1. Introduction and literature review

1.1 Alcohol

Alcohol represent one of the most serious worldwide socioeconomic and health problems . Alcohol ,or ethyl alcohol (ethanol) , refers to the intoxicating ingredient found in wine, beer and hard liquor. Alcohol arises naturally from carbohydrates when certain micro-organism metabolize them in the absence of oxygen, called fermentation In chemistry , alcohol is an organic compound in which hydroxyl functional group (_OH) is bound to a carbon atom. In particular , This carbon should be saturated , having single bonds to three other atoms (Room *et al* ,2005). Alcohol is classed as a 'sedative hypnotic' drug, (Kuhn, *et al* 2008) which means it acts to depress the central nervous system at high doses. At lower doses, alcohol can act as a stimulant, inducing feelings of euphoria and talkativeness, but drinking too much alcohol at one session can lead to drowsiness, respiratory depression (where breathing becomes slow, shallow or stops entirely),coma or even death .As well as its acute and potentially lethal sedative effect at high doses, alcohol has effects on every organ in the body, and These effects depend on the blood alcohol concentration (BAC) over time (Zakharo,2006).After a drink is swallowed, the alcohol is rapidly absorbed into the blood (20 percent through the stomach and 80 percent through the small intestine),with effects felt within 5 to10 minutes after drinking, It usually peaks in the blood after 30 to 90 minutes, (lohor,2005) and thus is carried through all the organs of the body percent) of the metabolism, or breaking down, of alcohol from a toxic substance to water and carbon dioxide is performed by the liver,(Lohor , 2005) with the rest excreted through the lungs allowing alcohol breath tests, through the kidneys in to urine and in sweat (Schuckit, 2005).

As well as potentially affecting the physical and mental health of individuals in many ways, chronic and heavy alcohol use can increase the risk of death (Rehm, *et al* 2009) either directly, for example through acute alcohol poisoning or because alcohol causes a fatal disease such as cancer, (Baan, *et al* 2007) or indirectly, such as alcohol being a factor in violent death or suicide. Alcohol contributes to a high burden of disease in society in terms of years that people spend with disability or in poor

health because of alcohol-related illnesses or injuries. (Connor *et al*, 2005).

1.1.1 History of alcohol in Sudan

I think it was from Sudanese customs and traditions that viewed proud Self- esteem, And not detect .We find in the North light wines such as Marisa, kasra, Walshrbot and heavy wines such as all kinds of race (ethnicity) and made from dates ,is most fames and powerful ethnic types and the percentage of alcohol is very high , and was made and What was his distillation (Butler) . And all of that kind of ignorance. Also find the same types of wines in various parts of the Sudan and the different raw material to manufacture and have spade, and all her wines are made from the area of agricultural products, for example, in the South the same type of Beirut but ethnic made from coffee and bananas. In West Sudan ethnic manufactures orange (Gebel Mara) and GEF corn. (Elamin, 1990).

In the colonial era, there were laws governing alcohol and work alanadi and hours of work, and was under police protection and close 5p.m. w whistle from rotating, balanadi they had local permits certification. Nanny still in the South and some Western Sudan are the staple food of the population the extend that the child When his weaning almeries and God forbid. . (Elamin, 1990).

1.1.2 Local Sudanese Drink (Sharboat Drink)

Carbonate, a fames Sudanese indigenous date juice, has-been used as drink for any centuries. Now adages it used as common drink in Eid Aladha and sometime in wedding celebration, especially by people from northern Sudan .Sharboat is mad either with addition of yeast extract or without. Flavoring material is also added to it. (Morton, 1987)

1.1.3 Date Palm

The date palm is a palm in the genus phoenix extensively cultivated for its edible fruit. (Morton, 1987)

1.1.4 Origin and distribution

The date palm is believed to have originated in the lands around the Persian Gulf and in ancient times was especially abundant between the Nile and Euphrates rivers. It was claimed that it angled in prehistoric times from Senegal to the basin of the Indus River in northern India,

especially between latitudes 15 and 30. There is archeological evidence of cultivation in eastern Arabia in 000B.C. Nomads planted the date at oases in the deserts and Arabs introduced it into Spain it has long been grow on the French Riviera, in southern Italy, Sicily Greece. Through the fruit does not reach perfection in these areas. Possibly it fares better in the cape Verde Islands, for program of date improvement was launched there in the late 1950s. Iraq has always led the world in date production. Presently, there are 22 million date palms in that country producing nearly 600000 tons of dates annually (Morton, 1987)

In Sudan date grow Predominately in northern parts where rainfall is scarce. (Musa, 1998). They grow near rivers and streams on silty soils where the water table is high and non stagnant along the River Nile. Many varieties cultivated in most parts of the Sudan (Elamin, 1990).

In the last ten years due to the Sudan of the Nile many trees in other areas such as Khartoum. (Musa, 1998).

1.1.5 Sugars Contents of Date Fruit

Date fruit contains a large of Sugar. A study of thirty four date varieties from start of maturity showed that the predominant Sugar were fructose (12.6- 43.3 g\100g) and glucose (16.4- 54.2 \100g). was found that two Omani date varieties , farad and Koalas contain about 44.75% and 43.6% glucose respectively . Source was not practically detected in most varieties (Musa, 1998).

1.1.6 Data Juice

Juice of date is one of richest food stuffs in neutral Compounds such as mono Saccharides, disaccharides, mineral as essential element for the growth of micro organism specially yeast and hence production of ethanol. (Musa, 1998).

1.1.7 Alcoholic beverage

An alcoholic beverage is a drink that contains ethanol. Alcoholic beverages are divided into three general classes for taxation and regulation of production: beers, wines, and spirits. (Brown and Lemay, 2006)

1.1.8 Distilled beverages

A distilled beverage, spirit, or liquor is an alcoholic beverage produced by distilling ethanol produced by means of fermenting grain, fruit, or vegetables. Unsweetened, distilled, alcoholic beverages that have an alcohol content of at least 20% ABV are called *spirits*. For the most common distilled beverages, such as whiskey and vodka, the alcohol content is around 40%. (Brown and Lemay, 2006)

1.1.9 Alcohol poisoning

A case of poisoning as a result of excessive consumption of a large amount of alcohol in a short time. Alcohol weakens the capacity of performance nerves that control breathing and heartbeat. Activate the gag reflex when the body cannot handle the out of alcohol consumed. In this case the opposite may be the puke, called gag. So goof, reflex weakens the body absorbs alcohol, which can cause alcohol poisoning. Alcohol poisoning requires immediate medical attention.(Barce and Kranzelok, 2002).

1.2 Hangover

A hangover is characterized by the constellation of unpleasant physical and mental symptoms that occur after a bout of heavy alcohol drinking .
Physical symptoms of a hangover include fatigue, headache,
Increased sensitivity to light and sound, redness of the eyes, muscle Aches and thirst. Signs of increase sympathetic nervous system activity can accompany a hangover, including increased systolic blood pressure, rapid heartbeat (i.e., tachycardia), tremor, and sweating. Mental symptoms include dizziness; a sense of the room spinning (i.e., vertigo); and possible cognitive and mood disturbs bances, especially depression, anxiety, and irritability. The particular set of symptoms experienced and their intensity may vary from person to person and from occasion to occasion. In addition, hangover characteristics may depend on the type of alcoholic beverage consumed and the amount a person drinks. Typically, a hangover begins within several hours after the cessation of drinking, when a person ’ s blood alcohol concentration (BAC) is falling. Symptoms usually peak about the time BAC is zero and may continue for up to 24 hours thereafter .Overlap exists between hangover and the symptoms of mild alcohol withdrawal (AW), leading to the assertion that

hangover is a manifestation of mild withdrawal. Hangovers, however, may occur after a single bout of drinking, whereas withdrawal occurs usually after multiple, repeated bouts. Other differences between hangover and AW include a shorter period of impairment (i.e., hours for hangover versus several days for withdrawal) and a lack of hallucinations and seizures in hangover. People experiencing a hangover feel ill and impaired. Although a hangover may impair task performance and thereby increase the risk of injury, equivocal data exist on whether hang over actually impairs complex mental tasks. When subjects with a BAC of zero were tested following alcohol intoxication with peak BAC 's in the range of 50 to 100 milligrams perdeciliter (mg/dL), most of them did not show significant impairments in the performance of simple mental tasks, such as reaction time (Lemon *etal.* 1993).

1.2.1 Prevalence of Hangover

Generally, the greater the amount and duration of alcohol consumption, The more prevalent is the hangover, although some people report experi ending a hangover after drinking low levels of alcohol (i.e., one to three Alcoholic drinks), and some heavy drinkers do not report experiencingHangovers at all. A survey by (Harburg *etal*1993) on the prevalence of hangovers found that approximately 75 percent of the subjects who drank to intoxication reported experiencing a hangover at least some of the time. In a study of 2,160 Finnish men, researchers found an association between increased weekly alcohol consumption and the frequency of hangover: 43.8 percent of the group of heaviest drinkers (i.e., study subjects who drank more than 106 grams [g] of alcohol per week or approximately9 drinks) reported experiencing a hang over monthly or more often, compared with 6.6 percent of the remaining study subjects (Kauhanen *et al*. 1997).

Similarly, in a study of 1,041 drinkers in New York State, 50 percent of the subjects who drank two or more drinks per day reported experiencing hangovers in the previous year, whereas subjects who consumed lower level of alcohol reported fewer hangovers (Smith and Barnes 1983). Other reports, however, claim that hangovers occur less often in heavy drinkers. In a study of 43 alcoholic drinkers admitted for inpatient treatment, 50 percent of the subjects reported experiencing no

hangovers within the previous year and 23 percent reported never experiencing a hangover (Pristach *etal*. 1983).

