Sudan University of Science & Technology

College of Graduate Studies

Association of ABO Blood Group/ Rhesus Factor with Upper Gastrointestinal Bleeding and Potential Risk Factors

الارتباط بين فصيلة الدم ABO و العامل الريصي بنزيف الجهاز الهضمي العلوي وعوامل الخطر المحتملة

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DEDICATION

I dedicate this work to:

My darling parents who are support me and encourage me

to success.

My brothers and my friends and my all family .

My colleagues who gave me the possibility of completing this dissertation

Everyone who has helped me to learn new things and to reach this level .

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First of all my gratitude and thanks to our Almighty Allah, most gracious and most merciful, whom gave me the serenity , means of strength and patience to finish this work

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Abstract

This is analytical Hospital based case control study conducted at Ibn Sina Hospital in Khartoum State aimed to assess the possible association of ABO blood group/Rhesus factor with upper gastrointestinal bleeding and potential risk factors in the period from March to June 2019. Two ml of remnant blood sample was used were collected from hundred endoscopically diagnosed UGIB patients and two ml of blood sample were collected from hundred healthy individuals.

A verbal consent had been taken from all the participants before the beginning of the study.Aquestionnaire was constructed to obtain some of the participants characteristics. ABO blood group and Rhesus factor were determined by the slide method . The obtained data were analyzed by Chi Square test and One Way Anova test using Statistical Package For Social Sciences (SPSS) version(20).Males represent 78% of the UGIB patients while females were 22%. The age range of the UGIB patients was (18-90) years, the highest percentage (40%) of GIB was found in patients aged (41-60) years old and the least percentage (27%) was found in patients aged more than 60 years. The highest percentage of UGIB occurrence (66%) was found in Gezira State and the least percentage (3%) was in North Sudan.The order of ABO blood group distribution in the patient was (O>B>A>AB) which is different from that of the control group (O>A>B>AB). ABO blood group occurrence in patients and control group was:(O 59% vs 50%),(B 20% vs 17%), (A 16% vs 26%), (AB 5% vs 7%).No association was found between ABO blood group and UGIB (P> 0.05). Blood group Rh +ve in the patients and control group are 94% vs 95% . Blood group Rh-ve in patients and control group were 6% vs 5%. No association was observed between Rhesus blood group and UGIB (P> 0.05). The endoscopic findings were oesophageal varices (57),peptic ulcer (34) and fundal varices(9). The highest frequency of all the endoscopic findings (59) was found in blood group O.There was a statistically significant association between UGIB and *H.pylori* infection (P.value 0.05) , use of NSAID (P.value 0.00),spicy food(P.value 0.002) and toombak dipping (P.value0.01).There is no significan association (P≤0.29), (P≤0.56), (P≤0.10), (P≤0.61),(P≤0.13) between endoscopic finding and bilharzias,coffee consumption ,tea consumption,alcohol consumption,cigarete smoking respectively.

The most common clinical outcome was hematemesis and melena (61%)and its highest frequency was (35) in blood group O patients.

المستخلص

هذه دراسة تحليلة للحالات والشواهد مستندة إلى مستشفى اجريت في مستشفى ابن سينا بولاية الخرطوم لتقييم الارتباط المحتمل بين فصيلة الدم ABO و العامل الريصي ونزف الجهاز الهضمي العلوي و وعوا مل الخطر المحتملة خلال الفترة من مارس إلى يونيو 2019، تم استعمال 2مل من عينة الدم المتبقية التي تم جمعها من مائة مريض بنزيف الجهاز الهضمي العلوي الذين شخصوا بالتنظير الداخلي وتم جمع 2مل من عينة الدم من مائة فرد سليم.

تم إنشاء استبيان للحصول على بعض خصائص المشاركين. تم تحديد فصيلة الدم ABO و العامل الريصي بطريقة الشريحة. حللت البيانات التي تم الحصول عليها عن طريق اختبار مربع كاي واختبار ون وي انوفا باستخدام برنامج الحزمة الإحصائية للعلوم الاجتماعية إصدار (20)

يمثل الذكور 78 ٪ من مرضى نزيف الجهاز الهضمي العلوي بينما كانت الإناث 22 ٪. كان النطاق العمري لمرضى نزيف الجهاز الهضمي العلوي (18-90) عامًا ، وكانت أعلى نسبة (40٪) من نزيف الجهاز الهضمي العلوي في المرضى الذين تتراوح أعمارهم بين (41-60) عامًا وأقل نسبة (27٪) في المرضى الأكبر من 60 سنة. أعلى نسبة حدوث نزيف الجهاز الهضمي العلوي (66٪) وجدت في ولاية الجزيرة وأقل نسبة (3٪) كانت في شمال السودان.

كان ترتيب توزيع فصيلة الدم / ABO في المرضى (AB<A<B<O) والذي يختلف عن ترتيب مجموعة التحكم (AB<B<A<O). كان حدوث فصيلة الدم ABO في المرضى ومجموعه التحكم: (59 ٪ O مقابل 50٪) ، (20٪ B مقابل 17٪) ، (16٪ A مقابل 26٪) ، (5٪ AB مقابل 7٪). لم يوجد ارتباط بين فصيلة الدم ABO و نزيف الجهاز الهضمي العلوي (ب > 0.05). فصيلة الدم Rh + ve في المرضى ومجموعة التحكم هي 94٪ مقابل 95٪. كانت فصيلة الدم Rh-ve في المرضى والمجموعة الضابطة 6٪ مقابل 5٪. لم يلاحظ أي ارتباط بين العامل الريصي ونزف الجهاز الهضمي العلوي (ب > 0.05).

