs of retinopathy that reflect the exudative stage, such as retinal hemorrhage or microaneurysm, may be seen in eyes that do not have features of the sclerotic stage, *(*Tso *2005)* The exudative signs are nonspecific, since they are seen in diabetes and other conditions.

2.1.6.4Complications affecting the kidneys (Hypertensive nephropathy):

Hypertension is a risk factor for chronic kidney disease and end-stage kidney disease (ESKD*)*, kidney risk appears to be more closely related to systolic than to diastolic blood pressure, and black men are at greater risk than white men for developing ESRD at every level of blood pressure, *(*Niang *et al 2008)*

The atherosclerotic, hypertension-related vascular lesions in the kidney primarily affect the preglomerular arterioles, resulting in ischemic changes in the glomeruli and postglomerular structures, *(*Loscalzo, Joseph *et al 2008)* gomerular injury may also be a consequence of direct damage to the glomerular capillaries due to glomerular hyperperfusion. glomerular pathology progresses to glomerulosclerosis, *(*Stoian Radulian , *2007)* and eventually the kidney tubules may also become ischemic and gradually atrophic. the kidney lesion associated with malignant hypertension consists of fibrinoid necrosis of the afferent arterioles, sometimes extending into the glomerulus, and may result in focal necrosis of the glomerular tuft (Linz *et al 2004).*

Clinically, macroalbuminuria (a random urine albumin/creatinine ratio > 300 mg/g) or microalbuminuria (a random urine albumin/creatinine ratio 30–300

mg/g) are early markers of kidney injury. These are also risk factors for kidney disease progression and for cardiovascular disease, *(*Loscalzo, Joseph *et al 2008).*

2.1.6.5 Complications associated to diabetes:

Diabetes has several complications of which one is hypertension or high blood pressure. data indicate that at least 60-80 percent of individuals whom develop diabetes will eventually develop high blood pressure. the high blood pressure is gradual at early stages and may take at least 10–15 years to fully develop. besides diabetes, other factors that may also increase high blood pressure include obesity, insulin resistance and high cholesterol levels. in general, fewer than 25 percent of diabetics have good control of their blood pressure. the presence of high blood pressure in diabetes is associated with a 4 fold increase in death chiefly from heart disease and strokes, *(Diabetes and Hypertension Medical Journal of Australia. 2010).*

The chief reason why people with diabetes develop high blood pressure is hardening of the arteries. diabetes tends to speed up the process of atherosclerosis. the other fact about diabetes is that it affects both large and small blood vessels in the body. over time, blood vessels become clogged with fatty depots, become non-compliant and lose their elasticity. the process of atherosclerosis is a lot faster in diabetic individuals whom do not have good control of their blood sugars. the high blood pressure eventually leads to heart failure, strokes, heart attacks, blindness, kidney failure, loss of libido and poor circulation of blood in the legs. when the blood supply to the feet is compromised, the chances of infections and amputations also increases. all diabetics should know that even mild elevations in blood pressure can be detrimental to health. studies have shown that diabetics with even a slight elevation in blood pressure have 2-3 times the risk of heart

disease compared to individuals without diabetes, *(Diabetes associated to Hypertension About health portal 2010).*

Blood pressure readings do vary but experts recommend that blood pressure should not range above 140/80. secondly, high blood pressure is a silent disease and thus it is vital for all diabetics to regularly check their blood pressure or have it checked at a doctor's office on a regular basis. the american diabetes association recommends that all diabetics get their blood pressure measured by a health care professional at least 2-5 times a year, *(Medical Journal of Australia Hypertension and Diabetes overview 2010).*

2.2 liver:

The liver is an organ only found in vertebrates which detoxifies various metabolites, synthesizes proteins and produces biochemicals necessary for digestion,*(* Lee *et al 2016)(* Aleksandrova *et al 2016) (* Komatsu *2014)* In humans, it is located in the right upper quadrant of the abdomen, below the diaphragm. Its other roles in metabolism include the regulation of glycogen storage, decomposition of red blood cells and the production of hormones,*(*Komatsu *2014).*

The liver is an accessory digestive organ that produces bile, a fluid containing cholesterol and bile acids, and an alkaline compound which helps the breakdown of fat. bile aids in digestion via the emulsification of lipids. the gallbladder, a small pouch that sits just under the liver, stores bile produced by the liver which is afterwards moved to the small intestine to complete digestion, *(*samal *2012)* the liver's highly specialized tissue consisting of mostly hepatocytes regulates a wide variety of high-volume biochemical reactions, including the synthesis and breakdown of small and complex molecules, many of which are necessary for normal vital functions, estimates regarding the organ's total number of functions vary, but textbooks

generally cite it being around 500,*(*Williams *et al 2014).*

Terminology related to the liver often starts in hepat- from ἡπατο-, from the Greek word for liver, It is not yet known how to compensate for the absence of liver function in the long term, although liver dialysis techniques can be used in the short term. artificial livers are yet to be developed to promote long-term replacement in the absence of the liver liver transplantation is the only option for complete liver failure,*(*Kim *et al 2014).*

2.2.1Anatomy of Liver:

The liver is grossly divided into two parts when viewed from above – a right and a left lobe - and four parts when viewed from below (left, right, caudate, and quadrate lobes). *(*Tilg *et al 2016).*

The falciform ligament divides the liver into a left and right lobe. from below, the two additional lobes are located between the right and left lobes, one in front of the other. A line can be imagined running from the left of the vena cava and all the way forward to divide the liver and gallbladder into two halves, *(*Tripodi *et al 2011)* This line is called Cantlie's line *(*Leslie *et al 2006).*

Other anatomical landmarks include the ligamentum venosum and the round ligament of the liver (ligamentum teres), which further divide the left side of the liver in two sections. An important anatomical landmark, the porta hepatis, divides this left portion into four segments, which can be numbered starting is only visible in the visceral view, *(*Oyama *et al 2010)* at the caudate lobe as I in an anticlockwise manner. from this parietal view, seven segments can be seen, because the eighth segment and microscopically, each liver lobe is seen to be made up of hepatic lobules. the lobules are roughly hexagonal and consist of plates of hepatocytes radiating from a central vein, the central vein joins to the hepatic vein to carry blood out from the liver. a

distinctive component of a lobule is the portal triad, which can be found running along each of the lobule's corners. the portal triad, misleadingly named, consists of five structures: a branch of the hepatic artery, a branch of the hepatic portal vein, and a bile duct, as well as lymphatic vessels and a branch of the vagus nerve, *(*Niedernhofer *2016)* Between the hepatocyte plates are liver sinusoids, which are enlarged capillaries through which blood from the hepatic portal vein and hepatic artery enters via the portal triads, then drains to the central vein, (Ivanov *et al 2017).*

histology, the study of microscopic anatomy, shows two major types of liver cell: parenchymal cells and nonparenchymal cells. About 70–85% of the liver volume is occupied by parenchymal hepatocytes. nonparenchymal cells constitute 40% of the total number of liver cells but only 6.5% of its volume, *(*Dizdaroglu *2012)* the liver sinusoids are lined with two types of cell, sinusoidal endothelial cells, and phagocytic kupffer cells,*(* Nishida *2013)* hepatic stellate cells are nonparenchymal cells found in the perisinusoidal space, between a sinusoid and a hepatocyte, additionally, intrahepatic lymphocytes are often present in the sinusoidal lumen. *(*Dizdaroglu *2012).*

2.2.2**Function of Liver:**

The various functions of the liver are carried out by the liver cells or hepatocytes. the liver is thought to be responsible for up to 500 separate functions, usually in combination with other systems and organs. currently, no artificial organ or device is capable of reproducing all the functions of the liver. Some functions can be carried out by liver dialysis, an experimental treatment for liver failure. The liver also accounts for about 20% of resting total body oxygen consumption. The liver receives a dual blood supply from the hepatic portal vein and hepatic arteries. The hepatic portal vein delivers around 75% of the liver's blood supply, and carries venous blood drained

from the spleen, gastrointestinal tract, and its associated organs. the hepatic arteries supply arterial blood to the liver, accounting for the remaining quarter of its blood flow. oxygen is provided from both sources; about half of the liver's oxygen demand is met by the hepatic portal vein, and half is met by the hepatic arteries,*(*Samal *et al 2012)* The hepatic artery also has both alpha- and beta-adrenergic receptors; therefore, flow through the artery is controlled, in part, by the splanchnic nerves of the autonomic nervous system.

Blood flows through the liver sinusoids and empties into the central vein of each lobule. The central veins coalesce into hepatic veins, which leave the liver and drain into the inferior vena cava, *(*Yu Y, Cui *et al 2016).*

2.2.3Liver disease:

Liver disease (also called hepatic disease) is a type of damage to or disease of the liver, (Shibata *et al 2014)* whenever the course of the problem lasts long, chronic liver diseasese ensues.

2.2.3.1Signs and symptoms of liver disease:

- Some of the signs and symptoms of liver disease are the following:[citation needed]
- Jaundice
- Confusion and altered consciousness caused by hepatic encephalopathy.
- Thrombocytopenia and coagulopathy, *(*Ozen *et al 2013)*
- Risk of bleeding symptoms particularly taking place in gastrointestinal tract (Yu HS *et al 2010)*
- Ascites, the accumulation of fluid in the abdominal cavity.

2.2.3.2Causes of liver disease:

Ground glass hepatocyte, primary biliary cirrhosis, budd-chiari syndrome. There are more than a hundred different kinds of liver disease. these are some of the most common, *(*Lee *et al 2016).*

fascioliasis, a parasitic infection of liver caused by a liver fluke of the genus fasciola, mostly the fasciola hepatica, *(*Wang *et al 2012).*

hepatitis, inflammation of the liver, is caused by various viruses (viral hepatitis) also by some liver toxins (e.g. alcoholic hepatitis), autoimmunity (autoimmune hepatitis) or hereditary conditions, (Shukla *2013).*

Alcoholic liver disease is a hepatic manifestation of alcohol overconsumption, including fatty liver disease, alcoholic hepatitis, and cirrhosis. Analogous terms such as "drug-induced" or "toxic" liver disease are also used to refer to disorders caused by various drugs, *(*Aleksandrova *et al 2016).*

Fatty liver disease (hepatic steatosis) is a reversible condition where large vacuoles of triglyceride fat accumulate in liver cells, *(*Benova *et al 2014)* non-alcoholic fatty liver disease is a spectrum of disease associated with obesity and metabolic syndrome, *(*Komatsu *2014).*

Hereditary diseases that cause damage to the liver include hemochromatosis,involving accumulation of iron in the body, and wilson's disease. Liver damage is also a clinical feature of alpha 1-antitrypsin deficiency (Hirschfield et al 2011) and glycogen storage disease type II *(*Suchy *et al 2014).*

In transthyretin-related hereditary amyloidosis, the liver produces a mutated transthyreti protein which has severe neurodegenerative and/or cardiopathic effects. Liver transplantation can give a curative treatment option, *(* Cheng *et al 2017).*

Gilbert's syndrome, a genetic disorder of bilirubin metabolism found in a small percent of the population, can cause mild jaundice, *(Yu* HS *et al 2010).*

Cirrhosis is the formation of fibrous tissue (fibrosis) in the place of liver cells that have died due to a variety of causes, including viral hepatitis, alcohol overconsumption, and other forms of liver toxicity. Cirrhosis causes chronic liver failure,*(* Ozen *et al 2013).*

Primary liver cancer most commonly manifests as hepatocellular carcinoma and/or cholangiocarcinoma; rarer forms include angiosarcoma and hemangiosarcoma of the liver, (many liver malignancies are secondary lesions that have metastasized from primary cancers in the gastrointestinal tract and other organs, such as the kidneys, lungs) (Shibata *2014).*

Primary biliary cirrhosis is a serious autoimmune disease of the bile capillaries *(Nishida 2013).*

Primary sclerosing cholangitis is a serious chronic inflammatory disease of the bile duct, which is believed to be autoimmune in origin,(Dizdaroglu *2012).*

Budd–chiari syndrome is the clinical picture caused by occlusion of the hepatic vein, *(*Yu Y, Cui Y *et al 2016).*

2.2.3.3Mechanism of liver disease:

Liver disease can occur through several mechanisms:

DNA damage:

One general mechanism, increased DNA damage, is shared by some of the major causes of liver disease. These major causes include infection by hepatitis B virus or hepatitis C virus, alcohol abuse, and obesity,*(* Ivanov *et al 2017).*

2.2.4 Liver enzymes:

A number of liver function tests (LFTs) are available to test the proper function of the liver. This test for the presence of enzymes in blood those are normally most abundant in liver tissue, metabolites or products. Serum proteins, serum albumin, serum globulin, alanine transaminase, aspartate transaminase, prothrombin time, partial thromboplastic time. every single enzyme reflect a specific function related to the liver organ some of them reflect the amount of damage that has been taken place in liver, and the other reflect amount of obstruction,(Lee SM *et al 2016).*

2.2.4.1. Alanine transaminase (ALT):

Alanine transaminase (ALT) is a transaminase enzyme (EC 2.6.1.2). It is also called alanine aminotransferase (ALAT) and was formerly called serum glutamate-pyruvate transaminase (SGPT) or serum glutamic-pyruvic transaminase (SGPT) and was first characterized in the mid-1950s by arthur karmen and colleagues ALT is found in plasma and in various body tissues but is most common in the liver. It catalyzes the two parts of the alanine cycle. Serum ALT level, serum AST (aspartate transaminase) level, and their ratio (AST/ALT ratio) are commonly measured clinically as biomarkers for liver health. The tests are part of blood panels,(Karmen A et al 2009).