1.2.2 Physiological Factors Contributing to Hangover

Hangover symptoms have been attributed to several causes , including the direct physiological effects of alcohol on the brain and other organs; the effects of the removal of alcohol from these organs after alcohol exposure (i.e., withdrawal); the physiological effects of compounds produced as a result of alcohol's metabolism (i.e., metabolites), especially acetaldehyde; and non alcohol factors, such as the toxic effects of other biologically active chemicals (i.e., congeners) in the beverage, behavior s associated with the alcohol-drinking bout (e.g., other drug use, restricted in food intake, and disruption of normal sleep time), and certain personal char acteristics (e.g., temperament, personality, and family history of alcoholism Although current evidence suggests that more than one factor most likely contributes to the overall hangover state, the following sections address each of the postulated causes in turn .hormone (i.e., antidiuretic hormone, or vasopressin) from the pituitary gland.
In turn, reduced levels of antidiuretic hormone prevent the kidneys from Reabsorbing (i.e., conserving) water and thereby increase urine production. Additional mechanisms must be at work to increase urine production, however, because antidiuretic hormone levels increase as BAC levels decline to zero during hangover (Eisenhofer *etal* ,1985).

1.2.3 Gastrointestinal Disturbances

Alcohol directly irritates the stomach and intestines, causing inflammation of the stomach lining (i.e., gastritis) and delayed stomach emptying, especially when beverages with a high alcohol concentration (i.e., greater than 15percent) are consumed (Lieber 1995).

1.2.4 Low Blood Sugar

Several alterations in the metabolic state of the liver and other organs occur in response to the presence of alcohol in the body and can result in low blood sugar levels(i.e., low glucose levels, or hypoglycemia) (National Institute on Alcohol Abuse and Alcoholism 1994). Alcohol metabolism leads to fatty liver and a build up of an intermediate metabolic product, lactic acid, in body fluids (i.e., lactic acidosis). Both

of these effects can inhibit glucose production. Alcohol-induced hypoglycemia generally occurs after binge drinking several days in alcoholics who have not been eating. In such a situation, prolonged alcohol consumption, coupled with poor nutritional intake, not only decreases glucose production but also exhausts the reserves of glucose Stored in the liver in the form of glycogen, thereby leading to hypoglycemia. Because glucose is the primary energy source of the brain, hypoglycemia can contribute to hangover symptoms such as fatigue, weakness, and mood disturbances. Diabetics are particularly sensitive to the alcohol-induced alterations in blood glucose. However, it has not been documented whether low blood sugar concentrations con tribute to hangover symptomatically (Lieber, 1995).

1.2.5 Effects of Alcohol on Metabolites

Alcohol undergoes a two-step process in its metabolism First, an enzyme (i.e., alcohol dehydrogenase) metabolizes alcohol to an intermediate product, acetaldehyde; then a second enzyme (aldehyde dehydrogenase [ALDH]) metabolizes acetaldehyde to acetate. Acetaldehyde is a chemically reactive substance that binds to proteins and other biologically important compounds. At higher concentrations, it causes toxic effects, such as a rapid pulse, sweating, skin flushing, nausea, and vomiting. In most people, ALDH metabolizes acetaldehyde quickly and efficiently, so that this intermediate metabolite does not accumulate in high concentrations, although small amounts are present in the blood during alcohol intoxication. In some people, however, genetic variants of the ALDH enzyme permit acetaldehyde to accumulate. Those people routinely flush, sweat, and become ill after consuming small amounts of alcohol. Because of the similarity between the acetaldehyde reaction and a hangover, some investigators have suggested that acetaldehyde causes hangovers. Although free acetaldehyde is not present in the blood after BAC's reach zero, the toxic effects of acetaldehyde produced during alcohol metabolism may persist into the hangover period. (Lieber, 1995).

1.2.6 Effects of factors other Than Alcohol

Factors other than alcohol also may contribute to a hangover. These factors include the following possibilities. Congeners among other

reasons; people consume alcoholic beverages for their ethanol content. Most alcoholic beverages contain smaller amounts of other biologically active compounds, however, including other alcohols. These compounds, known as congeners, contribute to the taste, smell, and appearance of alcoholic beverages. Congeners may be produced along with ethanol during fermentation, generated during aging or processing through the degradation of the beverage's organic components, or added to the beverage during the production process. Investigators now believe that congeners may contribute to a beverage's intoxicating effects and to a subsequent hangover. Research has shown that beverages composed of more pure ethanol, such as gin or vodka; induce fewer hangover effects than do beverages containing a large number of congeners, such as whiskey, brandy, or red wine (Chapman 1970; Pawan 1973).

1.2.7 Use of other Drugs

The use of other drugs often accompanies heavy alcohol consumption. Most heavy drinkers smoke cigarettes and some also use marijuana, cocaine, or other drugs. Although certain drugs can themselves produce hangover symptoms and affect alcohol intoxication, the effects of the various alcohol and other drug combinations on alcohol hangover are unknown Personal Influences. Some evidence exists that increased hangover symptoms occur more often in people possessing certain personality traits, such as neuroticism, anger, and defensiveness. Negative life events and feelings of guilt about drinking also are associated with experiencing more hangovers (Harburg *etal*. 1993). In addition, Earle wine (1993) reports greater hangover symptoms in people who have a higher personality risk for the development of alcoholism (as measured by the Mac Andrew Scale (Mac Andrew 1965).Those studies suggest that people who have an elevated personality risk for alcoholism experience more acute withdrawal and hangover symptoms and may initiate further drinking in an effort to find relief. Research has shown that a history of alcoholism in a person's family (i.e., a positive family history) is associate with a decreased sensitivity to the intoxicating effects of alcohol and a greater risk for developing alcoholism (Schuckit and Smith 1996). Newline and Pretorius (1990) suggested that a positive family history for alcoholism may be associated with a tendency for increased hangover symptoms as well. Their research compared the self-reported hangover

symptoms in college-age sons of alcoholic fathers with symptoms in sons of nonalcoholic fathers and found that the subjects with a positive family history for alcoholism had had greater hangover symptoms during the previous year. The amount of drinking was comparable between the two groups, although the subjects with a positive family history reported consuming significantly more mixed drinks than the group with a negative family history Attentiveness to the quantity and quality of alcohol consumed can have a significant effect on preventing hangover. Hangover symptoms are less likely to occur if a person drinks only small, no intoxicating amounts. Even among people who drink to intoxication, those who consume lower amounts of alcohol appear less likely to develop a hangover than those who drink higher amounts. Hangovers have not been associated with drinking beverages with a low alcohol content or with drinking nonalcoholic beverages. The type of alcohol consumed also may have a significant effect on reducing hangover (Chapman 1970; Pawan1973).

1.3 Effect of alcohol on blood

1.3.1Hematological complication of alcoholism

The Alcohol has numerous adverse effects on the various types of blood cells and their functions. For example, heavy alcohol consumption can cause generalized suppression of blood cell production and the production of structurally abnormal blood cell precursors that cannot mature into functional cells. Alcoholics frequently have defective red blood cells that are destroyed prematurely, possibly resulting in anemia. Alcohol also interferes with the production and function of white blood cells, especially those that defend the body against invading bacteria. Consequently, alcoholics frequently suffer from bacterial infections. Finally, alcohol adversely affects the platelets and other components of the blood-clotting system. Heavy alcohol consumption thus may increase the drinker's risk of suffering a stroke. (Harold and Ballard, 1997).

1.3.2 Alcohol,s effects on the bone marrow and RBCs production

Alcohol is the most commonly used drug whose consequences include the suppression of blood cell production, or hematopoiesis. Because its toxic effects are dose dependent, however, significantly impaired hematopoietic usually occurs only in people with severe alcoholism, who

also may suffer from nutritional deficiencies of folic acid and other vitamins that play a role in blood cell development. Chronic excessive alcohol ingestion reduces the number of blood cell precursors in the bone marrow and causes characteristic structural abnormalities in these cells' resulting in fewer-than-normal or non-functional mature blood cells. As a result, alcoholics may suffer from moderate anemia, characterized by enlarged, structurally abnormal RBC's; mildly reduced numbers of WBC's, especially of neutrophils; and moderately to severely reduced numbers of platelets. Although this generalized reduction in blood cell numbers (i.e., pancytopenia) usually is not progressive or fatal and is reversible with abstinence, complex aberrations of hematopoietic can develop over time that may cause death.

Many bone marrow abnormalities occurring in severe alcoholics affect the RBC precursor cells. These abnormalities most prominently include precursors containing fluid-fill cavities (i.e., vacuoles) or characteristic iron deposits (Harold and Ballard, 1997)

1.3.3 Alcohol-related RBCs disorder

Alcohol-related abnormalities in RBC production manifest themselves not only in the bone marrow but also through the presence of defective RBC's in the blood. For example, grossly enlarged RBC"s can occur in the blood a condition called macrocytosis as well as oddly shaped RBC 'that are subject to premature or accelerated destruction (i.e., hemolysis) because of their structural abnormalities. As result alcoholic frequently diagnosed with anemia. (Harold and Ballard, 1997)

1.3.4 Megaloblastic anemia

Blood cell precursor requires folic acid and other B12 vitamins for their continued production. Under conditions of folic acid deficiency, precursor cells can not divided properly and large immature and non function cells (i.e., megaloblasts) accumulate in the bone marrow as well as in the bloodstream. This impaired hematopoiesis affects mainly RBC's, but also WBC's and platelets. The resulting deficiency in RBC's, WBC's, and platelets (i.e., pancytopenia) has numerous adverse consequences for the patient, including weakness and pallor from anemia, infections resulting from reduced neutrophil numbers, and bleeding as a result of the lack of platelets.