كانت النتائج بالمنظار هي دوالي المريء (57) ، القرحة الهضمية (34) ودوالي قاع المعدة (9). تم العثور على أعلى معدل تكرار لجميع نتائج المنظار الداخلي (59) في فصيلة الدم O

هناك علاقة ذات دلالة إحصائية بين نزف الجهاز الهضمي العلوي و: عدوى الحلزونية البوابية (ب 0.05) ، واستخدام مضادات الالتهاب غير الستيروئيدية (ب 0.00) ، والأطعمة الحارة (ب 002. 0) والتومباك (ب 1 0. 0). لم يوجد ارتباط معنوي (ب ≥ 29. 0) ، (ب ≥56. 0) ، (ب ≥10. 0) ،(ب ≥61 . 0) ، (ب ≥ 13. 0) بين نتائج البحث بالمنظار والبلهارسيا ، استهلاك القهوة ، استهلاك الشاي ، استهلاك الكحول ، تدخين السجائر على التوالي.

كانت النتيجة السريرية الأكثر شيوعًا هي القيء الدموي والبراز الدموي الاسود (61٪) وكانت أعلى نسبة حدوث لها في فصيلة الدم O (35).

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List of Abbreviations

Abbreviations	Full name
AT	A glycosyltransferases
ALGIB	Acute lower gastrointestinal bleeding
BT	B glycosyltransferases
CDNA	Complementary DNA
CVD	Cardiovascular disease
DNA	Deoxyribonucleic acid
EV	Esophageal varices
FMF	Familial mediterranean fever
GI	Gastrointestinal
GV	Gastric varices
Hb	Hemoglobin
IHD	Ischemic heart disease
LGIB	Lower gastrointestinal bleeding
mRNA	Messenger RNA
NSAID	Non steroidal anti inflammatory drugs
OGD	Oesophago-gastroduodenoscopy
PH	Portal hypertension
RBCs	Red blood cells
Rh	Rhesus
SJS	Sjogrens syndrome
SLE	Systemic lupus erythematosus
SSC	Systemic sclerosis
UGI	Upper gastrointestinal
UGIB	Upper gastrointestinal bleeding
USA	United states of America

CHAPTER I

INTRODUCTIION

Chapter one

1.1 Introduction

ABO blood group system was first discovered in 1900 by german scientist Landsteiner ,who demonstrated that people could be divided into three groups (A,B and O) based on the presence or absence of an inherited antigenic substance on the surface of the red blood cells that can be determined by specific antibodies, later the fourth group (AB) was detected, the ABO and RhD are the two most significant blood group systems in transfusion medicine, These blood groups are being tested for all healthy blood donors as well as all patients prior to blood transfusion to ensure that the patients are given the right blood for transfusion (Yousuf , *et. al*., 2018)**.** It was documented that there is an association between ABO/Rh blood group and different types of diseases viz, blood group A was associated with head , neck and gastric cancers and blood groups B and AB with tuberculosis and blood group O with pancreatic cancer (Teshome, *et al*., 2019).

UGIB was defined as bleeding proximal to the ligament of treitz, the incidence of UGIB is approximately 100 cases per 100,000 populations per year (Fallah, *et al*, 2000).

Gastrointestinal bleeding is a very widespread condition at all ages, with high rates of morbidity and mortality, mainly in case of acute presentation(Federica, *et al* ., 2018). The visiting of emergency room was dramatically increased around the world by upper and lower gastrointestinal bleeding, gastrointestinal bleeding is expected to have an annual incidence of 48-160 per every 100,000 people, the most common causes of upper and lower GI bleeding include peptic ulcer disease ,varices and peri-anal disorders (that is hemorrhoids and fissures), moreover, *Helicobacter Pylori* infection and NSAIDs use are known to play a significant role in the incidence of UGI bleeding, it seems that the presence of etiologic factors along with genetic susceptibilities is the main predictive factors in patients with UGI bleeding(Bahardoust, *et. al*., 2018).

Abdulridha,(2013) have shown that ABO blood group is associated with UGIB; especially blood group O ,which is considered an additional risk factor to the known etiologic factors, risk and development of UGI bleeding were suggested to be affected by ABO blood group antigens such as a genetic factor(Bahardoust, *et al*., 2018).

1.2 Rationale

UGIB is becoming a health problem with an economical impact on the economy.The mortality rate of UGIB in the Sudan was 3.8% according to a study done at Ibn-Sina Hospital (Salih, *etal* .,2009). *H.pylori* is an etiologic factor for UGIB. In Sudan the prevalence of *H.pylori* infection was estimated to be between 65.8% and 80% . The overall incidence of acute upper GIB has been estimated to be 50 to 100 per 100000 persons per year. Many previous studies abroad have proven the association of ABO/Rh blood group and UGI bleeding. In Sudan there is a paucity of data concerning the association of ABO/Rh blood group and risk, severity and development of UGI bleeding. So this study was undertaken to assess whether ABO/Rh blood group can be of value for early diagnosis and prognosis of UGIB.

1.3 Objectives

1.3.1 General objective:

To study the possible association between ABO blood group /Rhesus factor and upper gastrointestinal bleeding at Ibn Sina Hospital.

1.3.2 Specific objective:

1. To determine the frequency of ABO Blood Group in UGI bleeding patients.

2. To investigate whether of *Helicobacter pylori* ,NSAID, toombak dipping, cigarette smoking , alcohol consumption, Bilhrazia, coffee drinking, tea drinking and spicy food are potential risk factors for UGI bleeding .

3. To determine the endoscopic outcomes of UGIB.

CHAPTER II
LITERATURE REVIEW

Chapter Tow

Literature Review

2.1 Blood groups system

Blood group refers to the entire blood group system comprising red blood cell antigens whose specificity is controlled by a series of genes, blood type refers to a specific pattern of reaction to testing antisera within a given system (Mitra,*et al*.,2014).