ALT function:

ALT catalyzes the transfer of an amino group from L-alanine to α-ketoglutarate, the products of this reversible transamination reaction being pyruvate and L-glutamate.

L-alanine + α-ketoglutarate ⇌ pyruvate + L-glutamate ALT (and all aminotransferases) require the coenzyme pyridoxal phosphate, which is converted into pyridoxamine in the first phase of the reaction, when an amino acid is converted into a keto acid, *(* Karmen *et al 2009).*

Clinical significance of ALT:

ALT is commonly measured clinically as part of liver function tests and is a component of the AST/ALT ratio,When used in diagnostics, it is almost always measured in international units/liter (IU/L) *(* Ghouri *2010)* or µkat. While sources vary on specific reference range values for patients, 0-40 IU/L is the standard reference range for experimental studies, *(*Lala *2018).*

Elevated levels of ALT:

Test results should always be interpreted using the reference range from the laboratory that produced the result. However typical reference intervals for ALT are:

patient type reference ranges *(Association for Clinical Biochemistry and Laboratory Medicine. Retrieved 7 October 2013).*

Female ≤ 34 IU/L

Male ≤ 45 IU/L

Significantly elevated levels of ALT (SGPT) often suggest the existence of other medical problems such as viral hepatitis, diabetes, congestive heart failure, liver damage, bile duct problems, infectious mononucleosis, or myopathy, so ALT is commonly used as a way of screening for liver problems. Elevated ALT may also be caused by dietary choline deficiency. 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 they can also increase in response to strenuous physical exercise, *(*Paul . Giboney American Family Physician *2014).*

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 hepatocyte damage can be distinguished from bile duct problems by measuring alkaline phosphatase.

Also, myopathy-related elevations in ALT should be suspected when the aspartate transaminase (AST) is greater than ALT; the possibility of muscle disease causing elevations in liver tests can be further explored by measuring muscle enzymes, including creatine kinase. many drugs may elevate ALT levels, including zileuton, omega-3 acid ethyl esters, *(*Dubbeldam *et al 2008)* anti-inflammatory drugs, antibiotics, cholesterol medications, some antipsychotics such as risperidone, and anticonvulsants. [citation needed] paracetamol (acetaminophen) may also elevate ALT levels, *(*Watkins *2006).* For years, the american red cross used ALT testing as part of the battery of tests to ensure the safety of its blood supply by deferring donors with elevated ALT levels. The intent was to identify donors potentially infected with hepatitis C because no specific test for that disease was available at the time. Prior to July 1992, widespread blood donation testing in the USA for hepatitis C was not carried out by major blood banks. With the introduction of second-generation ELISA antibody tests for hepatitis C, the Red Cross changed the ALT policy. As of July 2003, donors previously disqualified for elevated ALT levels and no other reason may be reinstated as donors when they contact the donor-counseling department of their regional Red Cross organization, *(from the original on 2005).*

In 2000, the american association for clinical chemistry determined that the appropriate terminology for AST and ALT are aspartate aminotransferase and alanine aminotransferase. the term transaminase is outdated and no longer used in liver disease (Dufour *2000).*

2.2.4.2 Aspartate transaminase (AST):

Aspartate transaminase (AST) or aspartate aminotransferase, also known as AspAT/ASAT/AAT or (serum) glutamic oxaloacetic transaminase (GOT, SGOT), is a pyridoxal phosphate (PLP)-dependent transaminase enzyme

(EC 2.6.1.1) that was first described by arthur karmen and colleagues in 1954, *(*KARMEN *et al 2009),* AST catalyzes the reversible transfer of an α-amino group between aspartate and glutamate and, as such, is an important enzyme in amino acid metabolism. AST is found in the liver, heart, skeletal muscle, kidneys, brain, and red blood cells. Serum AST level, serum ALT (alanine transaminase) level, and their ratio (AST/ALT ratio) are commonly measured clinically as biomarkers for liver health. the tests are part of blood panels.

Function of AST:

Aspartate transaminase catalyzes the interconversion of aspartate and α-ketoglutarate to oxaloacetate and glutamate.

1L-Aspartate (Asp) + α-ketoglutarate ↔ oxaloacetate + L-glutamate (Glu)

Reaction catalyzed by aspartate aminotransferase

as a prototypical transaminase, AST relies on PLP (Vitamin B6) as a cofactor to transfer the amino group from aspartate or glutamate to the corresponding ketoacid. In the process, the cofactor shuttles between PLP and the pyridoxamine phosphate (PMP) form. *(from the original on 2005),* The amino group transfer catalyzed by this enzyme is crucial in both amino acid degradation and biosynthesis. In amino acid degradation, following the conversion of α-ketoglutarate to glutamate, glutamate subsequently undergoes oxidative deamination to form ammonium ions, which are excreted as urea. In the reverse reaction, aspartate may be synthesized from oxaloacetate, which is a key intermediate in the citric acid cycle, (Dubbeldam *et al 2008).*

Clinical significance of AST:

AST is similar to alanine transaminase (ALT) in that both enzymes are associated with liver parenchymal cells. 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, *(*Goldberg *2004)*, As a result, ALT is a more specific indicator of liver inflammation than AST, as AST may be elevated also in diseases affecting other organs, such as myocardial infarction, acute pancreatitis, acute hemolytic anemia, severe burns, acute renal disease, musculoskeletal diseases, and trauma,(Hirotsu *et al., 2005).*

AST was defined as a biochemical marker for the diagnosis of acute myocardial infarction in 1954. However, the use of AST for such a diagnosis is now redundant and has been superseded by the cardiac troponins, (Berg, *et al., 2006)*

AST is commonly measured clinically as a part of diagnostic liver function tests, to determine liver health. However, it is important to keep in mind that the source of AST (and, to a lesser extent, ALT) in blood tests may reflect pathology in organs other than the liver. In fact, when the AST is higher than ALT, a muscle source of these enzymes should be considered. For example, muscle inflammation due to dermatomyositis may cause AST>ALT. This is a good reminder that AST and ALT are not good measures of liver function because they do not reliably reflect the synthetic ability of the liver and they may come from tissues other than liver (such as muscle).

Laboratory tests should always be interpreted using the reference range from the laboratory that performed the test. example reference ranges are shown below: an aspartate aminotransferase (AST) test measures the amount of this enzyme in the blood. AST is normally found in red blood cells, liver, heart, muscle tissue, pancreas, and kidneys. AST formerly was called serum glutamic oxaloacetic transaminase (SGOT).

Low levels of AST are normally found in the blood. When body tissue or an organ such as the heart or liver is diseased or damaged, additional AST is released into the bloodstream. The amount of AST in the blood is directly related to the extent of the tissue damage. After severe damage, AST levels rise in 6 to 10 hours and remain high for about 4 days.

The AST test may be done at the same time as a test for alanine aminotransferase, or ALT. The ratio of AST to ALT sometimes can help determine whether the liver or another organ has been damaged. both ALT and AST levels can test for liver damage. *(*McPhalen *et al 2011).*

High amount of AST: the aspartate aminotransferase (AST) test is a blood test that checks for liver damage. The doctor might order this test to find out if you have liver disease and to monitor your treatment.

your liver is an organ that has many important jobs.

It makes a fluid called bile that helps the body digest food. it also removes waste products and other toxins from your blood. it produces proteins, as well as substances that help your blood clot. Alcohol or drug use and diseases such as hepatitis can damage your liver and keep it from doing these jobs, *(*Gaze *2007).*

AST is an enzyme your liver makes. Other organs, like your heart, kidneys, brain, and muscles, also make smaller amounts. AST is also called SGOT (serum glutamic-oxaloacetic transaminase).

Normally, AST levels in your blood are low, when your liver is damaged, it puts more AST into your blood, and your levels rise.

A high AST level is a sign of liver damage, but it can also mean you have damage to another organ that makes it, like your heart or kidneys. that's why doctors often do the AST test together with tests of other liver enzymes, *(*Muriana *et al., 2008).*

2.3 Albumin:

Albumin is the most abundant plasma protein with a concentration ranging from 35 to 50 g/L.*(* Cabrerizo *et al., 2015).* Albumin represents 50% of the total protein content of plasma, with globulins making up most of the rest. It is a single peptide chain of 585 amino acids in a globular structure. The molecular weight of albumin is approximately 66 kDa, and it has a half-life of 21 days. Albumin is exclusively synthesized by the liver, initially a pre-proalbumin and then proalbumin, which in the golgi apparatus is converted to albumin, which is the final form secreted by the hepatocyte, very little albumin is stored in the liver. The synthetic rate is about 10 to 15 grams per day and then secreted into the circulation of which around 40% remains in circulation with a fraction moving from the intravascular to the interstitial space (Brock *et al., 2016*). Factors that stimulate albumin synthesis include the action of hormones such as insulin and growth hormone. Albumin production may be inhibited by pro-inflammatory mediators such as interleukin-6 (IL-6), interleukin-1 (IL-1) and tumor necrosis factor *(*Ballmer *2001*). Albumin has several physiological roles. One of the most important is to maintain the oncotic pressure within the vascular compartments preventing leaking of fluids into the extravascular spaces. Albumin functions as a low-affinity, high-capacity carrier of several different endogenous and exogenous compounds. Also, albumin binds at least 40% of the circulating calcium, fatty acid, bilirubin and many drugs, and is a transporter of hormones such as thyroxin, cortisol, testosterone, fatty acid, bilirubin and many drugs albumin is also involved with maintaining acid-base balance as it acts as a plasma buffer. (Brock *et al 2016*). Renal and gut loss of albumin may account for around 6% and 10% respectively of albumin loss in healthy

individuals. a decrease in serum albumin levels below the reference interval hypoalbuminemia (William *2012*).

2.3.1 Relationship between albumin and age:

Some studies have shown a negative association between age and serum albumin. Several of these studies included older people with known disease, *(*Dubbeldam *et al 2008)* disease may reduce albumin in any age group. Other studies have shown no association between age and albumin. To investigate the association of age and albumin, albumin levels were determined in 241 apparently healthy subjects aged 55 to 101. A small but consistent negative regression slope of about 4% per decade was found for those aged over 70. Because the relationship to age was small, the finding of hypoalbuminemia in an elderly patient generally should be attributed to disease rather than age alone, *(*Watkins *et al 2006).*

Chapter Three

3-Materials and Methods

3.1 Materials

3.1.1 Study design:

This study is analytical hospital base-case control study

3.1.2 Study Area:

The study will be conducted in in North Kordofan state in ELobied city in 2019.

3.1.3 Study population:

The study will be consisted of 50 Patients diagnosis with Hypertension (HTN or HT) and 50 controls group (healthy volunteer) will be involved in the study, age will be matched.

3.1.4 Inclusion criteria:

Hypertension (HTN or HT) women and men who are clinically diagnosed with different ages and tripe were included in this study.

3.1.5 Exclusion criteria:

Patients with any other causes of liver injury were excluded from this study.

Smokers

Alcoholism

Diabetic patients

All patients with liver diseases or other diseases that may affect liver enzymes

3.1.6 Ethical issues:

All patients and controls were informed about the aim of the study and accepted the diagnostic procedure. Their participation in this study was fully voluntary and a verbal consent was taken from all patients included in the study.

3.1.7 Data collection tools:

3.1.7.1 Questionnaire:

The data will be collected from all participants through closed ended questionnaire; patient's records will be reviewed to confirm diagnosis and information.

3.1.7.2 Sample collection:

After informed consent a sample were collected by using dry, plastic syringes, 5ml blood sample was collected from each respective case and control subject in plain container. The samples were centrifuged and separated in epindorf tube and stored at -20 until analysis.

3.2 Methodology:

Estimation of ALT, AST and ALBUMIN are done by using BA400(BIOCHEMISTRY ANALYZER)

Principle of BA400 (Biochemistry analyzar):

Each sample was measured for Aspartate transaminase (AST), Alanine transaminase (ALT) and Alkaline Phosphatase. The three enzymes were meaured by using BA400 (Biochemistry analyzar) procedure.

3.2.1 Estimation of ALT

Principle:

ALT catalyzes the reaction between L-alanine and 2-oxoglutarate. The pyruvate formed is reduced by NADH in a reaction catalyzed by lactate dehydrogenase (LDH) to form L-lactate and NAD+. The rate of NADH oxidation is directly proportional to the catalytic ALT activity. It is determined by measuring the decrease in absorbance.

3.2.2 Estimation of AST

Principle:

AST in the sample catalyzes the transfer of an amino group between L-aspartate and 2-oxoglutarate to form oxaloacetate and L-glutamate. The oxaloacetate then reacts with NADH, in the presence of malate dehydrogenase (MDH), to form NAD+ . The rate of the NADH oxidation is directly proportional to the catalytic AST activity. It is determined by measuring the decrease in absorbance.

3.2.3 Estimation of albumin

Principle:

Albumin reacts with BCG at acidic PH 4.2 to give blue - green color complex that can be measured by photoelectric colorimeter.