Megaloblasts occur frequently in the bone marrow of alcoholics; they are particularly common among alcoholics with symptoms of anemia,

affecting up to one-third of these patients. These alcoholics generally also have reduced folic acid levels in their RBC's. The most common cause of this deficiency is a diet poor in folic acid, a frequent complication in alcoholics, who often have poor nutritional habits. In addition, alcohol ingestion itself may accelerate the development of folic acid deficiency by altering the absorption of folic acid from food. (Haroldand Ballard,1997).

1.3.5 Macrocytosis

The routine examination of blood samples from alcoholic and nonalcoholic patients using automated blood cell counters has resulted in the identification of many people in whom the mean size of individual RBC's the mean corpuscular volume (MCV) is significantly larger than normal. However, an increased MCV does not automatically lead to a diagnosis of macrocytosis. For example, cells with an increased MCV can be found in patients with folic acid or vitamin B12 deficiency (as in the case of megaloblastic anemia) or with chronic liver disease. Moreover, the presence of enlarged RBC's in the blood can be indicative of a variety of disorders in addition to alcoholism, including different kinds of anemia and a dysfunction of the thyroid gland. To establish a diagnosis of macrocytosis, the physician must examine the blood cells under microscope to identify structural features characteristic for each disorder.

Thus, the enlarged RBC's in patients with macrocytosis generally are uniformly rounded, in contrast to the more oval cells characteristic of megaloblastic anemia. People who drink excessive amounts of alcohol can develop macrocytosis even in the absence of other factors associated with RBC enlargement, such as alcoholic liver disease or folic acid deficiency. In fact, alcohol abuse is the disorder most commonly associated with macrocytosis: Up to 80 percent of men and 46 percent of women with macrocytosis have been found to be alcoholics. The precise mechanism underlying macrocytosis still is unknown . (Harold and Ballard, 1997).

1.3.6 Effect of Alcohol on WBCs

Since the 1920's clinicians have noted an association between excessive alcohol ingestion and the development of infections. These observations

suggest that alcohol interferes with the normal production and/or function of WBC's, which form the body's defense against microorganisms and other foreign substances. Because alcoholics commonly develop bacterial infections, much research has focused on alcohol s effects on neutrophils; the primary cell of defense against bacterial infection, alcohol also impairs the function of monocytes and macrophages, which attack bacteria and other microorganisms, and of lymphocytes, which mediate the immune response. Neutrophils severe bacteria infection occurs, the body's response usually includeslly neutrophils in the blood, a condition called leukocytosis. In contrast, bacterial infections often exhibit a reduced number of neutrophils in the alcoholics with severe bacterial pneumonia or other bacterial infections, neutropenia was present in 5 patients when they were admitted to the hospital and developed in the other patients within 24 to 48 hours was transient, however, and in several patients a rebound leukocytosis occurred between 5 and 10 days after hospital admission. Thus, bone marrow analysis of alcoholic patients during the neutropenic stage demonstrated that virtually none of the neutrophil precursors had matured beyond an early developmental stage. Moreover, the neutrophil stores that are maintained in the bone marrow to allow a quick response to a bacterial infection were depleted more rapidly in active alcoholics than in healthy control subjects. Alcohol consumption also interferes with the neutrophils ability to reach the site of an infection or inflammation (i.e., neutrophil delivery).then traveling to such a site, the neutrophils adhere to the walls of the blood vessels before migrating out of ted tissue. In tissue culture experiments using nylon fibers to mimic this adherence, neutrophils could not adhere to the fibers if the blood samples were incubated with alcohol. This effect was more pronounced the higher the alcohol doses were. Neutrophils obtained from intoxicated volunteers had the same defect. The degree and duration of this adherence defect correlated with the inhibition of neutrophil delivery observed in the body. Moreover, drugs that corrected the adherence defect in tissue-culture experiments also improved neutrophil delivery in humans. The function of neutrophils, including their adhesion ability, is regulated by hormone like substances called leukotrienes. Thus, the impaired neutrophil functioning observed after alcohol treatment could be attributable to reduced leukotriene production or to the neutrophils' inability to respond to the leukotrienes. Some research results indicate

that alcohol can interfere with leukotriene production. In an effort to overcome or prevent the alcohol-induced impairment of the body's antibacterial defense, researchers have studied the effects of a growth factor called granulocyte-colony stimulating factor (G-CSF) in animal experiments. During normal neutrophil production in the bone marrow, G-CSF promotes the multiplication and functional activity of neutrophils. The studies found that G-CSF stimulated neutrophil recruitment specifically to the site of an infection and ameliorated the alcohol-induced impairment in the defense against bacterial infections Monocytes and Macrophages .the monocyte-macrophage system, like neutrophils, constitutes an important line of defense against infections.

Monocytes and macrophages clear invading microorganisms as well as foreign or defective proteins from the blood by engulfing and subsequently destroying them. Alcohol interferes with the function of the monocyte-macrophage system, with clinically significant consequences. For example, compared with healthy people, alcoholics are less resistant to infections by microorganisms that normally are eradicated by monocytes and macrophages, such as the bacteria that cause tuberculosis and various forms of pneumonia. Similarly, studies of intoxicated laboratory animals demonstrated reduced elimination of bacteria by the monocyte-macrophage system.

These effects generally appear to be temporary Thus, in alcoholic patients whose monocyte-dependent elimination of a defective form of a albumin (Harold and Ballard, 1997).

1.3.7 Effect of alcohol on blood clotting system

Blood clotting, or coagulation, an important physiological process that Ensures the integrity of the vascular system, involves the platelets, or Thrombocytes, as well as several proteins dissolved in the plasma. When a blood vessel is injured, platelets are attracted to the site of the injury, where they aggregate to form a temporary plug. The platelets secrete several proteins (i.e., clotting factors) that together with other proteins either secreted by surrounding tissue cells or present in the blood initiate a chain of events that results in the formation of fibrin. Fibrin is a stringy protein that forms a tight mesh in the injured vessel; blood cells become

Trapped in this mesh, there by plugging the wound. Fibrin clots, in turn, can be dissolved by a process that helps prevent the development of thrombosis (i.e., fibrinolysis). (Harold&Ballard, 1997).

Alcohol can interfere with these processes at several levels, causing, for example, abnormally low platelet numbers in the blood (i.e., thrombocy-topenia), impaired platelet function (i.e. thrombocytopathy), and diminished fibrinolysis. These effects can have serious medical consequences, such as an increased risk for strokes Thrombocytopenia Thrombocytopenia is a frequent complication of alcoholism, affecting 3 to 43 percent of non acutely ill, well nourished alcoholics and 14 to 81percent of acutely ill, hospitalized alcoholics. Thus, apart from acquired immune deficiency syndrome (AIDS), alcoholism probably is the leading cause of thrombocytopenia. Except for the most severe cases, however, the patients generally do not exhibit manifestations of excessive bleeding. Moreover, alcohol-related thrombocytopenia generally is transient, and platelet counts usually return to normal within 1 week of abstinence. Only in patients whose thrombocytopenia is severe and associated with excessive bleeding are platelet transfusions indicated n many patients with thrombocytopenia, rebounding platelet numbers even exceed normal values. This re-bound thrombocytosis after cessation of alcohol consumption also occurs in the majority of patients whose platelet counts are normal at the time of hospitalization. In these patients, the extent of the excess in circulating platelets usually is higher than in patients presenting with thrombocytopenia .The exact mechanisms underlying alcohol-related thrombocytopenia remain unknown. Some researchers have suggested that alcohol intoxication itself, rather than alcohol-related nutritional deficiencies, causes the decrease in platelet numbers .This view is supported by findings that thrombocytopenia developed in healthy subjects who received diet containing adequate protein and vitamin levels (including large doses of folic acid) and consumed the equivalent of 1.5 pints (i.e. 745 milliliters) of 86-proof whiskey for at least 10 days (Linden baum 1987). The subjects' platelet levels returned to normal when alcohol consumption was discontinued. Similarly, platelet counts can be reduced in well-nourished alcoholics who do not suffer from folic acid deficiency. The available data also suggest that alcohol can interfere with a late stage of platelet production as well as shorten the life span of existing platelets. Individual drinkers

appear to differ in their susceptibility to alcohol-induced thrombocytopenia. Thus, clinicians have noted that some people who consume alcohol in excess repeatedly develop thrombocytopenia (often severely), whereas other drinkers maintain normal platelet levels. In addition to differences in the quantity of alcohol consumed, inherited or acquired variations in an individual drinker's biochemistry may account for these differences in susceptibility. (Harold and Ballard, 1997).

1.3.8 Hematological markers on alcoholism

Such adverse reactions, health care professionals should proactively counsel patients who regularly consume alcohol about the proper choice and safe use of aspirin and other over the counter NSAID'. Alcohol also can interact with anticoagulants, prescription medications that prevent blood clotting and which are used to treat patients who are at increased risk of developing thrombosis or an embolism in the lung. One commonly used anticoagulant is warfarin. However, warfarin treatment is not indicated for alcoholic patients, because alcohol ingestion can significantly interfere with the proper management of warfarin maintenance therapy. Fibrinolysis The body's ability to prevent excessive bleeding using the coagulation system is balanced by the fibrinolytic system, which helps ensure blood flow in peripheral organs and tissues by dissolving inappropriate fibrin clots. Alcohol's effect on fibrinolysis is controversial. Whereas some older studies reported an increase in fibrinolytic activity after alcohol consumption, more recent, better controlled studies have demonstrated that alcohol diminishes fibrinolysis the day after alcohol ingestion or during prolonged alcohol consumption. These observations suggest that alcoholics may be at increased risk for thrombosis (Harold and Ballard, 1997).