2.1.1 ABO blood Group System

More than 20 distinct blood group systems have been identified but the ABO and Rhesus blood groups remain clinically the most important, blood group or blood type is based on the presence or absence of inherited antigenic substance on the surface of red blood cells that can be determined by specific antibodies ,based on the presence or absence of antigen ABO blood group there are two antigens A and B antigen and there are four blood group A,B ,AB and O, the distribution of ABO blood group is different among different ethnic groups, this system has strong antigens and had natural occurring antibodies that make intravascular hemolysis (Zaman, *et al*. , 2015). The first blood group is ABO blood group system and remain the most important system, the scientist Landsteiner mixed sera and RBCs from his colleagues ,and then agglutination was observed, he named the first two blood group antigens A and B, using alphabetical nomenclatures (Hillyer, *etal*.,2007). A blood group was also defined as an inherited character of the red cell surface, detected by a specific alloantibody, polymorphisms suspected of being present on the red cell surface, but only detected by DNA Sequencing (Daniels and Bromilow, 2007). The blood group found in red blood cells and tissues is controlled by specific gene known as H gene , red blood cell antigens are the basis of blood grouping, consist of proteins and carbohydrates attached to lipids or proteins,the most clinical significant lies in safety blood transfusions (Alanazi, *etal.,* 2018). The importance of blood group discovery lies in the transfusion of blood amongst different populations irrespective of their ethnic origin, in organ transplantation and in the development of legal medicine, genetic research and anthropology (Zaman, *et al*. , 2015).

Table (2.1) .The ABO blood group antigens.

ABO group	Antigens on red cells	Antibodies in serum	Genotype
A	A	Anti-B	A/A or A/O
B	B	Anti-A	B/B or B/O
AB	A and B	None	A/B
O	None	Anti-A,B	O/O

(Daniels, 2002).

2.1.1.1 Inheritance and Molecular Genetics of ABO blood group

Blood group antigens (A and B) are inherited as codominant autosomal fashion, epstein and Ottenberg were the first to report that ABO blood groups might be inherited in 1908, the first genetic blood group used in paternity testing and in forensic medicine is ABO blood group,unlike the majority of blood groups, the antigens of the six currently known carbohydrate systems are not coded by genes directly, instead, these blood group genes encode glycosyltransferases that in turn manufacture the oligosaccharide epitopes, the A and B antigens are made by A and B glycosyltransferase, respectively, the ABO gene is located on chromosome nine , like other blood group genes, the position of the ABO locus was known for many years before the gene was cloned, the genes encoding the A-synthesizing 3-α-N-acetylgalactosaminyltransferase and B-synthesizing 3-α-N-galactosaminyltransferase were cloned by Yamamoto and colleagues after purification and partial amino acid sequencing of A transferase from lung tissue, cDNA libraries obtained from human adenocarcinoma cell lines of different ABO types (Denomme, *et al*., 2009).

2.1.1.2 The synthesis of ABO antigens

The precursor of the A and B antigen is H substance, the biosynthetic pathways and the structurally related oligosaccharide antigen, the functional A and B alleles at the ABO genetic locus encode A and B glycosyltransferases which catalyze the last biosynthetic step to form A and B oligosaccharides, group A individuals have 1 or 2 A alleles encoding AT that synthesize A antigen, group B individuals have 1 or 2 B alleles encoding BT that synthesize B antigen, group AB individuals have A and B alleles and express both AT and BT, group O individuals have two non functional O alleles but no A or B allele, type O RBCs express H substance (Cid, *et al*.,2018).

2.1.2 Rhesus blood group system

After the ABO blood group system the Rh system is regarded as the second most important blood group system and consists of over 50 antigens, the main Rh antigens are D,C, c,E and e that involve most clinically significant transfusion complication ,the RBC surface of an individual may or may not have Rh factor that means the individual may be Rh-positive or Rh-negative (Mitra, *et al*.,2014) .The RhD protein expresses the D antigens,while the Rh CcEe protein carries either C or c antigens concerning the second extracellular loop together with E or e antigens involving the fourth extracellular loop on the same protein(Avent and Reid,2000). The Rh antigens are encoded by two homologous, closely linked, genes on the short arm of chromosome 1, RhD producing the D antigen, RhCE producing the Cc and Ee antigens, the first discovered and clinically most important antigen is D, Rh antigens are very essential for confirmation of proteins in the red blood cell membrane (Daniels, 2002) . The RhD was originally identified in Rhesus monkeys, Later the same antigen was discovered in human beings,the Rh negative blood type is moderately uncommon, representing less than 15% of the population,the so-called "natural" antibodies to Rh do not exist in humans, Rh+ cells infused into an Rh negative recipient can give rise to a strong antibody response, the Rh antigens are located only on red blood cells unlike the A and B antigens,therefore, while these antigens are important for blood transfusion, they do not normally play a role in organ transplantation(Teshome, *et al*.,2019). Over a period of time understanding on blood groups has evolved to encompass not only transfusion related problems but also specific disease association with RBC surface antigens (Mitra, *etal*.,2014). Rh antigens'roles for

RBCs are preventing aggregation and adhesion to endothelial cells, protecting against mechanical damage and pathogen invasion which makes them reasons for the association ABO blood group with diseases(Teshome, *et al* .,2019).

2.1.3 Association of ABO/Rh blood groups with some diseases

2.1.3.1 Diabetes Mellitus

Diabetes mellitus commonly known diabetes, as is a group of metabolic disorders with unknown underlying cause,there are common types of diabetes mellitus, insulin dependent diabetes associated with absolute insulin deficiency and external insulin should be administered to the patient and the second type is non- insulin dependent diabetes where there is resistance to the action of insulin , it is a very complicated disease and there are sevral factors that play very important role in the causes of disease such as environmental, genetic and immunological where the interaction occur between all these factor lead to diabetes (Albaroodi,*et al*.,2019). The morbidity and mortality is increased in un controlled diabetes mellitus patients,diabetes mellitus has a genetic problem and environmental factors play role in its genetic expression, as many other inherited traits, the blood groups also genetically predetermined and therefore have an association between the blood group and diabetes mellitus,the AB blood group is more common in diabetic subjects, followed blood group O and less common in blood groups A and B, the majority of diabetic subjects are Rh Negative and few are Rh positive , a lower percentage of Blood group A and B and a higher percentage of blood group AB in the diabetic group in comparison with normal controls and concluded that here is a positive association between Rh negative blood groups and diabetes (Waseem, *et al*., 2012).

2.1.3.2 Rheumatic diseases

Rheumatic disease are a group of systemic disorders with a chronic course and with an unknown etiopathogenesis,recent studies have concerned environmental factors and genetic background in the etiology of rheumatic diseases(Karadag, 2019).