3.2.4 Quality control:

The precision and accuracy of all method used in this study will be checked by commercially prepared control sample before its application for the measurement of test and control samples.

3.2.5 Statistical analysis:

Statistical procedure will be followed using statistic package for social science (SPSS) version 20 on programmed computer. T-test and person correlation were used for analysis of results.

Chapter Four

4.1 Result:

This study included 50 female and male with hypertension (HTN or HT) and 50 without hypertension (HTN or HT) age matched, the result illustrated in tables and figures as follow, The mean concentration of AST,ALT and albumin were significantly increased among Hypertension (HTN or HT) patient (35.154±2.3184) (35.858±2.6679) (4.000±.3105) in comparison with control group (23.354±4.5197) (25.478±4.7412) (3.702±.1985) with p value 0.000 respectively which presented in table 4.1,

The mean concentration of AST,ALT were significantly increased among male group (36.188±1.8608) (36.671±2.9243) in comparison with female group (34.200±2.31190) (35.108±2.2053) with p value 0.002 , 0.037 respectively which presented in table 4.2, in contracts there is significant increase in the mean concentration of albumin in female group (4.089±0.3627) in Comparison with male group (3.904±0.2095) with (p value=0.034) is presented in table 4.2.

Person's correlation showed no correlation observed when associated serum AST,ALT and albumin with age of hypertension (HTN or HT) patient (r 0.013 , P value 0.927) (r 0.078 P value 0.550) (r=0.107, p-value 0.459) presented in figure 4.1,4.2,4.3 respectively, and there is week correlation observed when associate serum AST,ALTwith duration of hypertension (HTN or HT) (r 0.204 P value 0.156) (r 0.239 , P value 0.095) presented in figure4.4, 4.5 respectively but serum albumin not correlated with duration of hypertension (HTN or HT) patient(r 0.112 p value 0.440) presented in figure 4.6.

Table 4.1

Comparison between the mean of AST, ALT and Albumin in patients with Hypertension disease as (Case) and (Control) group.

Variable	**Case (n=50) Mean ± SD**	**Control (n = 50) Mean ± SD**	**p. value**
AST U/ L	**35.154 ±2.3184**	**23.354 ±4.5197**	**.000**
ALT U/ L	**35.858 ±2.6679**	**25.478 ±4.7412**	**.000**
Albumin g/dl	**4.000 ±.3105**	**3.702 ± .1985**	**.000**

- The table show the mean ± SD and P value.
- T-test was used for comparison.
- P value < 0.05 considered Significant.

Table 4.2

Comparison AST, ALT, and Albumin between Male group and Female group with Hypertension disease

Variables	**male n =24 Mean ± SD**	**Female n =26 Mean ± SD**	**P. value**
AST(U/L)	**36.188+ 1.8608**	**34.200+ 2. 31190**	**0.002**
ALT(U/L)	**36.671 + 2.9243**	**35.108+ 2.2053**	**0.037**
Albumin (g /dl)	**3.904 + 0.2095**	**4.089+ 0.362**	**0.034**

- The table show the mean ± SD and P. value.
- T-test was used for comparison.
- P value < 0.05 considered Significant.

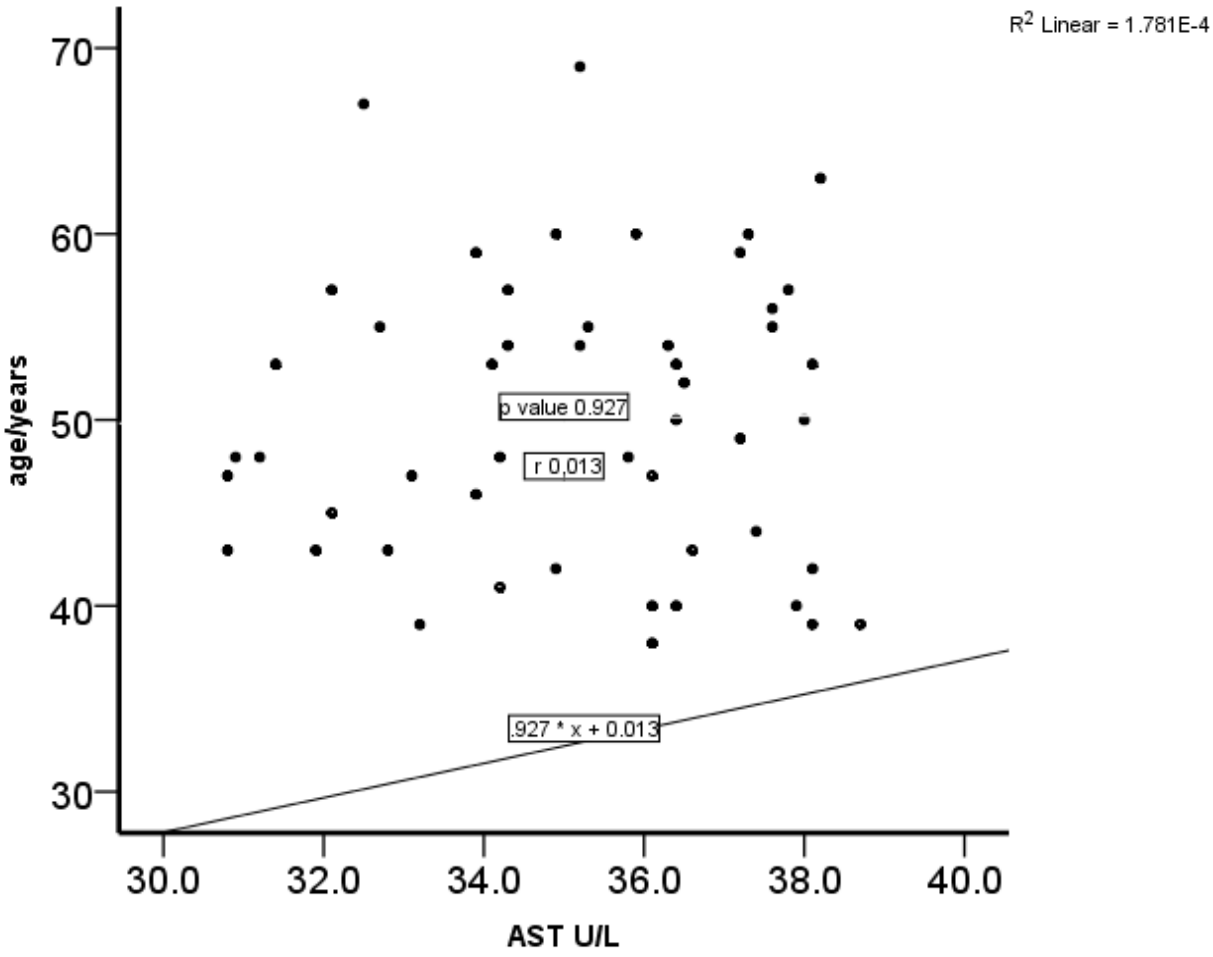

Figure 4.1

Correlation between AST and age (r = 0.013, p = 0.927)

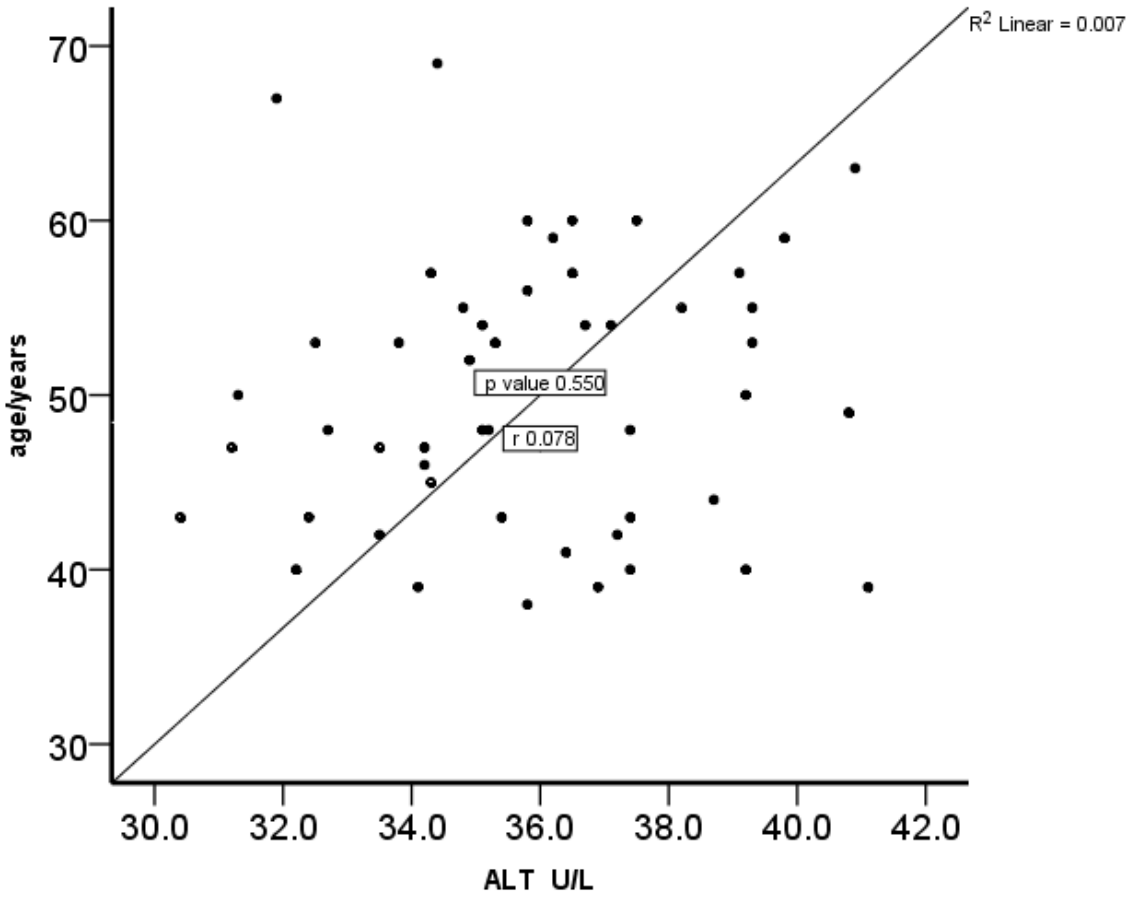

Figure 4.2

Correlation between ALT and age (r = 0.078, p = 0.550)

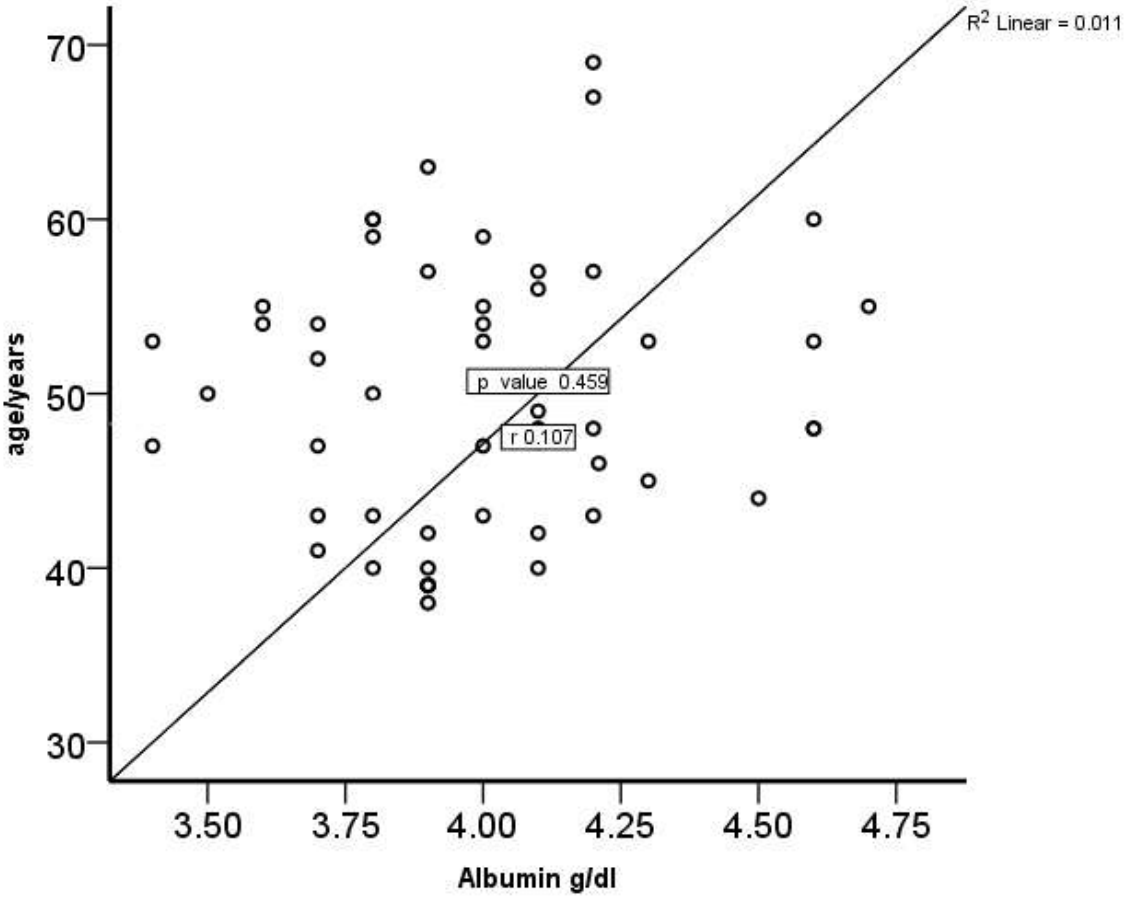

Figure : 4.3

Correlation between Albumin and age (r = 0.107, p = 0.459)