1.3.9 Alcohol health & Research World

An important focus of alcohol research is the search for biological markers that could be used in simple screening tests to identify people who are at risk for alcoholism or who already are chronic heavy drinkers. Two categories of biological markers exist: state markers, which reflect a person's alcohol consumption, and trait markers, which indicate a predisposition for alcoholism.

State markers fall into two main groups: screening markers and relapse markers. Screening markers, which detect chronic alcohol consumption, could complement information obtained from patients in the course of taking their medical history. This physical information could provide important diagnostic clues because, as clinical observations suggest, many people do not accurately report their level of alcohol consumption Thus, screening markers could be useful in the early identification of Alcoholism, especially in patients who consume alcohol in amounts that do not lead to acute medical problems but that could have long-term behavioral or medical consequences. In contrast, relapse markers, which are sensitive to acute alcohol consumption, could play an important role in monitoring recovering alcoholics and other heavy drinkers. State markers that would permit the identification of heavy drinkers even when alcohol is no longer present in the blood would be particularly valuable diagnostic tools .Trait markers could help identify people at risk for alcoholism who could benefit most from early, targeted prevention and intervention approaches .These high-risk populations most prominently include first-degree Relatives of alcoholics. Trait markers also could provide important research tools for evaluating the genetic and environmental factors that may predispose a person to alcoholism State Markers Chronic ingestion of large quantities of alcohol alters many physiological and biological processes and compounds, including several blood-related (i.e., hematological) variables. Because blood samples are relatively easy to obtain, structural and functional changes in circulating blood cells and plasma proteins potentially can form the basis of laboratory tests for screening, diagnosing, and monitoring alcoholism. Two hematological state markers commonly used for these purposes are the presence of carbohydrate-deficient transferring (CDT) in the blood and an increase in the size of red blood cells (RBC's), as measured by the mean corpuscular volume (MCV).(Harold and Ballard,1997).

1.4 Benefits of drink Alcohol

Moderate alcohol consumption has significant health benefits. These benefits include reducing the risk of heart attack, reduce the risk of diabetes, reduce the risk of Alzheimer's disease, reduce the risk of stroke, and to increase the health and life of consumers in General, there are a number of evidence that several moderate doses reduce the risk of blood

clotting, stroke, but an Australian study showed that drinking alcohol moderately equivalent of two glasses of alcohol a day increases the risk of breast and bowel cancer, throat and mouth by a large.(Kay, 1989)
Alcohol reduces heart attacks, ichemic strokes and circulatory problems through a number of identified ways. They include:

1. Improving blood lipid profile by increasing HDL ("good") cholesterol and decreasing LDL ("bad") cholesterol.
2. Decreasing thrombosis by reducing platelet aggregation, reducing fibrinogen.
3. Other ways such as reducing blood pressure, and reducing blood insulin level (Kay,1989).

1.4.1 Reduce Stress, Anxiety and Tension

Research shows that the consumption of alcohol in moderate amounts can lead to certain psychological benefits.
Low levels of alcohol can trigger stress reduction, easy feelings of anxiety and help consumers to reduce tension. These psychological effects of moderate drinking are positive ones that can be beneficial to theconsumer (Kay,1989).

1.4.2 A Longer Life

Studies from a number of different countries including China, the United States and England indicate that longevity is highest among groups of people who drink alcohol in moderation. (Kay,1989).

1.5 Folic acid

Folic acid is required for the purine and pyrimidine nucleotides synthesis, for the metabolism of several amino acids including homocysteine and for methylation of biological molecules (Wani *et al*, 2008) and (Zhaor, *et al*, 2009). Folate deficiency is a public health problem that is the most no in its association with neural tube defect in developing embryo, megaloblastic anemia, cancers and cardiovascular disease1. Since mammals cannot synthesize folate *de novo*, they must obtain these derivatives from the outside environment, necessitating an efficient intestinal absorptive mechanism. The intestine is exposed to folate from two sources: dietary source, where absorption of vitamin occurs in small intestine, and a large intestinal bacterial source, where the

vitamin is synthesized by the normal micro flora and absorbed by the large intestine.(Wanina and Kaurj 2011) (Dudeja *etal* 1997)).

1.5.1 Biochemical functions

Folates (as the intracellular polyglutamate derivatives) act as coenzymes in the of single-carbon units from one compound to another). Two of these reactions are involved in purine and one in pyrimidine synthesis necessary for DNA and RNA replication. Folate is coenzyme in another reaction, methionine synthesis, in which cobalamin is also involved and THF is regenerated THF is the acceptor of single carbon units newly entering the active pool via conversion of serine to glycine. Methionine, the other product of the methionine synthase reaction, is the precursor for *S*-adenosyl methionine (SAM), the universal methyl donor involved in over 100 methyltransferase reactions.During thymidylate synthesis, 5,10-methylene-THF is converted to DHF (dihydrofolate) . The enzyme DHF reductase converts this to THF. The drugs methotrexate, pyrimethamine and, mainly in bacteria, trimethoprim inhibit reductase, and this prevents formation of the active folate coenzymes from DHF. A small fraction of the folate coenzyme is not recycle during thymidylate synthesis but is degraded at the C-9–N-10 bond (Amazon *et al* ,2008).

1.5.2 Causes of folate deficiency

Dietary Particularly in: old age, infancy, poverty, alcoholism, chronic invalids kwashiorkor

1-Malabsorption

Major causes of deficiency Tropical sprue, gluten-induced enteropathy in children and adults, and in association with dermatitis herpetiformis, specific malabsorption of folate, intestinal megaloblastosis caused by severe cobalamin or folate deficiency *Minor causes of deficiency* Extensive jejunam resection, Crohn's disease, partial mastectomy, congestive heart failure, Whipple's disease, scleroderma, amyloid, diabetic enteropathy, systemic bacterial infection, lymphoma.

2- Excess utilization or loss

A-Physiological

Pregnancy and lactation, prematurity

b- Pathological Hematological diseases: chronic hemolytic anaemias, sickle cell anemia, thalassemia major, myelofibrosis Malignant diseases: carcinoma, lymphoma, leukemia, myeloma Inflammatory diseases: tuberculosis, Crohn's disease, psoriasis, exofoliative dermatitis, malaria Metabolic disease: homocystinuria Excess urinary loss: congestive heart failure, active liver disease Hemodialysis, peritoneal dialysis antifolatedrugs.

Anticonvulsant drugs (dephenylhydantoin, primidone, barbiturates), sulphasalazine Nitrofurantoin, tetracycline, anti-tuberculosis (Amazonetal2008).

1.5.3 Absorption

The principal site of folate absorption is the upper small intestine, and there is a steep fall-off in absorptive capacity in the lower jejunum and ileum. The absorption of all forms tested is rapid, a rise in blood level occurring within 15–20 min of ingestion. The small intestine has a tremendous capacity to absorb folate monoglutamates, as about 90% of a single dose is absorbed regardless of whether this is small (100g) or large (15 mg).Absorption of pteroylglutamic acid occurs by a saturable process, although it is unclear whether an active mechanism or facilitated diffusion is involved. The existence of patients with a specific defect in absorption of folates, including pteroylgltamic acid itself, however, does suggest that a special mechanism exists. The absorption of folate polyglutamates with higher numbers of glutamate residues is reduced. This may be due to the limited capacity of the small intestine to hydrolyze these compounds or to their limited transfer in the mucosal cell. On mean, about 50% of food folates are absorbed. Polyglutamate forms are hydrolysed by teroylpolyglutamate hydrolase (PPH, also known as folylpoly-gamma-glutamate car- boxypeptidase) to the monoglutamate derivatives, either in the lumen of the intestine or within the mucosa; they do not enter portal blood intact. The exact intracellular site of hydrolysis pteroylpolyglutamates in the enterocytes is unknown, although PPH has been shown to be concentrated in the lyso-somes of the cells and is also present on the brush border. Mono-or polyglutamate forms of dietary folate, which is already partly or completely reduced, is converted to 5-methyltetrahy-drofolate within the small intestinal mucosa before entering the portal plasma. The monoglutamates are actively

Pteroylglutamic acid at doses greater than 400g is absorbed largely unchanged and converted to natural folates in the liver. Theses are converted to 5 tetrahydrofolate during absorption through the intestine. (Amazon *etal* 2008).

1.5.4 Transport

Folate is transported in plasma; about one-third is loosely bound to albumin and two-thirds is unbound. In all body fluids (plasma, cerebrospinal fluid, milk, bile) folate is largely, if not entirely, 5-methyl-THF in the monoglutamate form. A carrier-mediated active process is involved in the entry of folate in to cells, the rate of uptake being linked to the rate of folate polyglutamate synthesis in the cell, which in replicating cells is related to the rate of DNA synthesis. Reduced folates are more rapidly taken up than oxidized folates. In most cells, folates are retained with tight binding to folate-binding proteins, three of which are enzymes involved in methyl group metabolism, sarcosine dehydrogenase , dimethylglycine dehydrogenase and glycine n-methyltransferase, until the cell dies. Intact liver cells can release folate. Two types of folate-binding protein are involved in entry of methyl-THF into cells. A high-affinity folate receptor takes folate into cells internalized in a vesicle (caveola), which is then acidified, releasing folate into the vesicle lumen. Folate is then carried by the membrane folate transporter into the cytoplasm; the caveola recycles to the cell surface, where its high affinity receptors are re-utilized. The high-affinity receptor is attached to the outer surface of the cell membrane by glycosyl phosphatidylinositol link ages. They may be involved in transport of oxidized folates and folate breakdown products to the liver for excretion in bile. The congenital disease of folate specific malabsorption, in which there is also a transport defect, may be a defect of a specific folate binding protein, but this has yet to be established. (Amazon *et al* ,2008).