Several genetic and environmental risk factors have been related to be associated with the incidence of rheumatic diseases, ABO blood groups was to be associated with the types of rheumatic diseases such as spondyloarthropathy ,vasculitis, undifferentiated connective tissue disease , behcet's diseases, familial mediterranean fever , systemic lupus erythematosus , systemic sclerosis , sjogren's syndrome , and rheumatoid arthritis , 42.5%

patients had blood group A type, 33.2% had O type, 15.4% had B type, and 8.9% had AB type, there was significant difference in the distribution of blood types in rheumatic diseases, while spondyloarthropathy, vasculitis, undifferentiated connective tissue disease , behcet's disease and rheumatoid arthritis were more common in the patients with the A blood type, FMF, SLE, SSc and SjS were more common in patients with O blood type (Cildag, *et al*.,2017).

2.1.3.3 Ischemic heart disease

Ischemic heart disease means that organ is not getting enough blood and oxygen, it is one of the most critical problems of the world, of the 16.7 million deaths from CVDs every year, 7.2 million are due to IHD, many reports have appeared shown an association of ABO blood groups with coronary heart disease and IHD, between different categories of IHD, the frequencies of stable angina and acute myocardial infarction were higher in AB blood group ,the order of percentage of ABO blood groups among IHD patients was found to be in the order A>B>O>AB and the order of the percentage for Rhesus factor in those patients was Rh+ve > Rh –ve, It was found that the prevalence of blood group AB was high among IHD group (34%), shows that there is a strong relation of blood group A with IHD (Sharif, *et al*. , 2014).

2.1.3.4 Hypertension

Hypertension also known as high blood pressure, it is a major health problem in the world it has no early specific signs and symptoms , so most of the people have hypertension without knowing it, hypertension is a situation of sustained increase in blood pressure and the systolic blood pressure is >120 mm and diastolic is >80 mm, prehypertension (high normal) systolic blood pressure is 120-139 mm and diastolic is 80-89 mm, several factors like obesity,high cholesterol level, sedentary life style, high fat and low fibers diet it main causes of hypertension (Rai and Sapkota, 2017).The individuals with B blood group are more susceptible to hypertension as compared to blood group O and A; whereas AB blood group had less chance of getting hypertension in males and in females (Sadiq, *et al*. , 2017).

2.1.3.5 Malaria

Approximately 694 million people in Africa are to be at risk of malaria, which represents 21% of the global population at risk, malaria occurred more frequently in ABO blood

group O individuals and non-blood group O cases were at increased risk of severe malaria, the frequency of ABO blood group distribution different in a similar way to other countries, with blood group O most common, followed by A, B and then AB (Bomou and Sevidzem, 2016). A study conducted in Bafeno area located in southern Ethiopia found that individuals of blood groups A, B and AB are more susceptible to *P. falciparum* infection as compared with individuals of blood group O (Zerihun, *etal*., 2011)

2.1.3.6 Gastrointestinal tract bleeding

The gastrointestinal tract is also called the digestive system, the length of this system is approximately 10 metres,beginning with the mouth and ending at the anus, it consists of the digestive system structures and the accessory organs, the gastrointestinal system structures include: mouth, pharynx, oesophagus, stomach, small intestine, large intestine, anus,the accessory organs make a contribution to the function of the gastrointestinal tract, these organs are:salivary glands,liver,gall bladder, pancreas,the gastrointestinal tract divided into two parts: the upper and lower gastrointestinal tract (Peate,2018).

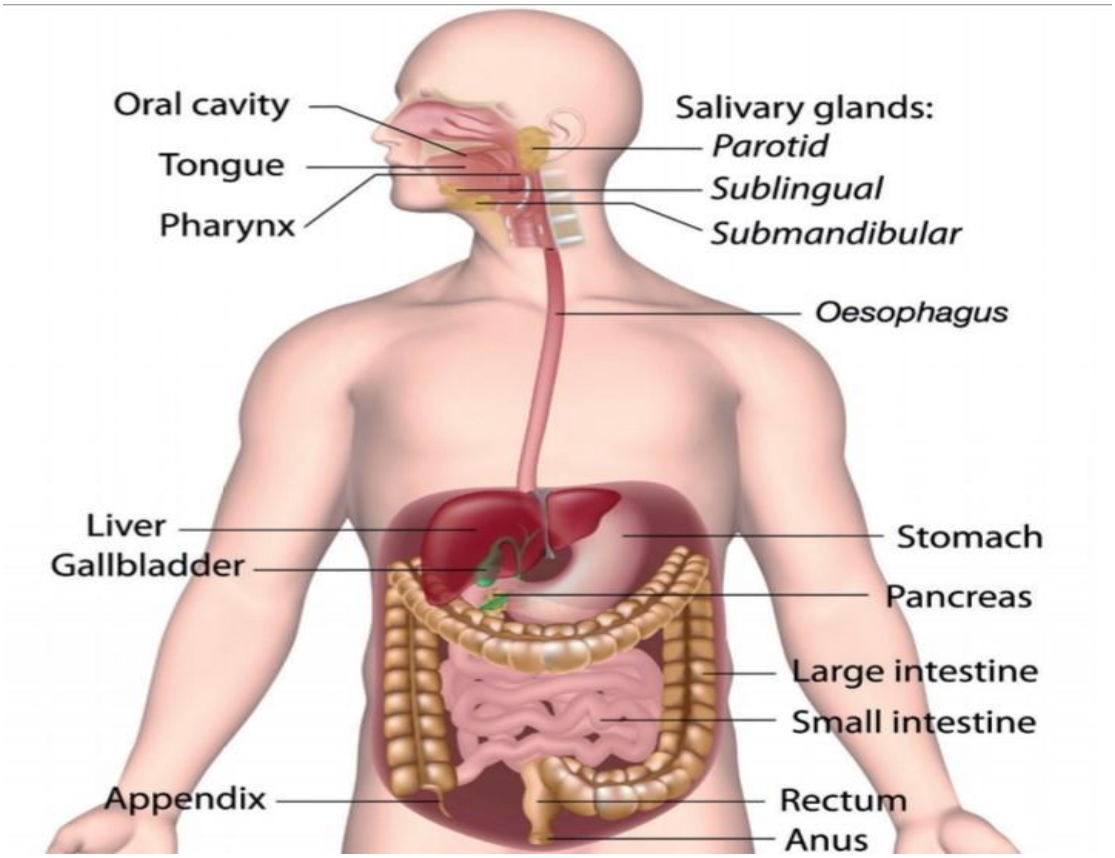

Figure 2.1 The gastorintestinal tract (Peate, 2018)