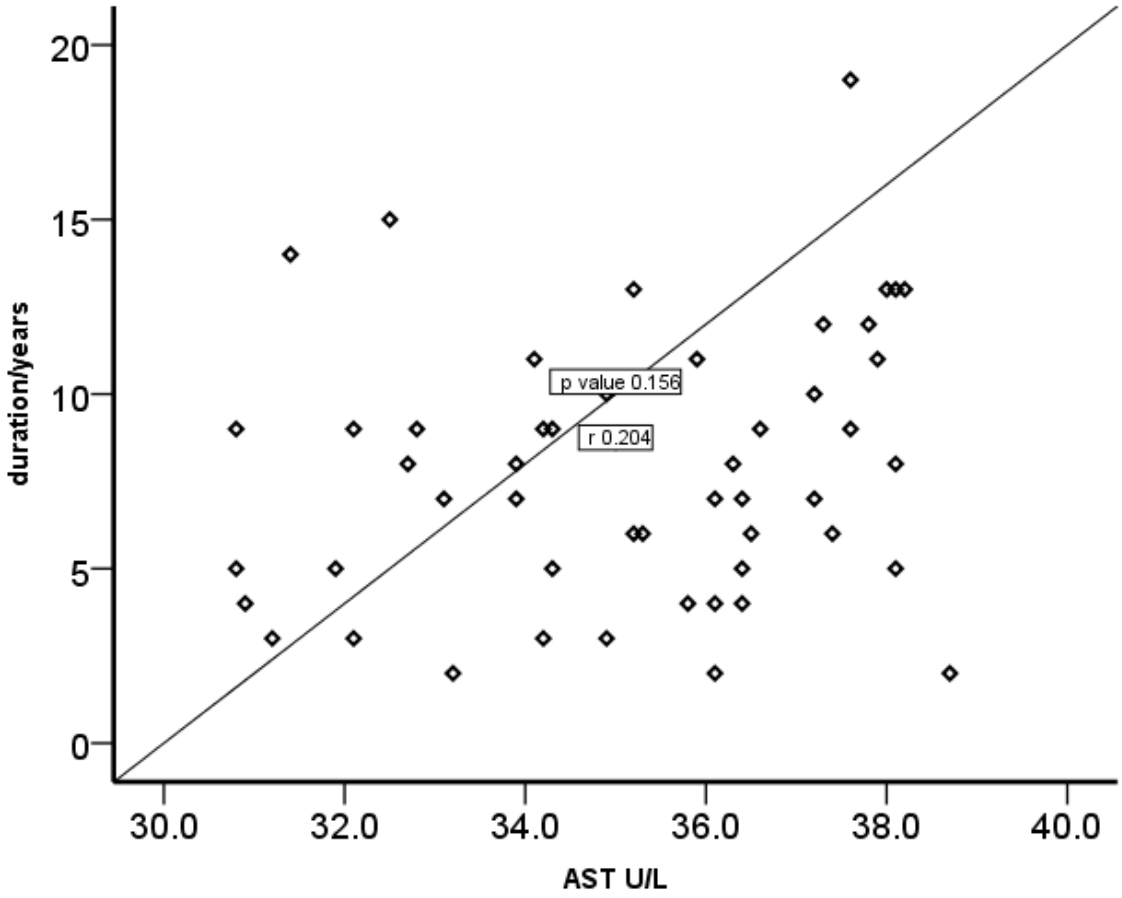

Figure: 4.4

Correlation between AST and duration (r = 0.204, p = 0.156)

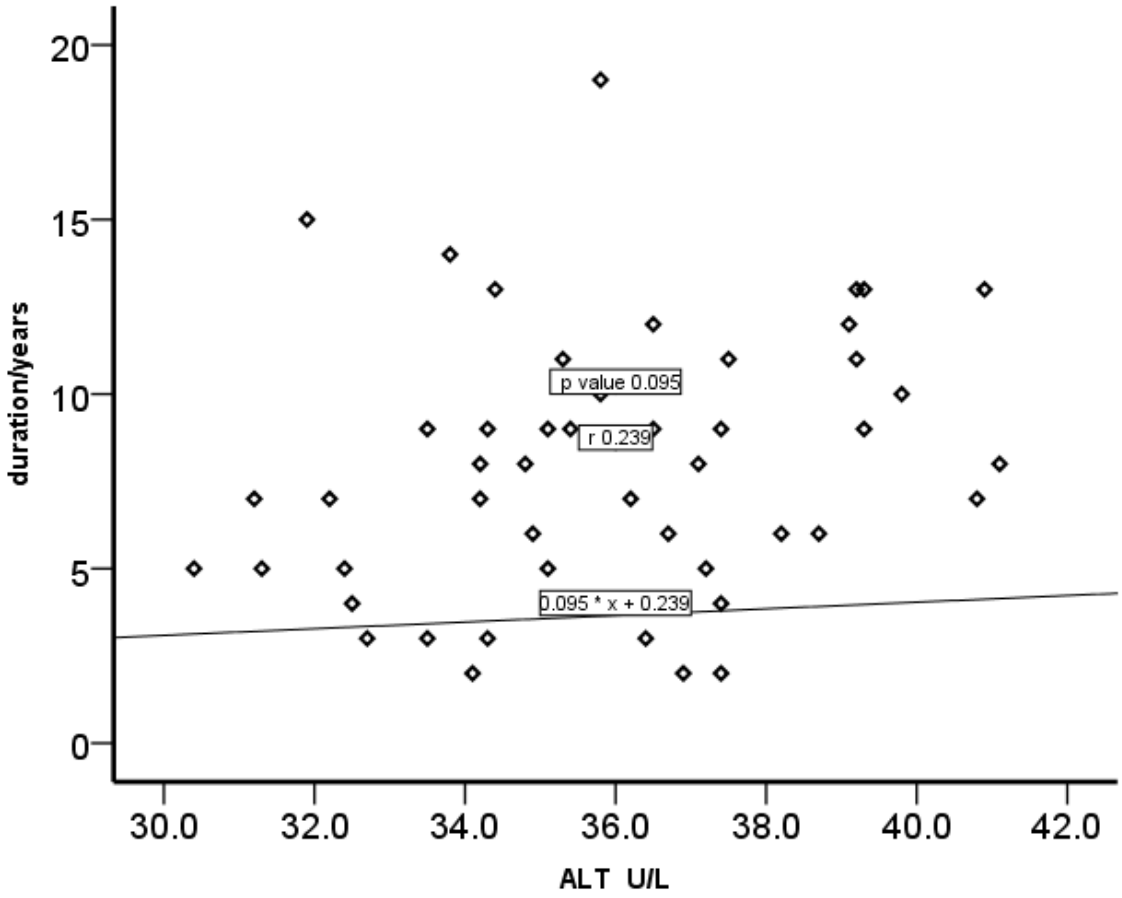

Figure 4.5

Correlation between ALT and duration (r = 0.239, p = 0.095)

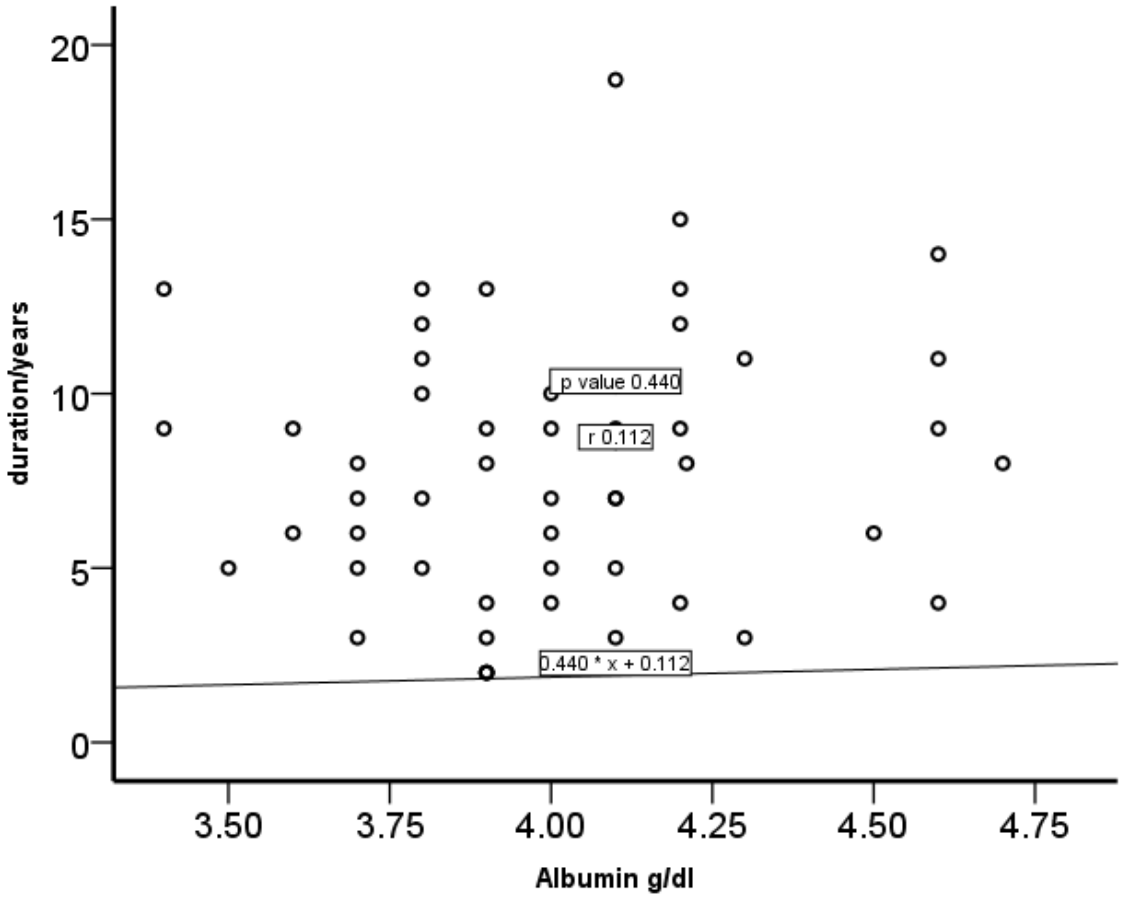

Figure 4.6

Correlation between Albumin and duration (r = 0.112, p = 0.440)

Chapter five

5. Discussion, Conclusion and Recommendation

5.1 Discussion

Hypertension (HTN or HT), is a long-term medical condition in which the blood pressure in the arteries is persistently elevated, *(*Hernandorena Duron *et al 2019)* Long-term high blood pressure, however, is a major risk factor for coronary artery disease, stroke, heart failure, atrial fibrillation, peripheral vascular disease, vision loss, chronic kidney disease, and dementia (Lackland and Weber *2015).*

In Sudan the prevalence of hypertension was around 35.7% and the newly diagnosed cases were 22.4% *(* Bushara *et al 2016)* Because hypertension affect many organs functions , this study was done to evaluate the liver functions.

The present study revealed that, serum albumin , serum ALT, serum AST were statistically significant increase in hypertension (p value<0.05) this agree with study done by *(*shalini sathiyamoorthy *et al 2016) (*donati, *et al 2017)* in relation to, AST,ALT with hypertension and disagree in the relation of Albumin and this result may be the level of hypertension in the patient were not reach to that high level which affect the synthetic function of liver (albumin) And *(* donati, *et al 2017)* never mentioned albumin he was taken other parameter in consideration.

Our study agree with in elevation of ALT,AST in male more than female, High hemoglobin level is a significant risk factor of ALT,AST elevation ,So Males have greater risk of abnormal liver function which may be associated with higher hemoglobin levels and also may be because of different in body mass *(* schwimmer *et al 2005),* low albumin was remarkably higher in men than in women and this agree with *(*Grimm *et al 2009)* study.

(Elinav et al 2006) study found that there is no correlation between AST with age, and Significant correlation between ALT and albumin with age, The present study agree in respect with AST , and disagree in respect with ALT and albumin,

The differences in the result between to studies may be due to different place and life style of the population of north kordofan state(elobied) and the population were included in these two different studies,

The study found that there is weak correlation between AST, ALT and duration of disease, and it showed that no correlation between albumin and duration, this agree with (Lei Wu, *et al 2017)* study in AST, and disagree with this study in association of ALT and duration. which shown significant association. And this different result may be due to different geographic area the study made in. our study disagree with *(*Michael Riordan *2008)*, so there were association between albumin and hypertension duration. And the differences might be according to the variation between population or due to different life style or because of different place the study were conducted.

5.2 Conclusion:

The study was concluded that, serum ALT, AST, albumin are higher among hypertensive patient compared to healthy.