1.5.5 Body stores and requirements

Total body folate in the adult is about 10 mg, the liver containing the largest store. Daily adult requirements are about 100 g. Up to 13 g of folate is lost as such in absorption the urine each day, but break down occur in sweat and skin; fecal folate is largely derived from colonic bacteria. Stores are only sufficient for about 4 months in normal adults, so

severe folate deficiency may develop rapidly. (The principal site of folate absorption is the upper small intestine, and there is a steep fall-off in absorptive capacity in the lower jejunum and ileum. The absorption of all forms tested is rapid, a rise in blood level occurring within 15–20 min of ingestion. The small intestine has a tremendous capacity to absorb folate monoglutamates, as about 90% of a single dose is absorbed regardless of whether this is small (100g) or large (15 mg).(Amazon *et al* ,2008)

1.5.6 Folate deficiency

Folate is the term encompassing all the different biologically active forms of the vitamin and folic acid is the synthetic form used in supplements, fortified foods, and for treatment. Both types are absorbed from the proximal small intestine and almost half of the body folate is found in the liver. The bioavailability of dietary folate is influenced by many factors within the intestinal lumen. Natural folates in food are also vulnerable to a variable degree of degradation by cooking processes (McKillop *et al,* 2002). These factors do not tend to affect folic acid and there is general consensus that the bioavailability of food folates is, on mean, about 50% lower than folic acid (Gregory, 1995). A low intake or poor absorption leads to a low serum folate level, which then leads to low tissue levels. Since folate is required for DNA synthesis, the earliest signs of deficiency are seen in rapidly proliferating cells such as those of the bone marrow and gastrointestinal tract. Severe folate deficiency can cause pancytopenia and megaloblastic anemia. Since serum folate reflects recent dietary intake, concerns have been raised about any assay taken after any oral folate intake, and therefore, masking underlying deficiency and giving a ‘false negative’ result. In addition, a ‘false positive’ reduced serum folate may be found in patients with anorexia, acute alcohol consumption, normal pregnancy and patients on anticonvulsant therapy (Beck, 1991). It is important to consider the result of the serum folate level within the context of the full clinical picture. There is no clearly defined progression from the onset of inadequate tissue folate status to development of megaloblastic anemia. Both biochemical and clinical evidence of folate deficiency can be observed in the absence of clinical symptoms. With increasing adoption of food fortification, the incidence of folate deficiency has declined significantly(Joelson *et al,* 2007), and

interpretation of folate status in patients has to be made in relation to presence of known risk factors causing efficiency (Vinker *et al,* 2013).

1.5.7 Influence of alcoholism on the membrane transport and bioavailability of folate

Folate deficiencies can occur for many reasons, including reduced folate intake, increased metabolism and increased requirements, malabsorption, and genetic defects (Baraona, 2001). Congenital errors in folate metabolism can related either to defective transport of folate through various cells, or to defective intracellular utilization of folate, because of some enzyme deficiencies (Hung *et al,* 2005). Folate malabsorption can be at the level of impaired intestinal absorption and renal tubular absorption. Such impairments occur in variety of conditions, including chronic ethanol consumption, intestinal diseases, and renal malfunction. Ethanol must be considered as one of the most important toxins consumed regularly and in large quantities by humans (Salasporo, 2003). Since ethanol intake has steadily increased during the last two decades, alcoholism has become one of the major health problems worldwide. Among the various other ethanol-associated disorders, folate deficiency is commonly associated with chronic alcoholism, because the processes involved in the absorption, transport and intracellular metabolism of this cofactor are complex and are quite susceptible to the cellular microenvironment (Vilanueva *et al,* 2004).

Niacin, thiamine and pyridoxine (vitamin B6) deficiencies have also been confirmed in alcoholics, but ethanol-induced folate deficiency has been extensively studied. It is clear from the available literature that ethanol-induced folate deficiency is caused, in part, by intestinal malabsorption of folate (Weir *et al* 1985).

Three decades ago, (Halsted *et al,* 1973) demonstrated that individuals who abuse ethanol on a regular basis malabsorb folate. The absorption of folic acid by the jejunum and duecum of ethanol-fed rats was found to be decreased (Fernandez *te al,* 1996) .There was a significant decrease in folate absorption and hepatic folate content in alcoholic monkeys (Barak *etal,* 1987).

In vitro studies on the effect of ethanol on the absorption of folate in the rat proximal jejunum suggested that the malabsorption of folate could

be related to the effect of ethanol on the acid micro climate (Weir *et al*, 1985) .However, there is no in vivo study to support such a finding. The reduced intestinal transport of folate in a chronic alcoholism model was found to be associated with a reduction in folic acid binding to intestinal Bmax might contribute to intestinal folate malabsorption during alcoholism(Hamid and Kaur,2005) BM, with a significant alteration in B max ,SH group status, and divalent and monocovalent caution dependency(Hamid and Kaur, 2007) . The deregulated kinetic characteristics of the folate uptake proceder.Moreover decreased RFC mRNA levels were observed in the primary absorptive surface of jejunal tissue with parallel changes in RFc protein levels at the brush border as well as at the BLM all across the crypt-villous axis(Hamid *et al*,2007).

These changes in functional activity of the membrane transport system could not be related to the general loss of intestinal architecture, but has been attributed to the specific effect of ethanol ingestion on the folate transport system. in contrast to the BBM surface, the neutral carrier mediated steerable folate transport at the basolateral surface showed sodium and ATP independence. Ethanol ingestion results in potassium and ATP dependence, besides affecting the status of S–S linkage of the folate transport system. Importantly, chronic ethanol ingestion reduced folate exit across the basolateral surface by a mechanism involving decreased affinity of RFC for folate and a decrease in the number of transporter molecules on the surface (Hamid *et al*, 2007).

Another factor contributing to the lower bioavailability of dietary folate that accompanies ethanol ingestion is increased renal excretion. Both acute (4 h) and chronic (12 weeks) ethanol ingestion seem to increase the loss of folate in the urine (Eiesenga *et al*, 1989).

Our recent findings showed that ethanol exerts its effect by altering the binding and kinetic characteristics of folate transport at both the BBM and the BLM of the kidney .In addition to this, the down regulation of RFC and FBP genes in the renal absorptive and conservative surfaces, respectively, along with that of RFC in the intestine might play a role in the observed reduced folate transport efficiency in the kidney and intestine during alcoholism , and result in low red blood cell (RBC) and serum folate levels. The role of PCFT and OATs in chronic ethanol-induced reduced folate transport in the absorptive epithelia has not been

exploredas yet. In addition, a significant decrease in folate uptake in intestinal epithelial cells in the presence of inhibitors of cAMP-dependent protein kinase implied a role of protein kinase in the efficiency of the transport process. The best defined target of cAMP is PKA, which in turn mediates most of the physiological effects of cAMP in eukaryotes. Moreover, dibutyryl cAMP, a compound that increases the intracellular cAMP levels, resulted in a significant increase in folic acid uptake, with 2.0-fold higher increase in the ethanol-fed group than in the control group. This suggested that cAMP may be an important regulatory component of signaling cascade that is affected inchronic a lcoholism . (Hamid *andKaur,* 2008).

Moreover, atropine, which causes decreased intracellular cAMP levels by inhibiting the activity of adenylylcyclase, inhibited folic acid transport in both groups of rats, but the decrease was less (51%) in the case of alcoholic rats. Importantly, many groups have demonstrated, in models of chronic alcoholism, that both the initial deconjugation and the subsequent transport of monoglutamic folate are impaired in alcoholic individuals (Purohit *et al*, 2005). In alcoholic pigs, loss of deconjugation activity at the brush border was observed (Halsted *et al*, 2001) & (Reisenaver *etal* ,1989) as was the partial loss of both FBPs that coordinately affect the transmembrane transport of folate (Piedrahita *et al*, 1999). Current data indicate that folate catabolism and folate polyglutamylation are competitive reactions that influence cellular folate concentrations, and that increased methenyl tetahydrofolate synthetase late concentrations, and may account, in part, for tissue-specific differences in folate accumulation (Suh, 2001).

1.5.8 Tests to diagnose folate deficiency

(a) Serum Folate:

The serum folate concentration reflects recent folate status and intake. Most clinical laboratories today measure serum folate by competitive folate binding protein assays (FBP) using chemilu-minescence or fluorescence detection systems. Despite considerable variation in performance between assays, using the isotope dilution-liquid chromatography-tandem mass spectrometry (ID-LC-MS/MS) international reference methods, there was close correlation of the

consensus mean in the United Kingdom NEQAS surveys (Black more, *et al* 2011). This offers the prospect of harmonization of reference ranges for serum folate assays. There is no clear consensus on the level of serum folate that indicates deficiency. Conventionally, clinicians have used serum folate lower than 7 n mol/L (3 μg/L) as a guideline since the risk of megaloblastic anemia greatly increases below this level However, there is a sizeable 'indeterminate zone' (between approximately 7 and 10 nmol /L (3 and 4.5 μg/L)).Therefore a low serum folate should be taken as suggestive of deficiency rather than as a highly sensitive diagnostic test.

(b) Red cell Folate:

The red cell folate gives an assessment of the tissue folate status over the lifetime of the red cells and is therefore regarded as an indicator of longer term folate status the serum folate assay.

A red cell folate level below 340 nmol/L (150 μg/L) has been regarded as consistent with clinical folate deficiency (Joelson *et al*, 2007) in the absence of cobalamin deficiency. Whether serum folate or red cell folate is better for assessing body folate status has been extensively argued. A pathology benchmarking review concluded that serum folate measurement provides equivalent information to red cell measurement (Galloway and Rushworth, 2003). However, it is suggested that in about 5% of patients the measurement of red cell folate may be useful in patients with macrocytosis who have a normal serum folate .Current red cell folate assays are affected by pre-analytical and analytical variables which preclude them as robust assays. There is a lack of standardization of current commercial red cell folate assays, which show very poor inter-method agreement in UKNEQAS red cell folate surveys.
A recent review also suggested serum folate measurement may be better than red cell folate since it is affected by fewer pre-analytical and analytical variables (Farrell *teal*, 2013).