2.1.3.6.1 Gastrointestinal bleeding

Gastrointestinal bleeding is a very widespread condition at all ages, with high rates of morbidity and mortality mainly in case of acute presentation (Federica, *et al* ., 2018).
Gastrointestinal bleeding is a common reason for acute hospitalization, with estimated rates of hospitalization at 375 per 100,000 per year in the united states,gastrointestinal bleeding is not a specific disease but rather a diverse set of conditions that lead to the clinical manifestations associated with bleeding into the gastrointestinal tract, gastrointestinal bleeding may occur at the upper or lower gastrointestinal tract ,the differentiation between upper and lower GIB is one of the most commonly used in organizing frameworks in gastrointestinal bleeding ,there are important differences in the etiologies between the tow sources, for example,acid related disease is a common etiology in UGIB but dose not occur in LGIB (Whelan, *et al*.,2010).
Bahardoust, *et. al*., (2018) investigated the possible relationship between ABO/Rh blood group and development of GI bleeding, they found patients with O blood group had a higher rate for the development of GI bleeding than the other blood groups, also they observed that risk and development of GI bleeding might be affected by ABO blood group antigens which suggests that the ABO/Rh blood group act as genetic predisposing factor to develop the GIB.

The optimal management of acute GIB requires a timely overview of vital signs and clinical presentation to stabilize the patient if necessary and set up the most adequate diagnostic and therapeutic approach based on the suspected etiology, endoscopy is considered most important role in both in diagnosis and treatment of acute GIB (Federica, *et al* ., 2018).

2.1.3.6.1.1 Upper gastrointestinal bleeding

The upper gastrointestinal tract is consist of the oral cavity and salivary glands, esophagus,stomach, and small intestine(duodenum, jejunum and ileum), the tract is essentially a smooth muscle enveloped tube with an innermost mucosa(barrier epithelium, lamina propria and muscularis mucosae), submucosa, tunica muscularis and variable serosa or adventitia, the functions of the upper GI tract include transport of the swallowed food bolus, enzymatic digestion and absorption of nutrients, in addition to protective barrier function against the external environment (Treuting, *et al*., 2018).Upper

gastrointestinal bleeding is very poorly described at primary health system, the most important aspect of control of GI bleeding is to locate the site and cause of bleeding, bleeding from the upper GI tract is around five times more common in comparison with lower GI tract bleeding, and males are affected twice as much as compared to females, clinically, upper GI bleeding often presents as hematemesis or melena, fresh blood per rectum usually indicates lower GI source of bleeding and massive upper GI bleeding in 15% of cases and is associated with worse prognosis, 80% of the GI bleedings stop spontaneously; only 20% continue or recur, diagnostic accuracy of endoscopy is 80-95% for upper GI bleeding, National Institute of Health and American Society of Gastrointestinal and Endoscopic surgeons preferred urgent endoscopy in a patient who is actively bleeding or has a high risk for re-bleeding (Rathod, *et al*., 2011).

2.1.3.6.1.1.1 Epidemiology of upper gastrointestinal bleeding

Vanleerdam, (2008) studied the epidemiology of upper gastrointestinal bleeding and found that upper gastrointestinal bleeding is an important crisis situation, population-based epidemiology data are important to obtain insight in the actual healthcare problem,several surveys focusing on peptic ulcer disease showed a significant decrease in admission and mortality of peptic ulcer disease, some more recent epidemiological surveys show a decrease in incidence of all cause upper gastrointestinal bleeding, the incidence of peptic ulcer bleeding remained stable, peptic ulcer bleeding is the most common cause of upper gastrointestinal bleeding, responsible for about 50% of all cases, followed by oesophagitis and erosive disease, variceal bleeding is the cause of bleeding in cirrhotic patients in 50–60%, rebleeding in upper gastrointestinal bleeding occurs in 7–16% after endoscopic therapy, rebleeding is especially high in variceal bleeding and peptic ulcer bleeding, mortality ranges between 3 and 14% and did not change in the past 10 years, mortality is increasing with increasing age and is significantly high in patients who are already admitted in hospital for co-morbidity, risk factors for peptic ulcer bleeding are NSAIDs use and *H. pylori* infection, *H. pylori* infection is found in about 50% of peptic ulcer bleeding patients so it is very essential verified for in all ulcer patients. Individual who infected with *H.pylori* has an estimated lifetime of 10-20% for development of peptic ulcer disease which is at least 3-4 fold higher than in non-infected individual,*H.pylori* can be detect in 90-100% of duodenal ulcer patients and in 60-100% of gastric ulcer patients (Mohammed, *et al*.,2015).

2.1.3.6.1.1.2 Causes of upper GI bleeding

2.1.3.6.1.1.2.1 Esophageal Varices

Normal portal pressure varies between 4–8 mm, in case of an obstruction, when natural connections needed to maintain normal flow from the celiac system to the inferiorvena cava become inadequate, the portal pressure increases greatly,the portal hypertensive classified into: Presinusoidal obstruction: **a)** extrahepatic (usually portal vein obstruction) and **b)** intrahepatic (such as schistosomatosis, bilharziosis), Sinusoidal obstruction**:** Wilson's disease and hepatic cirrhosis,extrasinusoidal obstruction: **a)** intrahepatic (postalcoholiccirrhosis), **b)**extrahepatic (Budd−Chiari syndrome), **c)** caused by cardiac dysfunctions (pericarditis,rightventricular insufficiency), **d)** caused by increased blood flow (arteriovenous fistulas), the etiology of PH among adults in Europe and in the USA is dominated by chronic liver diseases, when the PH present for a prolonged period of time it leads to the development of an extensive network of portosystemic collaterals, one of these collateral systems is through the vessels in the esophageal mucosa that collects blood from the left gastric vein,the blood is later drained to the azygos and hemiazygos veins and later to the superior vena cava,the submucosal vessels of the esophagus are surrounded by a small amount of perivascular tissue and do not have valves, these factors make themprone to increasing blood pressure, which leads to their di latation, called esophageal varices, varices can usually be found in the lower parts of the esophagus, just above the cardia, but may reach to the aortic arch (Bochnia, *et al*., 2008).