5.3 Recommendations:

From the findings of this study it is recommended that:

• Biochemical test ALT, AST and albumin should be done as early liver dysfunction tests and follow up especially to those who are diagnosed with have constant Hypertension and they taking regular drugs.

• Further studies should be done to investigate ALT, AST, Gamma-glutamyl transferase (GGT) – alkaline phosphatase(ALP), .serum globulin. among serum albumin.

• Life style modifications program such as exercise, healthy diets, low calories intake, and low salt intake and physical activities to be implemented in male and females especially people who are irritable and worm-blooded, to reduce the susceptibility to hypertension (HTN or HT).

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Appendixes

Appendix I

Sudan University of Science and Technology

College of graduate studies

Questionnaire of serum level of ALT, AST and Albumin in male and female with hypertension disease

Questionnaire

1. Sample number ……
2. Gender Male ☐ Female ☐
3. Ager group ……. Years
4. HTN

   Yes ☐ No ☐
5. Duration of HTN …….. years
6. History of having

a. D.M.	Yes	☐	No	☐
b. Hepatitis	Yes	☐	No	☐
c. Smoking	Yes	☐	No	☐
d. Alcoholism	Yes	☐	No	☐
e. Jaundice	Yes	☐	No	☐
f. Liver transplant	Yes	☐	No	☐
g. Others	Yes	☐	No	☐

Laboratory investigation

ALT ……u/l

AST ……u/l

Albumin ……g/dl

Appendix II

COD 11532 1 x 50 mL	COD 11533 1 x 200 mL	COD 11568 1 x 500 mL	COD 11562 1 x 1 L
STORE AT 2-8ºC			
Reagents for measurement of ALT/SGPT concentration. Only for in vitro use in the clinical laboratory			

ALANINE AMINOTRANSFERASE (ALT/GPT)

BioSystems

CE

ALANINE AMINOTRANSFERASE (ALT/GPT) IFCC

PRINCIPLE OF THE METHOD

Alanine aminotransferase (ALT or GPT) catalyzes the transfer of the amino group from alanine to 2-oxoglutarate, forming pyruvate and glutamate. The catalytic concentration is determined from the rate of decrease of NADH, measured at 340 nm, by means of the lactate dehydrogenase (LDH) coupled reaction[1,2].

$$\text{Alanine} + 2\text{-Oxoglutarate} \xrightarrow{\text{ALT}} \text{Pyruvate} + \text{Glutamate}$$

$$\text{Pyruvate} + \text{NADH} + \text{H}^+ \xrightarrow{\text{LDH}} \text{Lactate} + \text{NAD}^+$$

CONTENTS

	COD 11532	COD 11533	COD 11568	COD 11562
A. Reagent	1 x 40 mL	1 x 180 mL	1 x 450 mL	1 x 900 mL
B. Reagent	1 x 10 mL	1 x 40 mL	1 x 100 mL	1 x 200 mL

COMPOSITION

A. Reagent: Tris 150 mmol/L, L-alanine 750 mmol/L, lactate dehydrogenase > 1350 U/L, pH 7.3.

B. Reagent: NADH 1.0 mmol/L, 2-oxoglutarate 75 mmol/L, Sodium hydroxide 148 mmol/L, sodium azide 9.5 g/L.

WARNING: H300: Harmful if swallowed. EUH031: Contact with acids liberates toxic gas. P301+P312: IF SWALLOWED: Call a POISON CENTER or doctor/physician if you feel unwell. P330: Rinse mouth.

For further warnings and precautions, see the product safety data sheet (SDS).

STORAGE

Store at 2-8ºC.

Reagents are stable until the expiry date shown on the label when stored tightly closed and if contaminations are prevented during their use.

Indications of deterioration:

– Reagents: Presence of particulate material, turbidity, absorbance of the blank lower than 1.400 at 340 nm (1 cm cuvette).

AUXILIARY REAGENTS

C. Reagent (ref 11680): Pyridoxal phosphate 10 mmol/L, 5 mL.

REAGENT PREPARATION

Working Reagent: Pour the contents of the Reagent B into the Reagent A bottle. Mix gently. Other volumes can be prepared in the proportion: 4 mL Reagent A + 1 mL Reagent B (Note 1). Stable for 1 month at 2-8ºC.

Working Reagent with Pyridoxal Phosphate (Note 2): Mix as follows: 10 mL of Working Reagent + 0.1 mL of Reagent C (cod 11680). Stable for 6 days at 2-8ºC.

ADDITIONAL EQUIPMENT

– Analyzer, spectrophotometer or photometer with cell holder thermostatable at 30 or 37ºC and able to read at 340 nm.

– Cuvettes with 1 cm light path.

SAMPLES

Serum and plasma collected by standard procedures.

Alanine aminotransferase in serum and plasma is stable for 7 days at 2-8ºC. Use heparin or EDTA as anticoagulant.

PROCEDURE

1. Bring the Working Reagent and the instrument to reaction temperature.
2. Pipette into a cuvette (Note 3):

Reaction temperature	37ºC	30ºC
Working Reagent	1.0 mL	1.0 mL
Sample	50 µL	100 µL

3. Mix and insert the cuvette into the photometer. Start the stopwatch.
4. After 1 minute (Note 1), record initial absorbance and at 1 minute intervals thereafter for 3 minutes.
5. Calculate the difference between consecutive absorbances, and the average absorbance difference per minute (ΔA/min).

CALCULATIONS

The ALT/GPT concentration in the sample is calculated using the following general formula:

$$\Delta A/\text{min} \times \frac{\text{Vt} \times 10^3}{\varepsilon \times l \times \text{Vs}} = \text{U/L}$$

The molar absorbance (ε) of NADH at 340 nm is 6300, the lightpath (l) is 1 cm, the total reaction volume (Vt) is 1.05 at 37ºC and 1.1 at 30ºC, the sample volume (Vs) is 0.05 at 37ºC and 0.1 at 30ºC, and 1 U/L are 0.0166 µkat/L. The following formulas are deduced for the calculation of the catalytic concentration:

	37ºC	30ºC
ΔA/min	x 3333 = U/L x 55.55 = µkat/L	x 1746 = U/L x 29.1 = µkat/L

REFERENCE VALUES

Reaction temperature	37ºC	30ºC
Values per P. up to*	41 U/L = 0.68 µkat/L	25 U/L = 0.42 µkat/L
With per P. up to*	68 U/L = 1.08 µkat/L	35 U/L = 0.58 µkat/L

Concentrations in newborns and infant are slightly higher than in adults. Values in men are slightly higher than in women.

These ranges are given for orientation only; each laboratory should establish its own reference ranges.

QUALITY CONTROL

It is recommended to use the Biochemistry Control Serum level I (cod. 18005, 18009 and 18042) and II (cod. 18007, 18010 and 18043) to verify the performance of the measurement procedure.

Each laboratory should establish its own Internal Quality Control scheme and procedures for corrective action if controls do not recover within the acceptable tolerances.

METROLOGICAL CHARACTERISTICS

– Detection limit: 1.8 U/L = 0.027 µkat/L.

– Linearity limit: 600 U/L = 10.3 µkat/L. For higher values dilute sample 1/10 with distilled water and repeat measurement.

– Repeatability (within run):

Mean Concentration	CV	n
43 U/L = 0.73 µkat/L	1.8 %	20
192 U/L = 3.2 µkat/L	2.8 %	20

– Reproducibility (run to run):

Mean Concentration	CV	n
43 U/L = 0.72 µkat/L	5.3 %	25
192 U/L = 3.2 µkat/L	4.7 %	25

– Sensitivity: 0.3 ΔmA-U/U·min = 0.00502 ΔmA·L/µkat·min.

– Trueness: Results obtained with this reagent did not show systematic differences when compared with reference reagents. Details of the comparison experiments are available on request.

– Interferences: Hemolysis (hemoglobin 10 g/L) and bilirubin (20 mg/dL) do not interfere. Lipemia (triglycerides 2 g/L) may affect the results. Other drugs and substances may interfere[3].

These metrological characteristics have been obtained using an analyzer. Results may vary if a different instrument or a manual procedure are used.

DIAGNOSTIC CHARACTERISTICS

The aminotransferases catalyze the formation of glutamic acid from 2-oxoglutarate by transfer of amino groups. ALT is normally present in various tissues but its higher concentrations are found in liver and kidney.

The serum concentration of ALT is elevated in hepatitis and other forms of hepatic disease associated with necrosis: infectious mononucleosis, cholestasis, cirrhosis, metastatic carcinoma of the liver, delirium tremens, and after administration of various drugs, such as opiates, salicylates or ampicillin[4].

Serum ALT concentration can also be elevated in skeletal or cardiac muscle disease[4,5].

Clinical diagnosis should not be made on the findings of a single test result, but should integrate both clinical and laboratory data.

NOTES

1. The initial absorbance of the reaction mixture may be out of range in some photometers with a low maximum absorbance reading. For these photometers it is recommended to prepare the Working Reagent by mixing in the proportion: 5 mL Reagent A + 1 mL Reagent B.
2. The IFCC recommended method specifies the addition of pyridoxal phosphate. This delay time before measurements should then be increased to 2 minutes.
3. These reagents may be used in several automatic analysers. Instructions for many of them are available on request.

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M119335-23

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Quality System certified according to EN ISO 13485 and EN ISO 9001 standards

CODE 11532 1 x 50 mL	CODE 11533 1 x 200 mL	CODE 11568 1 x 500 mL	CODE 11562 1 x 1 L
CONSERVER A 2-8ºC			
Réactifs pour mesurer la concentration d'ALT/SGPT. A utiliser uniquement in vitro dans les laboratoires cliniques			

ALANINE AMINOTRANSFERASE (ALT/GPT)

BioSystems

CE

ALANINE AMINOTRANSFERASE (ALT/GPT) IFCC

PRINCIPE DE LA METHODE

L'alanine aminotransférase (ALT ou GPT) catalyse le transfert du groupement amino de l'alanine au 2-oxoglutarate, en formant le pyruvate et le glutamate. La concentration catalytique est déterminée en utilisant la réaction couplée de la lactate-déshydrogénase (LDH), à partir de la vitesse de disparition du NADH, mesuré à 340 nm[1,2].

$$\text{Alanine} + 2\text{-Oxoglutarate} \xrightarrow{\text{ALT}} \text{Pyruvate} + \text{Glutamate}$$

$$\text{Pyruvate} + \text{NADH} + \text{H}^+ \xrightarrow{\text{LDH}} \text{Lactate} + \text{NAD}^+$$

CONTENU

	CODE 11532	CODE 11533	CODE 11568	CODE 11562
A Réactif	1 x 40 mL	1 x 180 mL	1 x 450 mL	1 x 900 mL
B Réactif	1 x 10 mL	1 x 40 mL	1 x 100 mL	1 x 200 mL

COMPOSITION

A. Réactif: Tris 100 mmol/L, L-alanine 750 mmol/L, lactate-déshydrogénase > 1350 U/L, pH 7.3.

B. Réactif: NADH 1,0 mmol/L, 2-oxoglutarate 75 mmol/L, Hydroxyde de sodium 148 mmol/L, sodium azide 9,5 g/L.

ATTENTION: H300: Mortel en cas d'ingestion. EUH031: Au contact d'un acide, dégage un gaz toxique. P301+P312: EN CAS D'INGESTION: appeler un CENTRE ANTIPOISON ou un médecin en cas de malaise. P330: Rincer la bouche.

Pour d'autres mises en garde et précautions, voir la fiche de données de sécurité du produit (SDS).

CONSERVATION

Les réactifs doivent être conservés à 2-8ºC. Bien refermer les flacons et éviter toute contamination lors de l'utilisation. Dans ces conditions ils restent stables jusqu'à la date indiquée sur l'étiquette.

Indications de dégradation:

– Réactifs: Présence de particules, turbidité, absorbance du blanc inférieure à 1,400 à 340 nm (cuvette de 1 cm).

REACTIFS SUPPLEMENTAIRES

Réactif (C): (Code: 11680) Phosphate de Pyridoxal 10 mmol/L, 5 mL.

PREPARATION DES REACTIFS

Réactif de travail: Voler le contenu d'un flacon de Réactif B dans un flacon de Réactif A. Homogénéiser. D'autres volumes peuvent être préparés dans les proportions: 4 mL Réactif A + 1 mL Réactif B (Note 1). Le Réactif de travail est stable 1 mois à 2-8ºC.

Réactif de Travail avec Phosphate de Pyridoxal (Note 2): Mélangez dans la proportion: 10 mL de Réactif de Travail + 0,1 mL de Réactif C (Code: 11680). Stable 6 jours à 2-8ºC.

EQUIPEMENT SUPPLEMENTAIRE

– Analyseur, Spectrophotomètre ou photomètre à cuve thermostatable à 30 ou 37ºC, pour lectures à 340 nm.

– Cuve de 1 cm de trajet optique.

ECHANTILLONS

Sérum et plasma prélevés par des procédures standard.

L'Alanine aminotransférase dans le sérum et le plasma est stable 7 jours à 2-8ºC. L'héparine ou l'EDTA doit être utilisé comme anticoagulants.