(c) Homocysteine (in relation to folate disorders) Elevated plasma tHcy is a sensitive indicator of folate status and is strongly correlated with serum folate levels in the low physiological range (i.e. serum folate levels below about 10 nmol/L (4.5 μg/L). tHcy arises as a by-product of methionine metabolism and is normally present in plasma at concentrations below 12 μmol/L, depending on age, gender, renal function, genetic factors and the

nutritional status of several other vitamins. It is not, therefore, a specific marker of folate status. Furthermore, it has stringent requirements regarding sampling and technical analysis. As a result, it is not used for routine testing (Farrell *etal*, 2013).

1.6 Previous studies

ODUOLA was studded effect of Alcohol on 200 adult males categorized into four groups ;none drinkers , occasional drinkers , moderate drinkers and heavy drinkers .Fifty subjects were in each group ,their age ranged between 20 and 57 (mean 33.4) The values obtained for biochemical and hematological parameters in occasional and moderate drinkers showed no significant difference (p`0.05)to those obtained for non- drinkers which served as control group . However, in heavy drinkers, there were significant difference (p0.05) in some of the biochemical and hematological results when compared to those of abstainers, occasional and moderate drinkers (Odoula, 2005) Other study was conducted in Sudan by RIVARA to evaluate hematological abnormality in alcohol consumer, 121 chronic alcoholics admitted to a general medical service with a low hematocrit were evaluated. Megaloblastic marrow change was found in 33.9% of patients, MCV was of little value in predicting the presence of megaloblastic change unless markedly elevated (greater than 110 f1). Hematologic responses to folic acid were often inadequate in patients with magaloblastic morphologic changes, apparently because of associated a cute and chronic illness (Rivara, 2004)

Eichner and Hillman were Test the significance of the alcohol-induced fall in serum folate level in USA, two volunteers were given alcohol and a low folate diet for several weeks.

One subject was chosen because of normal folate stores which were further supplemented with folic acid) and the other subject was chosen Because Of marginal folate stores. The ingestion of alcohol caused a fall in serum Folate level in both subjects (Eichner and Hillman, 1971).

1.7 Rationale

Alcohol is a major risk factor for health harms and also contributes to a personal and social burden of disease and injury (Rehm,2009).also it is a major contributes to the global burden of disease ,disability and death in ,middle and low income countries (Amazan ,2008).

The aim of the study is determine effect of alcohol consumption on CBC and serum folate level to increased the availability of information that may help addict to stop drinking and other researcher to continue in research.

1.8 Objective

General objective

-To evaluate the effect of alcohol consumption on CBC and serum folate level.

Specific objective

- To measure CBC in blood among study group.
- To measure serum folate level in blood among study group.

2-Materials and Methods

2.1 Study design

This is case control study aimed to determine the effect of alcohol consumption on CBC and serum folate level–Khartoum State

2.2 Study population

Alcoholisms in Khartoum state

2.3 Inclusion criteria

Person that drink alcohol (mild- modrate and sever).

2.4 Exclusion criteria

Alcoholic with disease and participant's alcoholic under treatment.

2.5 Study area

Khartoum state

2.6 Sample size

Fifty cases of volunteer were chosen by non –probability sample 50 alcoholic male and control group of 20 healthy individual have been chosen.

2.7 Tool of data collection

Data collection using personal interview questionnaire to the participant s including age–education level- marital status and ethical consideration was conducted by interview discussion to get permission from the participants.

2.8 Methodology

2.8.1 Blood collection

70 sample are collected from participant and control ,5 ml of vinous blood was collected from each volunteer and controls via the anteabital vein using vacationer system . Vacationer tube contains ethylene di-amine tetra- acetic acid (EDTA) as anticoagulant. Other tube was plain container which contain 2.5 ml each sample was mixed genteelly and thoroughly to prevent cell lysis and clotting of blood ,

there complete blood counts (CBC) was determined with in 2 hours after collection the remainder 2.5 ml of blood was used to determined folate level by tosoh (full blood count analysis was done on the same day of collection) using system KX21N (manufactured by sysmex corporation Kobe ,Japan) three –part auto analyzer able to run 19 parameters per sample including hemoglobin concentration , packed cell volume , red blood cell concentration mean corpuscular hemoglobin , mean cells volume , mean corpuscular hemoglobin concentration , white blood cells and plate late values and the reference value of these parameter (*Lewis etal* ,2006).

2.8.2 Complete blood count

Evaluation of the blood counts, were performed by sysmex automated hematological analyzer which could perform 18 hematological parameters with high accuracy is based on the electronic resistance (impedance)detection method for counting and sizing recognition of leukocyte, erythrocyte and platelet .Through using three preliminary hydraulic systems for WBCs RBCs platelet and hemoglobin, and display the mode of cells bold count result on the liquid crystal displayer{LCD} with histogram and printed out results in thermal paper. (*Lewis etal, 2006*).

2.8.3 Principle of sysmex KX 21N hematological analyzer

Measurement of blood cells (RBCs, WBCs, and platelet)and hemoglobin concentration obtained by aspiration of small volume of well mixed (k2EDTA) blood by sample probe and mixed with isotonic diluents in nebulizer .Diluents aspiration delivered to RBCs aperture bath for providing information about RBCs and platelet .Other portion of aspirated sample induced in to WBCs bath in which hemolytic reagent tromatolyzer) added to break down RBCs and release of hemoglobin method (HICN) .The through three sensing apertures for each cell type ,cells counted and size information generated in triplicate pulses acting to electronic conductivity . Mentioned pulses converts in to digital number using in build calculator programmed and designed for RBCs, WBCs count come portion of diluted sample delivered to in build hemoglobin meter at the same time ,hence three values directly measured (RBCs, TWBCs, Hb) and displayed on (LCD). Other values of red cell indices

leukocyte differential and absolute count calculated from given information ,the result printed out aced to the setting mode .on the other hand platelet count and histogram determined from pulses acting to the platelet (*Lewis etal* ,2006).

2.8.4 Reagents and materials provided by sysmex many facture: and contain;

1-sample; well mixed k2EDA blood

2-cell

3-stromatolyzer

4-detergen

5-cell cleaner

2.8.5 Procedure of sysmex

- The reagent needed was checked and the power switch was turned.
- self-auto rinse, and back ground check was automatically performed and the vend (vend for analysis) will appear
- Whole blood mode was selected.
- Sample number and patient name were entered.
- Sample was mixed sufficiently.
- The tube was set to the sample prope, and in that condition the start switch was pressed.
- When the sucking of the sample was done, the tube was removed.
- After that automatic analysis was done and the result was displayed in the screen.

2.8.6 Preparation of thin blood film

Equipments

- Slides
- Spreaders
- Blood sample

Procedure

A small drop of blood was placed in the centre line of a slide about 1 cm from one end .then ,without delay , the spreader was placed in front of the drop at an angle of about 30 to the slide and was moved back to make contact ,with a steady m Movement of the hand ,the drop of blood was spread a long the slide the spreader did not lift off until the last trace of blood was spread out ,with a correctly sized drop ;the film was about 3 cm in length. The film was dried by air then stained.

Staining of thin blood film

Equipments

- Thin blood film
- Staining
- Lieshman, s-buffer (tap water).

Procedure

The film was placed on the stainig rack then flooded by the stain for two minutes.

Then the buffer was applied for additional eight minutes.

After that the slide was washed well by the buffer and let to dry by air .The film was examined under the microscope (*Lewis etal, 2006*).

2.8.7 Principe of tosoh aia system analyzer

The AIA –PACK FOLATE is a competitive enzyme immunoassay which, after sample pretreatment, is preformed with in the AIA-PACK FOLATE test cup. sample pretreatment reagents (containing sodium hydroxide and dithiothreitol) release folate from serum binding proteins in the sample .folate present in pretreated test sample Competes with enzyme –labeled folate for a limited number of binding site on a fluoresce in –labeled bovine folate binding protein which then binds to anti-FITC(fluorescent isothiocyanate) antibody immobilized on magnetic beads. The Beads are washed to remove the unbound enzyme-labeled folate and are then incubated With fluorogenic substrate,4-methylumbelliferyl phosphate .the amount of enzyme labeled Folate

that binds to the beads is inversely proportional to the folate concentration in the test sample . A standard curve using arrange of

Known standard concentration is constructed and unknown folate concentrations are calculated using this curve**.**

2.9 Ethical consideration

Ethical clearance was obtained in this study, and the sample collected after the consent of participant s whom were informed about the procedure of blood collection and the aim of the study. Data were obtained with high confidentiality and sure that data were used for research purposes only.