Esophageal variceal bleeding is the major complication of portal hypertensive in adults experiencing liver cirrhosis, bleeding responsible for 14% to 33% of deaths until 6 weeks after the first bleeding episode,the prevalence of esophageal varices(EV) in adults with liver cirrhosis ranges from 30% to 70% ,the risk of developing EV after diagnosis is 9% / year (Alcantara, *et al*., 2013).

Mortality was highest in those with variceal bleeding (Hearnshaw, *et al*., 2011).

2.1.3.6.1.1.2.2 Peptic ulcer

Kuna, *et. al*, (2019) study peptic ulcer and found that the peptic ulcer is a chronic disease affecting up to 10% of the worlds population, the formation of peptic ulcers depends on the presence of gastric juice PH and the decrease in mucosal defenses, NSAIDs and *H.pylori* infection are the two main factors disturbing the mucosal resistance to injury,peptic ulcer is an acid-induced lesion of the digestive tract that is usually located in the stomach or proximal duodenum, gastric and duodenal ulcers are two types of peptic

ulcers, a peptic ulcer is a sore that's inside the stomach lining is agastric ulcer or the upper part of the small intestine is a duodenal ulcer, peptic ulcer is characterized by denuded mucosa with the defect extending into the submucosa or muscularis propria, mucosal disruption in patients with the acid peptic disease is considered to be a result of a hypersecretory acidic environment together with dietary factors or stress,risk factors for developing peptic ulcer include *H.Pylori* infection, alcohol and tobacco consumption,non-steroidal anti-inflammatory drugs use,and zollinger-ellison syndrome, the main risk factors for both gastric and duodenal ulcers are *H.pylori* infection and NSAID use ,only a small proportion of people affected with *H.Pylori* or using NSAIDs develop peptic ulcer disease,meaning that individual susceptibility is important in the beginning of mucosal damage,functional polymorphisms in different cytokine genes are associated with peptic ulcers,for example, polymorphisms of interleukin 1 beta affect mucosal interleukin 1β production , causing *H.Pylori*-associated gastroduodenal disease.

2.1.3.6.1.1.2.3 Esophagitis

Esophagitis refers to an inflammatory condition of the esophageal mucosa, usually related with characteristic symptoms,such as heartburn,chest pain and dysphagia, gastroesophageal reflux disease is the main cause of esophagitis, it affects about 20% of the population in western countries and represents one of the most common conditions which gastroenterologists and general practitioners have to deal with,in fact the esophageal wall has low defense against gastric acid injury that can induce either erosive or non-erosive esophagitis,over the years esophagitis was considered almost synonymous with acid reflux, which lead to consequent therapeutic approaches mainly aimed at reducing gastric secretion(Grossi, *et al*., 2017).

2.1.3.6.1.1.2.4 Gastric Varices

Gastric varices are the most common cause of upper gastrointestinal bleeding in patients with portal hypertension after esophageal varices and commonly have more severe bleeding than EV, in the United States the majority of GV patients have underlying portal hypertension rather than splenic vein thrombosis,especially problematic are varices that occur in the fundal area of the stomach ,fundal varices may present as serpiginous obviously vascular structures or sometimes as polypoid masses occasionally resembling a cluster of grapes (Alosaimi and Caldwell,2011).

2.1.4 Association of ABO/Rh blood groups with upper gastrointestinal bleeding

There are many studies which have demonstrated association between ABO and Rh blood group with upper gastrointestinal bleeding, there is a positive correlation between group O and upper gastrointestinal bleeding and that blood group O have higher frequency in UGIB patients (Bayan, *et. al*., 2009). A study conducted in Tehran (Iran) found that blood group O was significantly more common in patients with GI bleeding and especially UGIB patients and suggested that it is a prognostic genetic risk factor for bleeding tendency in these patients, especially in those with upper GI bleeding (Bahardoust, *et. al*., 2018). In Irag Abdulridha, (2013) investigated the possible association between peptic ulcer disease and ABO/blood group and recorded a significant higher percentage of patients with both gastric and duodenal ulcer disease are those holding blood group O+ compared to other blood group phenotypes (57.5%) and this may consider that ABO/Rh blood group (mainly blood group O+) an additional risk factor for peptic ulcer to the other known factors.

2.1.3.6.1.2 Lower gastrointestinal bleeding

Lower gastrointestinal bleeding (LGIB) is defined as bleeding which originates from a site distal to the ligament of treitz and is usually suspected when patients present with haematochezia,or maroon stools per rectum,although some researchers defined LGIB as bleeding from a colonic source only and any bleeding from the small bowel has been shown to be a distinct entity , LGIB can present as an acute and life-threatening event or as chronic bleeding, which might evident as iron-deficiency anaemia and faecal occult blood,acute lower gastrointestinal bleeding (ALGIB) is a frequent gastrointestinal cause of hospital admission mainly in the elderly, and its incidence seems to be rising, in 15% of cases ALGIB and the incidence increases with age and comorbidity, and the discovery of the origin of bleeding may be difficult ,there are several factors which might contribute to increased mortality like a severe course of bleeding and repeated bleeding as well as advanced age,intestinal ischaemia, and haemodynamic instability, lower gastrointestinal bleeding is common among older patients and those with comorbidity, the common causes are diverticular disease, angiodysplasias, neoplasms,colitis, ischaemia and anorectal disorders(Arabi, *et al*., 2018). Lower gastrointestinal bleeding (LGIB) is a common clinical problem representing 20 to 30% of patients presenting with gastrointestinal bleeding (Clerc, *et al*., 2017).