PROCEDURE

1. Porter le réactif de travail et l'instrument à la température de réaction.
2. Pipeter dans la cuvette (Note 3):

Température de réaction	37ºC	30ºC
Réactif de travail	1,0 mL	1,0 mL
Échantillon	50 µL	100 µL

3. Mélangez et insérez la dans le porte-cuve thermostaté. Mettre le chronomètre en marche.
4. Au bout de 1 minutes (Note 1), notez l'absorbance initiale et effectuez des nouvelles lectures chaque minute pendant 3 minutes.
5. Calculez l'accroissement moyen d'absorbance par minute (ΔA/min).

CALCULS

La concentration en ALT/SGPT de l'échantillon est calculée selon la formule suivante:

$$\Delta A/\text{min} \times \frac{\text{Vt} \times 10^3}{\varepsilon \times l \times \text{Vs}} = \text{U/L}$$

Le coefficient d'extinction moléculaire (ε) du NaDH à 340 nm est de 6300, le trajet optique (l) de 1cm, le volume réactionnel total (Vt) est 1,05 à 37ºC et 1,1 à 30ºC, le volume d'échantillon (Vs) de 0,05 à 37ºC et 0,1 à 30ºC, et 1 U/L équivalent à 0,0166 µkat/L, on en déduit les facteurs suivants pour calculer la concentration catalytique:

	37ºC	30ºC
ΔA/min	x 3333 = U/L x 55,55 = µkat/L	x 1746 = U/L x 29,1 = µkat/L

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VALEURS DE REFERENCE

Température de réaction	37ºC	30ºC
Sans Phos-pyr. jusqu'à*	41 U/L = 0,68 µkat/L	25 U/L = 0,40 µkat/L
Avec Phos-pyr. jusqu'à*	68 U/L = 1,08 µkat/L	35 U/L = 0,59 µkat/L

Les concentrations chez les nouveaux-nés et l'enfant sont sensiblement plus élevées que chez les adultes. Les valeurs ont tendance à être légèrement plus élevées chez l'homme que chez la femme.

Ces valeurs ne sont données qu'à titre indicatif. Chaque laboratoire doit établir ses propres valeurs de référence.

CONTRÔLE DE QUALITE

Il est recommandé d'utiliser les Sérums Contrôles de Biochimie niveau I (Code: 18005, 18009 ou 18042) et II (Code: 18007, 18010 ou 18043) pour vérifier la qualité de la méthodologie.

Chaque laboratoire doit établir ses propres protocoles et schémas de Contrôle de Qualité Interne afin d'apporter les modifications nécessaires en cas de dépassement des tolérances.

CARACTERISTIQUES METROLOGIQUES

– Limite de détection : 1,8 U/L = 0,027 µkat/L.

– Limite de linéarité: 600 U/L = 10,3 µkat/L. Pour des valeurs supérieures diluer l'échantillon au 1/10 en eau distillée et répéter l'essai.

– Répétabilité (intra-série):

Concentration moyenne	CV	n
43 U/L = 0,73 µkat/L	1,8 %	20
192 U/L = 3,2 µkat/L	2,8 %	20

– Reproductibilité (intermédiaire):

Concentration moyenne	CV	n
43 U/L = 0,72 µkat/L	5,3 %	25
192 U/L = 3,2 µkat/L	4,7 %	25

– Sensibilité: 0,3 ΔmA-U/U·min = 0,00502 ΔmA·L/µkat·min.

– Justesse: Les résultats obtenus avec ce réactif n'ont pas montré de différences systématiques significatives par rapport aux réactifs de référence. Les détails des études comparatives sont disponibles sur demande.

– Interférences: L'hémolyse (hémoglobine 10 g/L) et la bilirubine (20 mg/dL) n'interfèrent pas. Les Lipides (triglycérides 2 g/L) peuvent affecter les résultats. Certains médicaments et substances peuvent interférer[3].

Ces caractéristiques métrologiques ont été obtenues en utilisant un analyseur, les résultats peuvent varier d'un instrument à l'autre ou en utilisant une technique manuelle.

CARACTERISTIQUES DIAGNOSTIQUES

Les aminotransférases catalysent la formation d'acide glutamique à partir de 2-oxoglutarate par transfert des groupements aminés. L'ATL est présente dans différents tissus, mais aux plus hautes concentrations se rencontrent dans le foie et les reins.

On observe des taux à concentrations élevées de ATL dans les hépatites avec nécroses: mononucléoses infectieuses, cholestases, cirrhoses, carcinome avec métastases du foie, délirium tremens et après l'administration de divers médicaments comme les opiacés, salicylates ou ampicilline[4].

La concentration en ATL du sérum peut aussi être élevé dans les maladies musculaires du squelette ou cardiaque[4,5].

Le diagnostic clinique ne doit pas être basé sur les conclusions d'un test unique mais il doit intégrer l'ensemble des données cliniques et de laboratoire.

NOTES

1. L'absorbance initiale du mélange de réaction peut être en dehors de la fourchette dans certains photomètres dont la lecture d'absorbance maximale est basse. Dans le cas de ces photomètres, il est conseillé de préparer le réactif de travail en mélangeant : 5 ml de réactif A + 1 ml de réactif B.
2. La méthode recommandée par la IFCC spécifie l'addition du phosphate de pyridoxal . Le temps de latence avant les mesures doit alors être augmenté de 2 minutes.
3. Ces réactifs peuvent être utilisés dans la plupart des analyseurs automatiques. Des adaptations sont disponibles sur demande.

BIBLIOGRAPHIE

1. IFCC primary reference procedures for the measurement of catalytic activity concentrations of enzymes at 37 °C. Part 4. Reference procedure for the measurement of catalytic concentration of alanine aminotransferase. *Clin Chem Lab Med* 2002; 40: 718-724.
2. IFCC reference procedure for measurement of catalytic concentrations of enzymes: corrigendum, notes and useful advice. *Clin Chem Lab Med* 2010; 48: 615-621.
3. Gella FJ, Olivella T, Cruz Pastor M, Arenas J, Moreno R, Durban R and Gómez JA. A simple procedure for routine determination of aspartate aminotransferase and alanine aminotransferase with pyridoxal phosphate. *Clin Chim Acta* 1985; 153: 241-247.
4. Young DS. Effects of drugs on clinical laboratory tests, 5th ed. AACC Press, 2000.
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6. Tietz Textbook of Clinical Chemistry and Molecular Diagnostics, 4th ed. Burtis CA, Ashwood ER, Bruns DE. WB Saunders Co, 2005.

Appendix III

COD 11630 1 x 50 mL	COD 11631 1 x 200 mL	COD 11567 1 x 500 mL	COD 11561 1 x 1 L
STORE AT 2-8ºC			
Reagents for measurement of AST/GOT concentration Only for *in vitro* use in the clinical laboratory			

ASPARTATE AMINOTRANSFERASE (AST/GOT)

BioSystems

CE

ASPARTATE AMINOTRANSFERASE (AST/GOT) IFCC

PRINCIPLE OF THE METHOD

Aspartate aminotransferase (AST or „GOT) catalyzes the transfer of the amino group from aspartate to 2-oxoglutarate, forming oxaloacetate and glutamate. The catalytic concentration is determined from the rate of decrease of NADH, measured at 340 nm, by means of the malate dehydrogenase (MDH) coupled reaction[1,2,3].

Aspartate + 2 – Oxoglutarate —AST→ Oxaloacetate + Glutamate

Oxaloacetate + NADH + H⁺ —MDH→ Malate + NAD⁺

CONTENTS

	COD 11630	COD 11631	COD 11567	COD 11561
A. Reagent	1 x 40 mL	1 x 100 mL	1 x 400 mL	1 x 800 mL
B. Reagent	1 x 10 mL	1 x 40 mL	1 x 100 mL	1 x 200 mL

COMPOSITION

A. Reagent: Tris 121 mmol/L, L-aspartate 362 mmol/L, malate dehydrogenase > 460 U/L, lactate dehydrogenase > 660 U/L, Sodium hydroxide 255 mmol/L, pH 7.8.
WARNING: H315: Causes skin irritation. H319: Causes serious eye irritation. P280: Wear protective gloves/protective clothing/eye protection/face protection. P305+P351+P338: IF IN EYES: Rinse cautiously with water for several minutes. Remove contact lenses, if present and easy to do. Continue rinsing. P332+P313: If skin irritation occurs: Get medical advice/attention.

B. Reagent: NADH 1.9 mmol/L, 2-oxoglutarate 75 mmol/L, Sodium hydroxide 148 mmol/L, sodium azide 9.5 g/L.
WARNING: H302: Harmful if swallowed. EUH031: Contact with acids liberates toxic gas. P301+P312: IF SWALLOWED: Call a POISON CENTER or doctor/physician if you feel unwell. P330: Rinse mouth.

For further warnings and precautions, see the product safety data sheet (SDS).

STORAGE

Store at 2-8ºC.
Reagents are stable until the expiry date shown on the label when stored tightly closed and if contaminations are prevented during their use.
Indications of deterioration:
– Reagents: Presence of particulate material, turbidity, absorbance of the blank lower than 1.400 at 340 nm (1 cm cuvette).

AUXILIARY REAGENTS

C. Reagent (cod 11566): Pyridoxal phosphate 10 mmol/L, 5 mL.

REAGENT PREPARATION

Working Reagent: Pour the contents of the Reagent B into the Reagent A bottle. Mix gently. Other volumes can be prepared in the proportion: 4 mL Reagent A + 1 mL Reagent B (Note 1). Stable for 1 month at 2-8ºC.
Working Reagent with Pyridoxal Phosphate (Note 2): Mix as follows: 10 mL of Working Reagent + 0.1 mL of Reagent C (cod 11566). Stable for 6 days at 2-8ºC.

ADDITIONAL EQUIPMENT

– Analyzer, spectrophotometer or photometer with cell holder thermostatable at 30 or 37ºC and able to read at 340 nm.
– Cuvettes with 1 cm light path.

SAMPLES

Serum and plasma collected by standard procedures.
Aspartate aminotransferase in serum and plasma is stable for 7 days at 2-8ºC. Use heparin as anticoagulant.

PROCEDURE

1. Bring the Working Reagent and the instrument to reaction temperature.
2. Pipette into a cuvette: (Note 3)

Reaction temperature	37ºC	30ºC
Working Reagent	1.0 mL	1.0 mL
Sample	50 µL	100 µL

3. Mix and insert the cuvette into the photometer. Start the stopwatch.
4. After 1 minute (Note 1), record initial absorbance and at 1 minute intervals thereafter for 3 minutes.
5. Calculate the difference between consecutive absorbances, and the average absorbance difference per minute (ΔA/min).

CALCULATIONS

The AST/GOT concentration in the sample is calculated using the following general formula:

$$\Delta A/min \times \frac{Vt \times 10^6}{\varepsilon \times l \times Vs} = U/L$$

The molar absorbance (ε) of NADH at 340 nm is 6300, the lightpath (l) is 1 cm, the total reaction volume (Vt) is 1.05 at 37ºC and 1.1 at 30ºC, the sample volume (Vs) is 0.05 at 37ºC and 0.1 at 30ºC, and 1 U/L are 0.0166 µkat/L. The following formulas are deduced for the calculation of the catalytic concentration:

	37ºC	30ºC
ΔA/min	x 3333 = U/L x 55.55 = µkat/L	x 1746 = U/L x 29.1 = µkat/L

REFERENCE VALUES

Reaction temperature	37ºC	30ºC
Without pyr-P, up to*	40 U/L = 0.67 µkat/L	25 U/L = 0.42 µkat/L
With pyr-P, up to*	60 U/L = 0.83 µkat/L	35 U/L = 0.60 µkat/L

Concentrations in newborns and infant are higher than in adults. Values in men are slightly higher than in women.
These ranges are given for orientation only; each laboratory should establish its own reference ranges.

QUALITY CONTROL

It is recommended to use the Biochemistry Control Serum level I (cod. 18005, 18008 and 18042) and II (cod. 18007, 18010 and 18043) to verify the performance of the measurement procedure.
Each laboratory should establish its own internal Quality Control scheme and procedures for corrective action if controls do not recover within the acceptable tolerances.

METROLOGICAL CHARACTERISTICS

– Detection limit: 1.1 U/L = 0.018 µkat/L.
– Linearity limit: 600 U/L = 13.3 µkat/L. For higher values dilute sample 1/ 10 with distilled water and repeat measurement.
– Repeatibility (within run):

Mean Concentration	CV	n
38 U/L = 0.63 µkat/L	1.4 %	20
119 U/L = 1.98 µkat/L	1.5 %	20

– Reproducibility (run to run):

Mean Concentration	CV	n
56 U/L = 0.93 µkat/L	3.9 %	25
119 U/L = 1.98 µkat/L	3.6 %	25

– Trueness: Results obtained with this reagent did not show systematic differences when compared with reference reagents. Details of the comparison experiments are available on request.
– Interferences: Bilirubin (20 mg/dL) does not interfere. Lipemia (triglycerides 2 g/L) and hemolysis may affect the results. Other drugs and substances may interfere[4].

These metrological characteristics have been obtained using an analyzer. Results may vary if a different instrument or a manual procedure are used.