2.10 Data analysis

The collected data was coded in master sheet and proceed for analysis using Independent t-test co- relation test SPSS version 15 computerized program and the data presented in tables and graphs

Results

70 of adult male were selected randomly 50 as alcoholic and 20 as non –alcohol

To measure the effect of alcohol consumption on CBC and serum folate level and the result obtained as follow:

-The mean± SD of Hemoglobin level for alcoholic was found to be (14.7±1.9) witch is not significantly different from the mean ± SD of hemoglobin for the control group (13.o±2.1) P.value(≥.05). Show table (1)

-The mean ± SD of PCV for alcoholic was found to be (45.0±5.6) witch is not significantly different from the mean± SD of PCV for the control group (40.6±6.1) P.value(≥.05).show table(1)

-The mean± SD of MCV for alcoholic was found to be (88.7±5.9) witch is not significantly different from the mean± SD of MCV for the control group (84.14) p.value (≥.05) show table (`1)

-The mean± SD of MCH for alcoholic was found to be (28.8±2.2) witch is not significantly different from the mean± SD of MCH for the control group. (26.0±2.9) P.value (≥.05). Show table (1)

-The mean ± SD of MCHC for alcoholic was found to be (32.6±1.6) witch is not significantly different from the mean± SDMCHC for the control group (32.0±1.0) P.value (≥.05). Show table (1)

-The mean± SD of TWBCs for alcoholic was found to be (6.1±2.0) show no significant effect when compare with mean± SD of TWBCs for the control group (7.2±3.2) P.value (≥05). Show table (2)

-The mean± SD of lymphocyte for alcoholic was found to be (47.62± 17.o) show significant effect when compare with mean± SD of lymphocyte for the control group(35.65±10.94)) P.value (≤05). Show table (2)

-The mean± SD of monocyte for alcoholic was found to be (.15± .18) show no significant effect when compare with mean± SD of monocyte for the control group (18±.19) p. value (≥05). Show table (2)

-The mean± SD of eosinophil for alcoholic was found to be (28± .18) show no significant effect when compare with mean± SD of eosinophil for the control group (.29±.300)) P.value (≥05). Show table (2)

-The mean± SD of basophil for alcoholic was found to be (0.08± .03) show no significant effect when compare with mean± SD of basophil for the control group(.04±.118) P.value (≥05). Show table (2)

-The mean± SD of neutrophil for alcoholic was found to be (47 .08± 17.1) show significant effect when compare with mean± SD of neutrophil for the control group (59.86±9.31) P.value (≤05). Show table (2)

--The mean± SD of platelets for alcoholic was found to be (2 .80± 114.93) show no significant effect when compare with mean± SD of platelets for the control group (2.66±65.8)) P.value (≥05). Show table (3)

-The mean± SD of Folate level for alcoholic was found to be (6.8±2.0) witch is not significantly different from the mean± SD of Folate level for the control group (8.9±3.1) P.value (≥.05). Show table (3)

- Study also show versus relationship between MCV and folate level among the study group but it is very weak show table no (4) and figure (4).

Macrocyte, target cells and crenated cells were found in the peripheral blood of some alcoholic subject.

Figure (1)Age:

The mean age for alcoholic group s was found to be 41 years witch is not significantly different from the mean age for the control group 39 years show (Fig. 1)

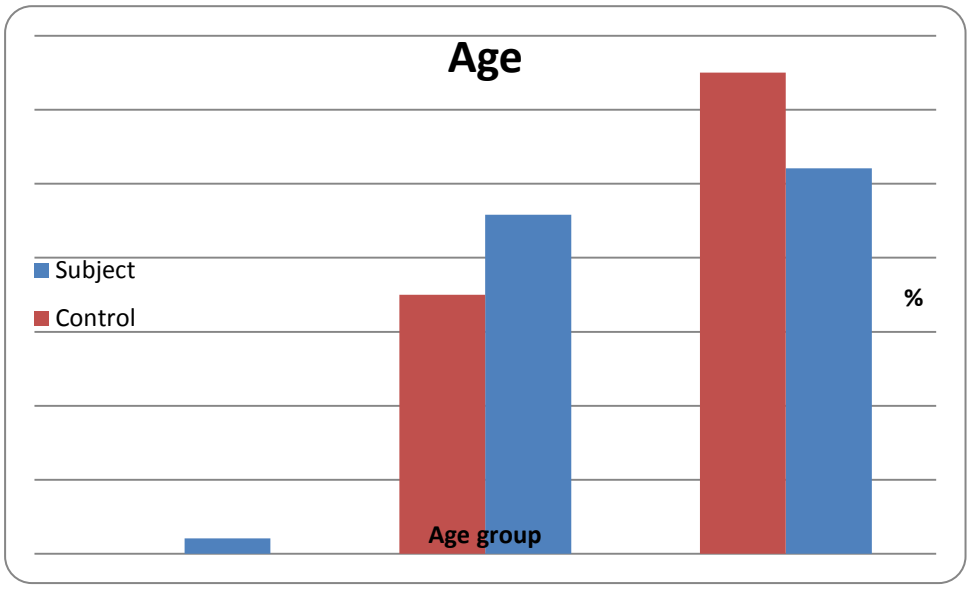


Figure (2) Education level: 54 % of alcoholic groups are educated up to the university level whereas only 12.5 % reported that the completed the basic level show (Fig.2)

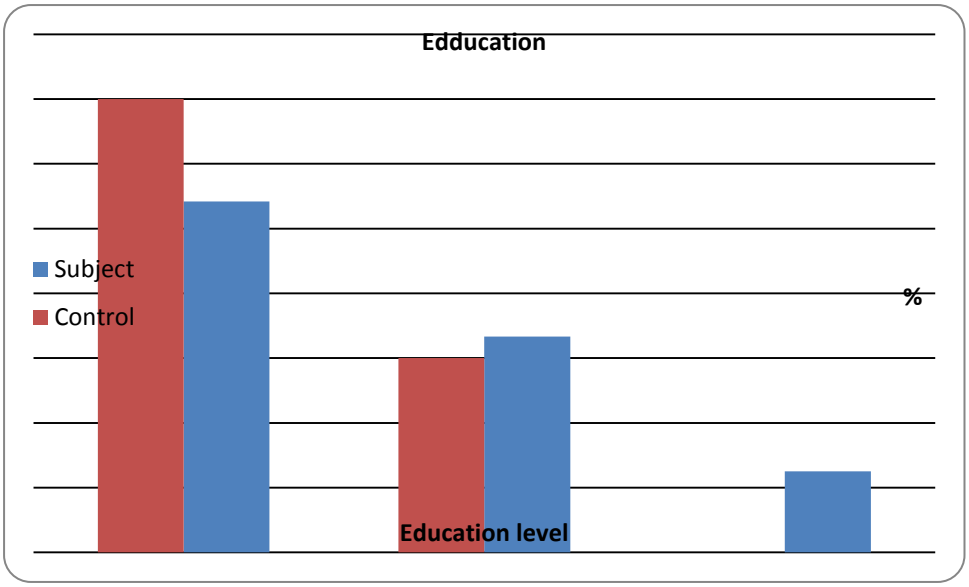


Figure (3) Marital Status: The % of the married and single respondent was found to be 64 and 36 for both the subject and control groups

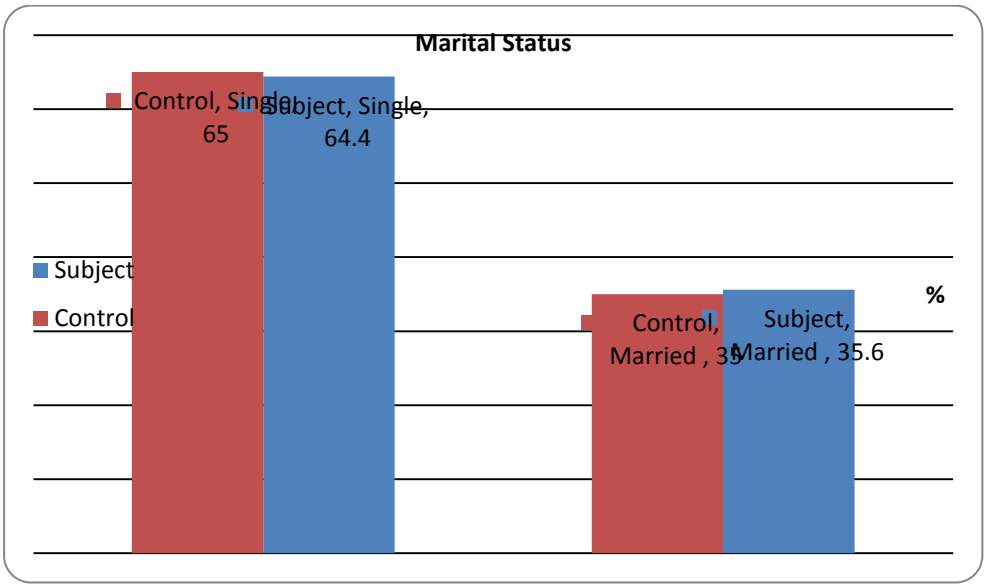
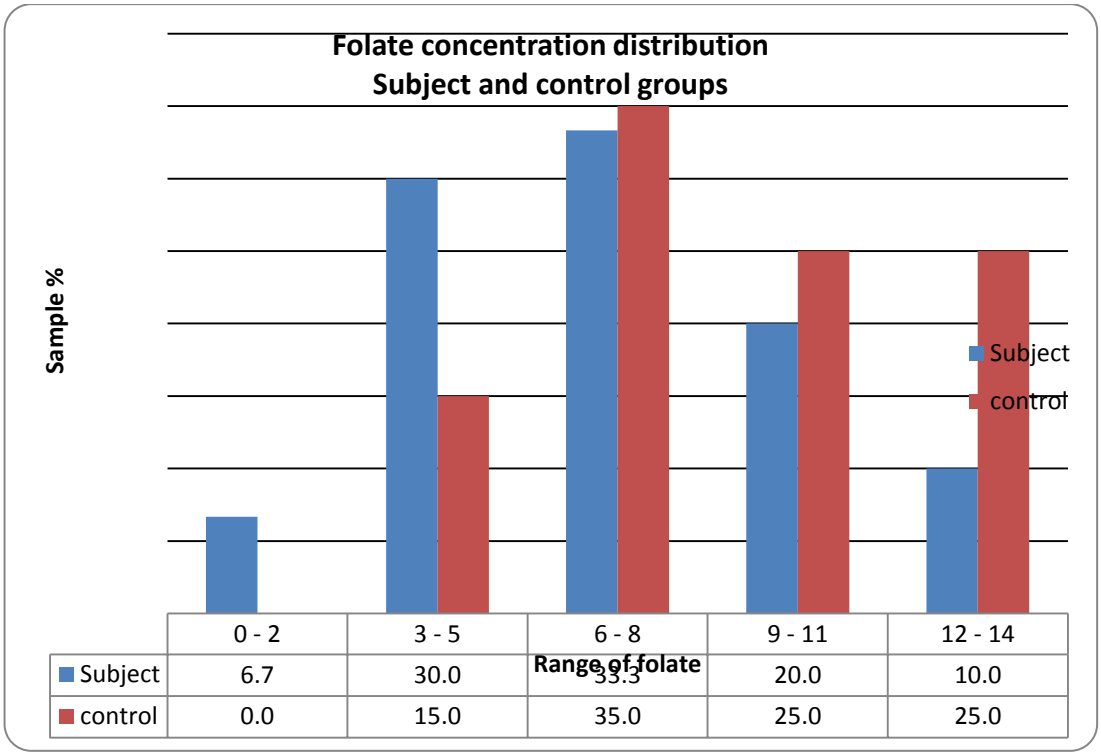