CHAPTER III

MATERIALS AND METHODS

Chapter three

Materials and methods

3.1 Study design

This was an analytical Hospital based case control study.

3.2 Study area

The study was conducted in Ibn Sina Hospital - Khartoum State.

3.3 Study duration

during the period from March to June 2019.

3.4 Study Population

Two Hundred participants were enrolled in this study . 100 patients were diagnosed with upper gastrointestinal bleeding (OGD endoscope) were as case group and 100 clinically healthy volunteers matched with the case group in age and gender were control group.

3.5 Inclusion Criteria

Endoscopically diagnosed upper gastrointestinal bleeding patients who attended Ibn Sina Hospital during the study period were enrolled in this study.

3.6 Exclusion criteria

Patients with different malignancies, autoimmune disease and bone marrow transplant.

3.7 Ethical consideration

The study was approved by the Ethical Committee of Medical Laboratory Science College SUST. The consent of the participants was taken after they were informed verbally about the result, Its benefits and method of sample collection. The participants were assured that the results will be kept confidential and will not be used for any other purpose than of this study .

3.8 Sampling

Non probability convenience sampling technique was used**.**

2 ml of EDTA remnant blood was used.

3.9 Data Collection

The patients were informed about the study purpose and were assured of. The confidentiality of the obtained data. Aquestionnaire was designed and the patients were interviewed to obtain:

a) The demographic data of the patients such as gender, age, education level, residence area,occupation and marital status.
b) Exposure to some potential risk factors such as *Helicobacter pylori* ,NSAID, toombak dipping, cigarette smoking , alcohol consumption, Bilhrazia, coffee drinking, tea drinking or spicy food.

3.10 Laboratory analysis:

3.10.1 ABO and Rh Blood Groups

ABO slide agglutination test was adopted as describe by Dietze, *et. al*., (1995).

3.10.1.1 Principle of Direct Slide Method

The principle is based on specific agglutination reaction between antigen on red blood cells and known antibodies (anti-A , anti-B and anti-D) (Tiwari, *et. al*., 2018).

3.10.1.2 Method

With a grease pencil two circle were drawn on a clean dry slide, and labeled one (A) and another (B), and on another slide a circle was drawn and labeled (D), a drop of blood was placed on each circle, then to circle (A) drop of anti-serum A was added, drop of anti-serum B also was added to circle (B), and drop of anti-serum D was added to circle (D). Then each suspension was mixed with a different wooden stick (Dietze, *et al*., 1995).

3.10.1.3 Interpretation of ABO blood groups

Dietze, *et. al*., (1995) was described the interpretation of ABO blood group is as follows:

- Agglutination on (A) circle and no agglutination on (B) circle mean the ABO blood group is A.

- Agglutination on (B) circle and no agglutination on (A) circle mean the ABO blood group is B.

- Agglutination on Both (A) circle and (B) circle mean the ABO blood group is AB.

- No agglutination on both (A) circle and (B) circle mean the ABO blood group is O.

- Agglutination on (D) circle means the Rhesus factor (Rh-factor) is positive (+ve).

- No agglutination on (D) circle must be followed by Due technique then if no agglutination in test tube that means the Rhesus factor (Rh-factor) is negative (-ve).

3.10.1.4 The weak D testing (Du) (**Confirmatory test**).

Every Rh negative sample was confirmed by Du method

3.10.1.4.1 Principle and Procedure

Some red cells possess the D antigen but it is expressed so weakly that the cells are not agglutinated directly by anti-D sera, an indirect antiglobulin test is necessary to identify patients with the weak D, prepare a washed, 3% suspension of participants cells, and add the anti D, record the D spin results.If the Rh test is negative, continue and incubate both tubes at 37C for 15 to 30 minutes. Then centrifuge and read for agglutination ,if the Rh test is negative continue and wash both tube 3-4 times with saline to remove any unbound globulins and then add one drop coombs to each tube and centrifuge , after centrifuge resuspend gently and examine for agglutination. Confirm all negative results by adding one drop coombs control cells(sensitized cells) to all tubes showing no agglutination and centrifuge 15-30 seconds and then gently resuspend and examine for agglutination. Agglutination should be present in this step or the test is invalid (Raman, *et al*., 2008).

3.10.1.5 Quality control of antisera

The anti-A should be tested against group O red blood cells as well as group A red cells and group B red cells to demonstrate reactivity and specificity; anti-A agglutinates only group A red blood cells and does not agglutinate group O or group B red blood cells. And also anti- B slould be tested against group O red blood cells as well as group B red blood cells and group A red cells to demonstrate reactivity and specificity; anti-B agglutinates only group B red blood cells and does not agglutinate group O or group A red blood cell. O-positive cells(positive control) and O-negative cells (Negative control) for antisera D (https://www.pathlabtalk.com,2012).

3.11 Data analysis

The data was described as percent and frequency. Pie chart was used to display demographic characteristics of the studied upper gastrointestinal bleeding patients. Chi square was used to determine the association of ABO/Rh blood group with UGIB patients.Association of ABO blood group with endoscopic findings,clinical outcomes was investigated use Chi square, association of endoscopic findings with possible risk factors also was investigated use Chi square. One way anova test was used to compare between laboratory and clinical finding of UGIB patients according to ABO blood group.The data was analyzed using statistical package for social sciences (SPSS version 20).

CHAPTER IV

RESULTS

Chapter four

Results

4.1. Characteristic of the studied patients

The demographic characteristics of 100 upper gastrointestinal bleeding patients attended Ibn Sina Hospital (in Khartoum) were displayed in figures (4.1, 4.2, 4.3, 4.4, 4.5 and 4.6).

Males represent 78% of the studied population (Figure 4.1).