DIAGNOSTIC CHARACTERISTICS

The aminotransferases catalyze the formation of glutamic acid from 2-oxoglutarate by transfer of amino groups. AST is found in highest concentration in the liver and heart muscle but it is also abundant in skeletal muscle, kidney and pancreas.
The serum concentration of AST is elevated in hepatitis and other forms of hepatic disease associated with necrosis: infectious mononucleosis, cholestasis, cirrhosis, metastasic carcinoma of the liver, delirium tremens, and after administration of various drugs[4,5].
Serum AST concentration is also elevated after myocardial infarction, in skeletal muscle disease (as progressive muscular distrophy), in acute pancreatitis or hemolytic disease and other[1,5].
Clinical diagnosis should not be made on the findings of a single test result, but should integrate both clinical and laboratory data.

NOTES

1. The initial absorbance of the reaction mixture may be out of range in some photometers with a low maximum absorbance reading. For these photometers it is recommended to prepare the Working Reagent by mixing in the proportion: 5 mL Reagent A + 1 mL Reagent B.
2. The IFCC recommended method specifies the addition of pyridoxal phosphate. The delay time before measurements should then be increased to 2 minutes.
3. These reagents may be used in several automatic analysers. Instructions for many of them are available on request.

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2. IFCC reference procedures for measurement of catalytic concentrations of enzymes: corrigendum, notes and useful advice. Clin Chem Lab Med 2010; 48: 615-621.
3. Gella FJ, Olivella T, Cruz Pastor M, Arenas J, Moreno R, Durban R and Gómez JA. A simple procedure for routine determination of aspartate aminotransferase and alanine aminotransferase with pyridoxal phosphate. Clin Chim Acta 1985; 153: 241-247.
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5. Young DS. Effects of drugs on clinical laboratory tests, 5th ed. AACC Press, 2000.
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Quality System certified according to EN ISO 13485 and EN ISO 9001 standards

08/2015

CODE 11630 1 x 50 mL	CODE 11631 1 x 200 mL	CODE 11567 1 x 500 mL	CODE 11561 1 x 1 L
CONSERVER À 2-8ºC			
Réactif pour mesurer la concentration de AST/GOT A utiliser uniquement *in vitro* dans les laboratoires cliniques			

PRINCIPE DE LA METHODE

L'aspartate-aminotransférase (AST) catalyse le transfert du groupement amino de l'aspartate au 2-oxoglutarate, en formant l'oxaloacétate et le glutamate. La concentration catalytique est déterminée, en utilisant la réaction couplée de la malate-déshydrogénase (MDH), à partir de la vitesse de disparition du NADH, mesuré à 340 nm[1,2,3].

Aspartate + 2 – Oxoglutarate —AST→ Oxaloacétate + Glutamate

Oxaloacétate + NADH +H⁺ —MDH→ Malate + NAD⁺

CONTENU

	CODE 11630	CODE 11631	CODE 11567	CODE 11561
A Réactif	1 x 40 mL	1 x 100 mL	1 x 400 mL	1 x 800 mL
B Réactif	1 x 10 mL	1 x 40 mL	1 x 100 mL	1 x 200 mL

COMPOSITION

A. Réactif: Tris 121 mmol/L, L-aspartate 362 mmol/L, malate-déshydrogénase > 460 U/L, lactate-déshydrogénase > 660 U/L, Hydroxyde de sodium 255 mmol/L, pH 7,8.
ATTENTION! H315: Provoque une irritation cutanée. H319: Provoque une sévère irritation des yeux. P280: Porter des gants de protection/des vêtements de protection/un équipement de protection des yeux/ du visage. P305+P351+P338: EN CAS DE CONTACT AVEC LES YEUX: rincer avec précaution à l'eau pendant plusieurs minutes. Enlever les lentilles de contact si la victime en porte et si elles peuvent être facilement enlevées. Continuer à rincer. P332+P313: En cas d'irritation cutanée: consulter un médecin.

B. Réactif: NADH 1,8 mmol/L, 2-oxoglutarate 75 mmol/L, Hydroxyde de sodium 148 mmol/L, sodium azide 9,5 g/L.
ATTENTION! H302: Nocif en cas d'ingestion. EUH031: Au contact d'un acide, dégage un gaz toxique. P301+P312: EN CAS D'INGESTION: appeler un CENTRE ANTIPOISON ou un médecin en cas de malaise. P330: Rincer la bouche.

Pour d'autres mises en garde et précautions, voir la fiche de données de sécurité du produit (SDS).

CONSERVATION

Les réactifs doivent être conservés à 2-8ºC. Bien refermer les flacons et éviter toute contamination lors de l'utilisation. Dans ces conditions ils restent stables jusqu'à la date indiquée sur l'étiquette.
Indications de dégradation:
Réactifs: Présence de particules, turbidité, absorbance du blanc inférieure à 1,400 à 340 nm (cuvette de 1 cm.

REACTIF AUXILIAIRE

Réactif (C): (code 11566): Phosphate de Pyridoxal 10 mmol/L, 5 mL.

PREPARATION DES REACTIFS

Réactif de Travail : Vider le contenu d'un flacon de Réactif B dans un flacon de Réactif A. Agitez doucement. Si on désire préparer des volumes petits, mélanger dans la proportion: 4 mL de Réactif A + 1 mL de Réactif B (Note 1). Stable 1 mois à 2-8°C.
Réactif de Travail avec Phosphate de Pyridoxal: (Note 2): Mélangez dans la proportion: 10 mL de Réactif de Travail + 0,1 mL de Réactif C. Stable 6 jours à 2-8ºC.

MATERIEL SUPPLEMENTAIRE

– Analyseur, spectrophotomètre ou photomètre avec cuve thermostatable à 30 ou 37ºC pour lectures à 340 nm.
– Cuves de 1,0 cm de trajet optique.

ECHANTILLONS

Sérum et plasma prélevés par des procédures standard.
L'aspartate-aminotransférase dans le sérum et le plasma est stable 7 jours à 2-8°C. L'héparine doit être utilisé comme anticoagulants.

PROCEDURE

1. Préchauffez le Réactif de Travail à la température de reaction et l'instrument.
2. Pipetez dans une cuve (Note 3):

Température de réaction	37ºC	30ºC
Réactif de travail	1,0 mL	1,0 mL
Echantillon	50 µL	100 µL

3. Mélangez et insérez-la dans le photomètre. Mettre le chronomètre en marche.
4. Au bout de 1 minute (Note 1), notez l'absorbance initiale et effectuez de nouvelles lectures chaque minute pendant 3 minutes.
5. Calculez l'accroissement moyen d'absorbance par minute (ΔA/min).

CALCULS

La concentration en AST/GOT dans l'échantillon est calculée à partir de la formule générale suivante :

$$\Delta A/min \times \frac{Vt \times 10^6}{\varepsilon \times l \times Vs} = U/L$$

L' absorbance molaire (ε) du NADH à 340 nm est 6,300, le pas de lumière est de 1 cm, le volume total de réaction (Vt) est 1,05 à 37ºC et 1,1 à 30ºC, le volume d'échantillon (Vs) est 0,05 à 37ºC et 0,1 à 30ºC, 1 U/L équivaut à 0,0166 µkat/L. On en déduit les formules suivantes pour calculer la concentration catalytique:

	37ºC	30ºC
ΔA/min	x 3333 = U/L x 55,55 = µkat/L	x 1746 = U/L x 29,1 = µkat/L

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ASPARTATE AMINOTRANSFERASE (AST/GOT)

BioSystems

CE

ASPARTATE AMINOTRANSFERASE (AST/GOT) IFCC

VALEURS DE REFERENCE

Température de réaction	37°C	30°C
Sans P-5P, jusqu'à[2]	40 U/L = 0,67 µkat/L	25 U/L = 0,42 µkat/L
Avec P-5P, jusqu'à[2]	50 U/L = 0,83 µkat/L	30 U/L = 0,50 µkat/L

Les concentrations chez les nouveau-nés et les enfants sont plus élevées que chez les adultes. Les valeurs sont légèrement plus hautes chez les hommes que chez les femmes.
Ces valeurs ne sont données qu'à titre indicatif. Chaque laboratoire doit établir ses propres valeurs de référence.

CONTRÔLE DE QUALITE

Il est recommandé d'utiliser les Sérums Contrôles de Biochimie niveau I (Code 18005, 18009 ou 18042) et II (Code 18007, 18010 ou 18043) pour vérifier la qualité de la méthodologie.
Chaque laboratoire doit établir ses propres protocoles et méthodes de Contrôle de Qualité interne afin d'apporter les modifications nécessaires en cas de dépassement des tolérances.

CARACTERISTIQUES METROLOGIQUES

- Limite de détection: 1,1 U/L = 0,018 µkat/L.
- Limite de linéarité: 600 U/L = 10,0 µkat/L. Pour les valeurs supérieures, diluer l'échantillon au 1/10 dans de l'eau distillée et répéter la mesure.
- Répétabilité (intra-essai):

Concentrations moyennes	CV	n
36 U/L = 0,63 µkat/L	1,4 %	20
119 U/L = 1,98 µkat/L	1,5 %	20

- Reproductibilité (intermédiaire):

Concentrations moyennes	CV	n
36 U/L = 0,63 µkat/L	5,3 %	20
119 U/L = 1,98 µkat/L	3,8 %	20

- Justesse: Les résultats obtenus avec ce réactif n'ont pas montré de différences systématiques significatives par rapport aux réactifs de référence. Les détails des études comparatives sont disponibles sur demande.
- Interférences: la bilirubine (20 mg/dL) n'interfère pas. La lipémie (triglycérides 2 g/L) et l'hémolyse peuvent affecter le résultat. D'autres médicaments ou substances peuvent interférer[3].

Ces données ont été obtenues en utilisant un analyseur. Les résultats peuvent varier d'un instrument à l'autre ou en utilisant une technique manuelle.

CARACTERISTIQUES DIAGNOSTIQUES

L'aminotransférase catalyse la formation de l'acide glutamique à partir de 2-oxoglutarate par transfert du groupement amine.
L'AST est trouvée en grande quantité dans le foie et le muscle cardiaque mais elle est aussi importante dans les muscles squelettiques, les reins, et le pancréas.
La concentration en AST dans le sérum est élevée dans les cas d'hépathites ou autres formes de maladies hépatiques associées à des nécroses: mononucléose infectieuse, cholestase, cirrhose, carcinome métastatique du foie, délirium tremens, et après l'administration de différents médicaments[4,5].
La concentration en AST dans le sérum est aussi élevée après un infarctus du myocarde, dans les cas de maladies des muscles squelettiques (comme dystrophie musculaire évolutive), lors de pancréatites aigües, maladies du sang ou autres[4,7].
Le diagnostic clinique ne doit pas être basé sur les conclusions d'un test unique mais il doit intégrer l'ensemble des données cliniques et de laboratoire.

NOTES

1. L'absorbance initiale du mélange de réaction peut être en dehors de la fourchette dans certains photomètres dont la lecture d'absorbance maximum est basse. Dans le cas de ces photomètres, il est conseillé de préparer le réactif de travail en mélangeant : 5 ml de réactif A + 1 ml, de réactif B.
2. La IFCC recommande l' utilisation du phosphate de pyridoxal. Dans ce cas, le temps de pré-incubation avant de commencer les mesures est 2 minutes.
3. Ces réactifs peuvent être utilisés avec la plupart des analyseurs automatiques. Demandez les informations à votre distributeur.

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2. IFCC reference procedures for measurement of catalytic concentrations of enzymes: corrigendum, notes and useful advice. Clin Chem Lab Med 2010; 48: 615-621.
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30, 08030 Barcelona (Spain)
tified according to
ISO 9001 standards

05/2013

COD 11530	COD 11531	COD 11567	COD 11561
1 x 50 mL	1 x 200 mL	1 x 500 mL	1 x 1 L
CONSERVAR A 2-8ºC			
Reagentes para medir a concentração de AST/GOT. Só para uso in vitro nos laboratórios clínicos			

FUNDAMENTO DO MÉTODO

O aspartato aminotransferase (AST ou GOT) catalisa a transferência do grupo amino do aspartato a 2-oxoglutarato, formando oxaloacetato e glutamato. A concentração catalítica determina-se, seguindo a reação abaixo descrita de desidrogenase málatos (MDH), a partir da velocidade de desaparecimento do NADH, medida a 340 nm[1,2,3].

$$\text{Aspartato} + 2\text{-Oxoglutarato} \xrightarrow{\text{AST}} \text{Oxaloacetato} + \text{Glutamato}$$

$$\text{Oxaloacetato} + \text{NADH} + \text{H}^+ \xrightarrow{\text{MDH}} \text{Málato} + \text{NAD}^+$$

CONTEÚDO

	COD 11530	COD 11531	COD 11567	COD 11561
A. Reagente	1 x 40 mL	1 x 160 mL	1 x 400 mL	1 x 800 mL
B. Reagente	1 x 10 mL	1 x 40 mL	1 x 100 mL	1 x 200 mL

COMPOSIÇÃO

A. Reagente: Tris 121 mmol/L, L-aspartato 362 mmol/L, desidrogenase málática ≥ 460 U/L, desidrogenase láctica ≥ 660 U/L, Hidróxido de sódio 255 mmol/L, pH 7,8.