Figure (4) Folate concentration distribution



	0 - 2	3 - 5	6 - 8	9 - 11	12 - 14
Subject	6.7	30.0	33.3	20.0	10.0
control	0.0	15.0	35.0	25.0	25.0

Figure (5) MCV against folate

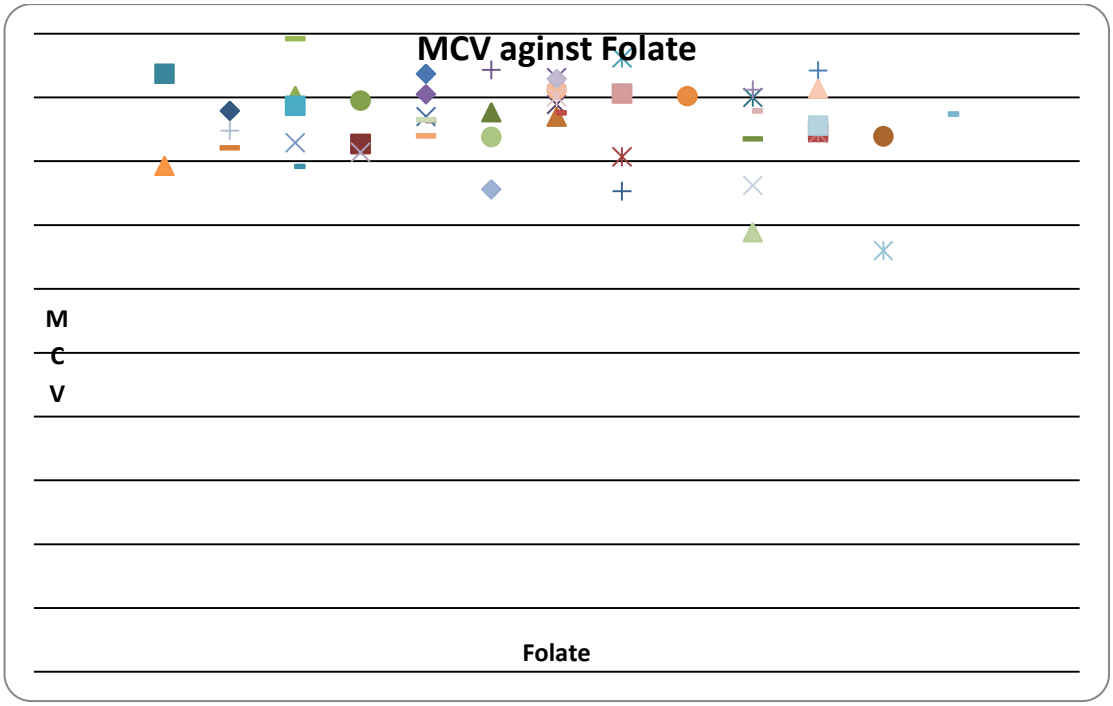


Table (1) Mean of erythrocytic series among the study group

Parameter	Alcoholic			Non-alcoholic			
	Mean	SD	No	Mean	SD	No	P-Value
RBCs×1012/l	5.067	0.614	50	4.841	0.653	20	0.325
HB g/dl	14.71	1.93214	50	13.09	2.17544	20	0.422
PCV%	45.034	5.6446	50	40.645	6.126	20	0.97
MCV fl	88.79	5.91367	50	84.14	7.41914	20	0.455
MCH pg	28.826	2.27298	50	26.985	2.97326	20	0.35
MCHC g/dl	32.606	1.67994	50	32.07	1.02552	20	0.2 03

Table (2) Mean of leucocyte series among the study group

Parameter	Alcoholic			Nonalcoholic			
	Mean	SD	No	Mean	SD	No	P-Value
TWBCs×109/l	6.198	2.02157	50	7.26	3.22937	20	0.600
Lymphocyte%	47.62	17.01607	50	47.62	17.01607	20	0.011
Monocyte%	0.15	0.18211	50	0.185	0.19808	20	0.58
Eosinophil%	0.28	0.18516	50	0.29	0.3007	20	0.054
Basophil5%	0.008	0.03959	50	0.04	0.11877	20	0.061
Neutrophil%	47.08	17.16051	50	59.685	9.31808	20	0.003

Table (3) Mean of platelets count and platelets indices among the study group

Parameter	Alcoholic			Non –Alcoholic			
	Mean	SD	No	Mean	SD	No	P-Value
Plt×109/l	2.80E+02	114.9378	50	2.66E+02	65.81433	20	0.064
Mpvfl	8.856	1.19986	50	8.235	0.92638	20	0.269
PDWfl	14.7184	1.9785	50	15.735	0.28335	20	0.002µ
Folate µg/L	6.8333	3.15227	50	8.9	3.16061	20	0.886

Table (4) Correlation between Folate and MCV among study group

	Group	N	p.value
Subject	Folate	30	0.129
	MVC		
Control	Folate	20	0.116
	MVC		

p.value (≤ .5)

4. Discussion conclusion .recommendation

4.1 Discussion

Alcohol contributed to a high burden of diseases in society in term of years that people spend with disability or in poor health because of alcohol related illness or injury (Connor *etal* ,2005).

This case control study used to assess the pathological effect of alcohol in complete blood count and folate level.

The result obtains from the study carried on 50 (cases) known as alcoholic in Khartoum State and 20 healthy volunteer (control).

-No effect of alcohol was found on HB, PCV ,RBCs and red cells indices this may be due to drinking alcohol in Sudan is illegal and so drinkers tend to stay at their homes. This might help in good nutrition and so opposite to the state of being neglected. This agree with a study in Nigeria 200 adults Nigerian males were categorized into four groups none drinkers , occasional drinkers , moderate drinkers and heavy drinkers The study concluded that only heavy drinkers were affected and so had low hematological parameters (Odoula *etal*, 2005). This may mean that occasional and moderate drinking were not affected in both blood biochemistry and hematology .

-Alcohol shows no significant effect in TWBCs among the study group p.value (0.600) .

-Neutropenia was documented in alcoholism decrease of neutrophils count when compared with control groups show significantly decrease pvalue (=0.003).

- Lymphocytosis reported in alcoholic was found significantly increase p.values(=0.011) compared to controls group .This increase is due to neutropenia. -

While there is no effects were found on monocyte, eosinophil, and basophil and this is disagree with latvala in USA which show that hematological examination of patient presenting with cytopenia and history of hazard drinking showed low incidence of anemia , but abnormal platelet and leukocyte level were common in alcoholic patient compared with control non- alcoholic .(latvala *etal,*2004).

Also disagree with heermans in UK which show that alcohol has widespread direct and indirect effect s on hematologic system which can mimic and/or obscure other disorder. Leukocyte, erythrocyte and

thrombocyte production and function are affected directly. Also impact red blood cells and hemostatic mechanisms (Heermans, 1998).

-Alcohol shows no significant effect in platelet indices among the study groups. P.value (0.04).except PDW shows significant effect p. value (0.002).
- Macrocyte, target cells and crenated cells were found in the peripheral blood of some alcoholic subject.

-Serum Folate level show no significant effected with alcoholism p.value (0.05). this result Disagree with Eichner and Hillman study done to test the significant of alcohol –induced serum e folate level ,one subject was chosen because of normal folate stores which were further supplemented with folic acid and other subject was chosen because of marginal folate stores . The ingestion of alcohol caused a fall in serum folate level in both subject (Eichner and Hillman, 1997).

4.2 Conclusion

-The study showed that Alcohol can not cause significant effect in all hematological parameter except neutrophil and lymphocyte.

-The study showed no significant effect of alcohol on serum folate level.

-Alcohol induces morphological change in RBCs.

4.3 Recommendation

-Prospective long term studies with large sample size must be done to give information about alcohol problem.

-Hematological investigation must be done early in alcoholic person to prevent a complication of alcohol.

- Research on discovery of more sensitive and specific tests on alcoholic person is needed.

- Raise the awareness of the university students about the risks of Alcohol abuse.

- Raise the awareness of the youth group about the importance of marriage.

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Appendix No (1)

Sudan University OF Science and Technology

College Of Graduate Studies

Department Of Hematology

Measurement Of Pathological Effect Of Alcohol in CBC and Folate Level Among Alcohol Consumer –Khartoum State (2015)

Questionnaire

ٍ الموضوع جمع عينات لاجراء البحث التكميلى

Sex	Male	

Age	0	1	2
	≤20	21-65	≥65

Education	**1**	**2**	**3**	**4**
	Primary	secondary	University	H.degree

Marital status	Marital	Single

امضاء الباحث: .....

امضاء المتبرع: .....

Appendex No (2)

Sysmex kx21N

Appendex No (3)

Tosoh AIA