ATENÇÃO: H315: Provoca irritação cutânea. H319: Provoca irritação ocular grave. P280: Usar luvas de proteção/vestuário de proteção/proteção ocular/proteção facial. P305+P351+P338: SE ENTRAR EM CONTACTO COM OS OLHOS: enxaguar cuidadosamente com água durante vários minutos. Se usar lentes de contacto, retire-as, se tal lhe for possível. Continuar a enxaguar. P332+P313: Em caso de irritação cutânea: consulte um médico.

B. Reagente: NADH 1,9 mmol/L, 2-oxoglutarato 75 mmol/L, Hidróxido de sódio 148 mmol/L, sódio azida 9,5 g/L.

ATENÇÃO: H302: Nocivo por ingestão. EUH031: Em contacto com ácidos liberta gases tóxicos. P301+P312: EM CASO DE INGESTÃO: caso sinta indisposição, contacte um CENTRO DE INFORMAÇÃO ANTIVENENOS ou um médico. P330: Enxaguar a boca.

Para mais advertências e precauções, ver a ficha de dados de segurança do produto (SDS).

CONSERVAÇÃO

Conservar a 2-8ºC.
Os reagentes são estáveis até à data de caducidade indicada na etiqueta, desde que se conservem bem fechados e se evite a contaminação durante o seu uso.
Indicações de deterioração:

- Reagentes: Presença de partículas, turvação, absorvência do branco inferior a 1,400 a 340 nm (cuvete de 1 cm).

REAGENTES AUXILIARES

C. Reagente (cod 11666): Fosfato de pridoxal 10 mmol/L, 5 mL.

PREPARAÇÃO DOS REAGENTES

Reagente de Trabalho: Transferir o conteúdo do frasco B no frasco A. Agitar suavemente. Se desejar preparar outros volumes, misturar na proporção: 4 mL de Reagente A + 1 mL de Reagente B (Nota 1). Estável 1 mês a 2-8ºC.
Reagente de Trabalho com Fosfato de Pridoxal (Nota 2): Misturar na proporção: 10 mL de Reagente de Trabalho + 0,1 mL de Reagente C (cod 11666). Estável 6 dias a 2-8ºC.

EQUIPAMENTO ADICIONAL

- Analisador, espectrofotómetro ou fotómetro com cuvete termostatizada a 30 ou 37ºC para leituras a 340 nm.
- Cuvetes de 1 cm de passo de luz.

AMOSTRAS

Soro e plasma recolhidos mediante procedimentos standard.
O aspartato aminotransferase no soro e plasma é estável durante 7 dias a 2-8ºC. A heparina deverá ser usado como anticoagulante.

PROCEDIMENTO

1. Pré-aquecer o Reagente de Trabalho e o equipamento à temperatura de reacção.
2. Pipetar numa cuvete: (Nota 3)

Temperatura de reacção	37ºC	30ºC
Reagente de Trabalho	1,0 mL	1,0 mL
Amostra	50 µL	100 µL

3. Misturar e introduzir a cuvete no fotómetro. Ligar o cronómetro.
4. Após 1 minuto (Nota 1), apontar a absorvância inicial e efectuar novas leituras em cada minuto durante 3 minutos.
5. Calcular a razão de incremento da absorvância por minuto (ΔA/min).

CÁLCULOS

A concentração de AST/GOT na amostra calcula-se a partir da seguinte fórmula geral:

$$\Delta A/\text{min} \times \frac{\text{Vt} \times 10^6}{\varepsilon \times l \times \text{Vs}} = \text{U/L}$$

O coeficiente de absorção molar (ε) de NADH a 340 nm é 6.300, o passo de luz (l) é 1 cm, o volume total de reacção (Vt) é 1,05 a 37ºC e 1,1 a 30ºC, o volume de amostra (Vs) é 0,05 a 37ºC e 0,1 a 30ºC, e 1 U/L equivale a 0,0166 µkat/L. Deduzem-se os seguintes factores para calcular a concentração catalítica:

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ASPARTATE AMINOTRANSFERASE (AST/GOT)

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CE

ASPARTATO AMINOTRANSFERASE (AST/GOT) IFCC

	37ºC	30ºC
ΔA/min	x 3333 = U/L x 55,55 = µkat/L	x 1748 = U/L x 29,1 = µkat/L

VALORES DE REFERÊNCIA

Temperatura de reacção	37ºC	30ºC
Sem fosfato piridoxal, até[1]	40 U/L = 0,67 µkat/L	25 U/L = 0,42 µkat/L
Com fosfato piridoxal, até[1]	50 U/L = 0,83 µkat/L	30 U/L = 0,50 µkat/L

As concentrações em crianças e recém nascidos são superiores às dos adultos. Encontram-se valores ligeiramente mais elevados nos homens que nas mulheres.
Estes valores dão-se unicamente a título orientativo; é recomendável que cada laboratório estabeleça os seus próprios intervalos de referência.

CONTROLE DE QUALIDADE

Recomenda-se o uso dos Soros Controle de Bioquímica níveis I (Cod. 18005, 18009 e 18042) e II (Cod. 18007, 18010 e 18043) para verificar a funcionalidade do procedimento da medida.
Cada laboratório deve estabelecer o seu próprio programa de Controle de Qualidade interno, assim como procedimentos de correcção caso em casos em que os controles não cumpram com as tolerâncias aceitáveis.

CARACTERÍSTICAS METROLÓGICAS

- Limite de detecção: 1,1 U/L = 0,018 µkat/L.
- Limite de linearidade: 600 U/L = 10,0 µkat/L. Quando se obtêm valores superiores, diluir a amostra 1/10 com água destilada e repetir a medição.
- Repetibilidade (intraensaio):

Concentração média	CV	n
36 U/L = 0,63 µkat/L	1,4 %	20
119 U/L = 1,98 µkat/L	1,5 %	20

- Reprodutibilidade (interensaio):

Concentração média	CV	n
36 U/L = 0,63 µkat/L	5,3 %	20
119 U/L = 1,98 µkat/L	3,8 %	20

- Veracidade: Os resultados obtidos com estes reagentes não mostram diferenças sistemáticas significativas quando comparados com reagentes de referência. Os detalhes do estudo comparativo estão abaixo disponíveis.
- Interferências: A bilirrubina (20 mg/dL) não interfere. A lipemia (triglicéridos 2 g/L) e a hemólise podem afectar os resultados. Outros medicamentos e substâncias podem interferir[3].

Estes dados foram obtidos utilizando um analisador. Os resultados podem variar ao mudar de equipamento ou ao realizar-se o procedimento manualmente.

CARACTERÍSTICAS DIAGNÓSTICAS

As aminotransferases catalizam a formação do ácido glutâmico a partir de 2-oxoglutarato mediante a transferência de grupos amino. As concentrações mais elevadas de AST encontram-se no fígado e no músculo cardíaco ainda que também seja abundante no músculo esquelético, rins e pancreas.
Encontram-se concentrações séricas elevadas de AST na hepatite e outras doenças hepáticas associadas com necroses: mononucleose infecciosa, cirrose, colestasis, carcinoma metastásico do fígado, delirium tremens, assim como após a administração de alguns medicamentos[4,5].
Também se encontram concentrações séricas elevadas de AST após um enfarte do miocardio, em doenças do músculo esquelético (como a distrofia muscular progressiva), em pancreatite aguda, doenças hemolíticas e outras[4,7].
O diagnóstico clínico não se deve realizar tendo em conta o resultado de um único teste, mas deve integrar-se nos dados clínicos e de laboratório.

NOTAS

1. A absorvância inicial da mistura de reação pode estar fora do intervalo em alguns fotómetros com uma leitura baixa de absorvância máxima. Para estes fotómetros recomenda-se preparar o reagente de trabalho com a mistura na seguinte proporção: 5 ml de reagente A + 1 ml de reagente B.
2. A IFCC recomenda a utilização de fosfato de piridoxal. Neste caso, antes de iniciar o período de medições, o tempo de pré-incubação, deve aumentar para 2 minutos.
3. Estes reagentes podem utilizar-se na maioria dos analizadores automáticos. Solicite informação ao seu distribuidor.

BIBLIOGRAFIA

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Appendix IV

COD 11547 2 x 250 mL	COD 11573 1 x 250 mL
STORE AT 2-8°C	
Reagents for measurement of albumin concentration Only for *in vitro* use in the clinical laboratory	

ALBUMIN

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ALBUMIN
BROMOCRESOL GREEN

PRINCIPLE OF THE METHOD

Albumin in the sample reacts with bromocresol green in acid medium forming a coloured complex that can be measured by spectrophotometry[1].

CONTENTS

	COD 11547	COD 11573
A. Reagent S. Standard	2 x 250 mL 1 x 5 mL	1 x 250 mL 1 x 5 mL

COMPOSITION

A. Reagent: Acetate buffer 100 mmol/L, bromocresol green 0.27 mmol/L, detergent, pH 4.1.

S. Albumin Standard: Bovine albumin. Concentration is given on the label. Concentration value is traceable to the Standard Reference Material 927 (National Institute of Standards and Technology, USA).

STORAGE

Reagent (A): Store at 2-8°C.

Albumin Standard (S): Store at 2-8°C, once opened.

Reagent and Standard are stable until the expiry date shown on the label when stored tightly closed and if contaminations are prevented during their use.

Indications of deterioration:

- Reagent: Presence of particulate material, turbidity, absorbance of the blank over 0.200 at 630 nm (1 cm cuvette).
- Standard: Presence of particulate material, turbidity.

REAGENT PREPARATION

Reagent and Standard are provided ready to use.

ADDITIONAL EQUIPMENT

- Analyzer, spectrophotometer or photometer able to read at 630 nm (610 - 670 nm).

SAMPLES

Serum or plasma (EDTA, citrate or heparine) collected by standard procedures.

Albumin in serum is stable for 3 days at 2-8°C.

PROCEDURE

1. Pipette into labelled test tubes: (Notes 1, 2)

	Blank	Standard	Sample
Albumin Standard (S)	—	10 µL	—
Sample	—	—	10 µL
Reagent (A)	1.0 mL	1.0 mL	1.0 mL

2. Mix thoroughly and let stand the tubes for 1 minute at room temperature.
3. Read the absorbance (A) of the Standard and the Sample at 630 nm against the Blank. The colour is stable for 30 minutes.

CALCULATIONS

The albumin concentration in the sample is calculated using the following general formula:

$$\frac{A\ Sample}{A\ Standard} \times C\ Standard = C\ Sample$$

REFERENCE VALUES

Serum[2]:

Newborn, 2 to 4 days	28-44 g/L
4 days to 14 years	38-54 g/L
Adult	35-50 g/L
> 60 years	34-48 g/L

These ranges are given for orientation only; each laboratory should establish its own reference ranges.

QUALITY CONTROL

It is recommended to use the Biochemistry Control Serum level I (cod. 18005, 18009 and 18042) and II (cod. 18007, 18010 and 18043) to verify the performance of the measurement procedure.

Each laboratory should establish its own internal Quality Control scheme and procedures for corrective action if controls do not recover within the acceptable tolerances.

METROLOGICAL CHARACTERISTICS

- Detection limit: 1.1 g/L.
- Linearity limit: 70 g/L.
- Repeatability (within run):

Mean Concentration	CV	n
26.2 g/L	1.4 %	20
42.1 g/L	1.0 %	20

- Reproducibility (run to run):

Mean Concentration	CV	n
26.2 g/L	1.9 %	25
42.1 g/L	1.9 %	25

- Trueness: Results obtained with this reagent did not show systematic differences when compared with reference reagents (Note 3). Details of the comparison experiments are available on request.
- Interferences: Bilirubin (>10 mg/dL), lipemia (triglycerides >7.5 g/L) and hemoglobin (>2.5 g/L) may affect the results. Other drugs and substances may interfere[3].

These metrological characteristics have been obtained using an analyzer. Results may vary if a different instrument or a manual procedure are used.

DIAGNOSTIC CHARACTERISTICS

Albumin is the most abundant protein in human plasma. It has three main functions: it contributes towards maintaining the colloid oncotic pressure of plasma, it acts as non-specific transport vehicle for many nonpolar compounds and it is a source of endogenous amino acids.

Hyperalbuminemia is of little diagnostic significance except in dehydration[2].

Hypoalbuminemia is found as a result of several factors: reduced synthesis caused by liver diseases; reduced absorption of amino acids due to malabsorption syndromes or malnutrition; increased catabolism as a result of inflammation or tissue damage; altered distribution between intravascular and extravascular space due to increased capillary permeability, overhydration or ascites; abnormal losses caused by renal disease (nephrotic syndrome, diabetes mellitus, chronic glomerulonephritis, systemic lupus erythematosus), gastrointestinal tract disease (ulcerative colitis, Crohn's disease) or skin damage (exfoliative dermatitis, extensive burns); congenital absence of albumin or analbuminemia[2,4].

Albumin plasma concentrations, although important for management and follow-up, have very little value in diagnosis[2].

Clinical diagnosis should not be made on the findings of a single test result, but should integrate both clinical and laboratory data.

NOTES

1. This reagent may be used in several automated analysers. Instructions for many of them are available on request.
2. Albumin reaction with bromocresol green is immediate. It is not recommended to delay readings, since other proteins react slowly.
3. Calibration with the provided aqueous standard may cause a matrix related bias, specially in some analyzers. In these cases, it is recommended to calibrate using a serum based standard (Biochemistry Calibrator, cod. 18011 and 18044).

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