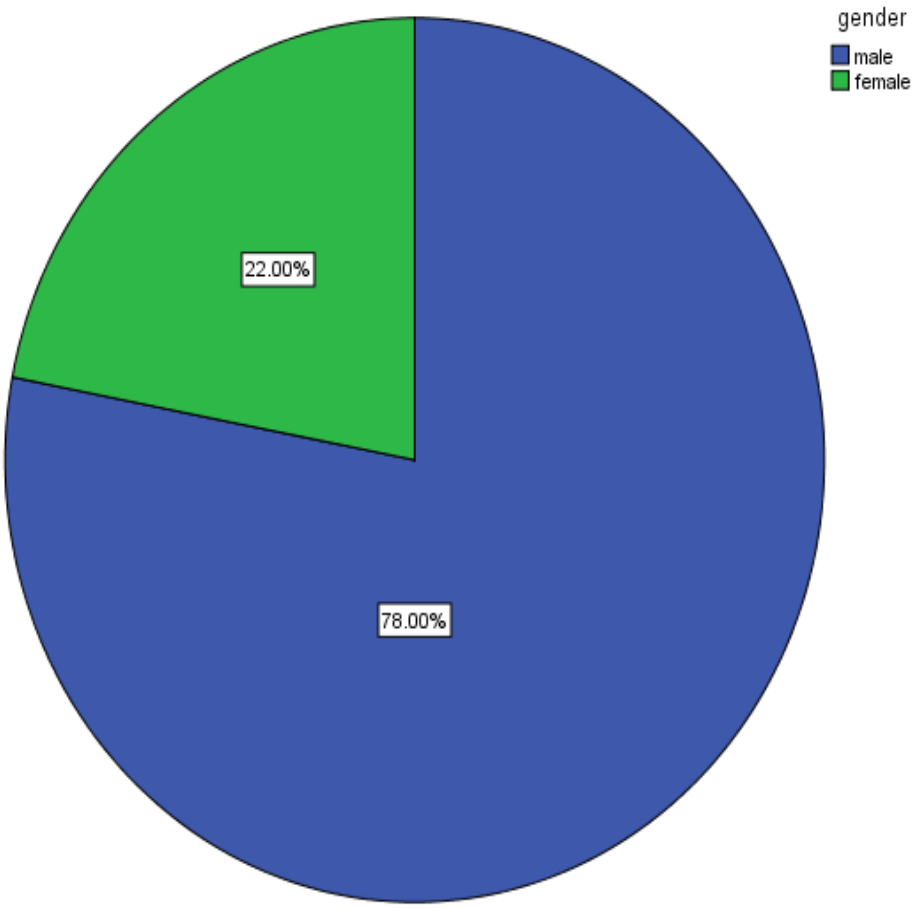

Figure (4.1) Distribution of the UGIB patients according to gender

The least occurrence of UGI bleeding (27%) was found among those aged more than sixty years and the highest rate (40%) was found in those aged from forty one to sixty(Figure 4.2).

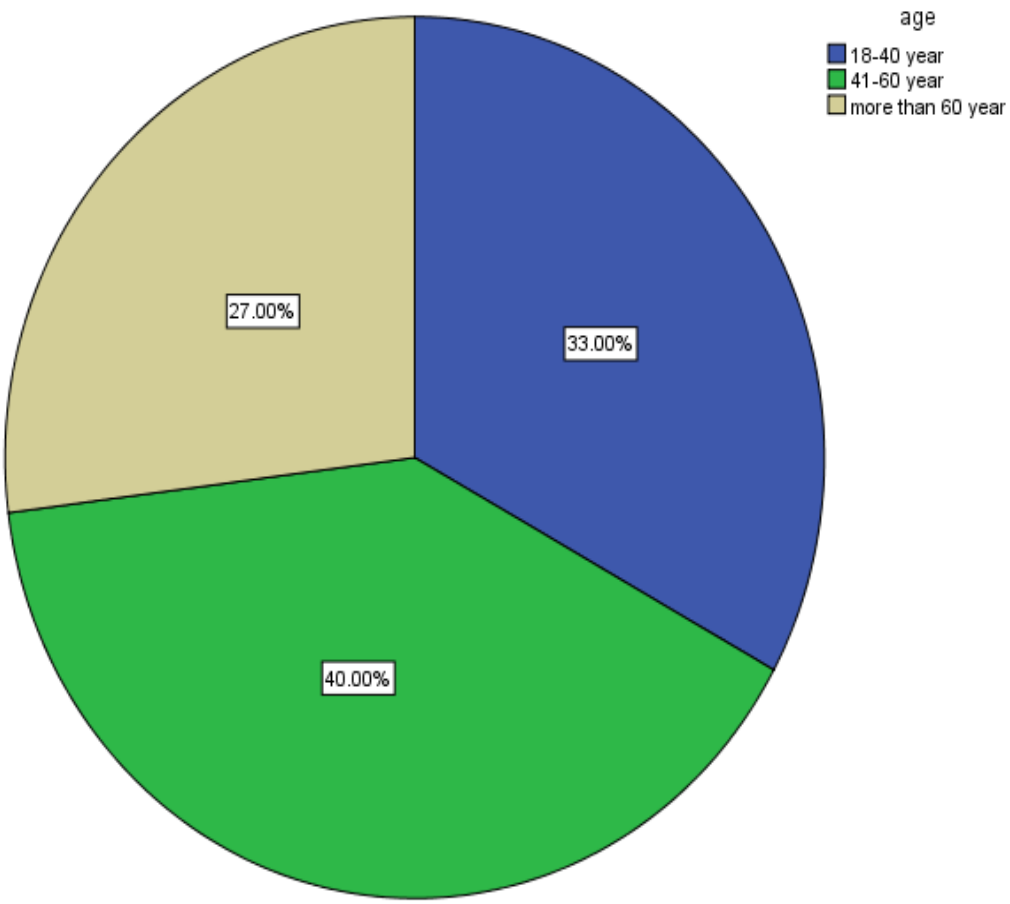

Figure (4.2) Distribution of the UGIB patients according to age

Most of the patients (66%) are resident at Gezira State while patients from North Sudan represent lowest percentage (3%) of the studied patients(Figure 4.3).

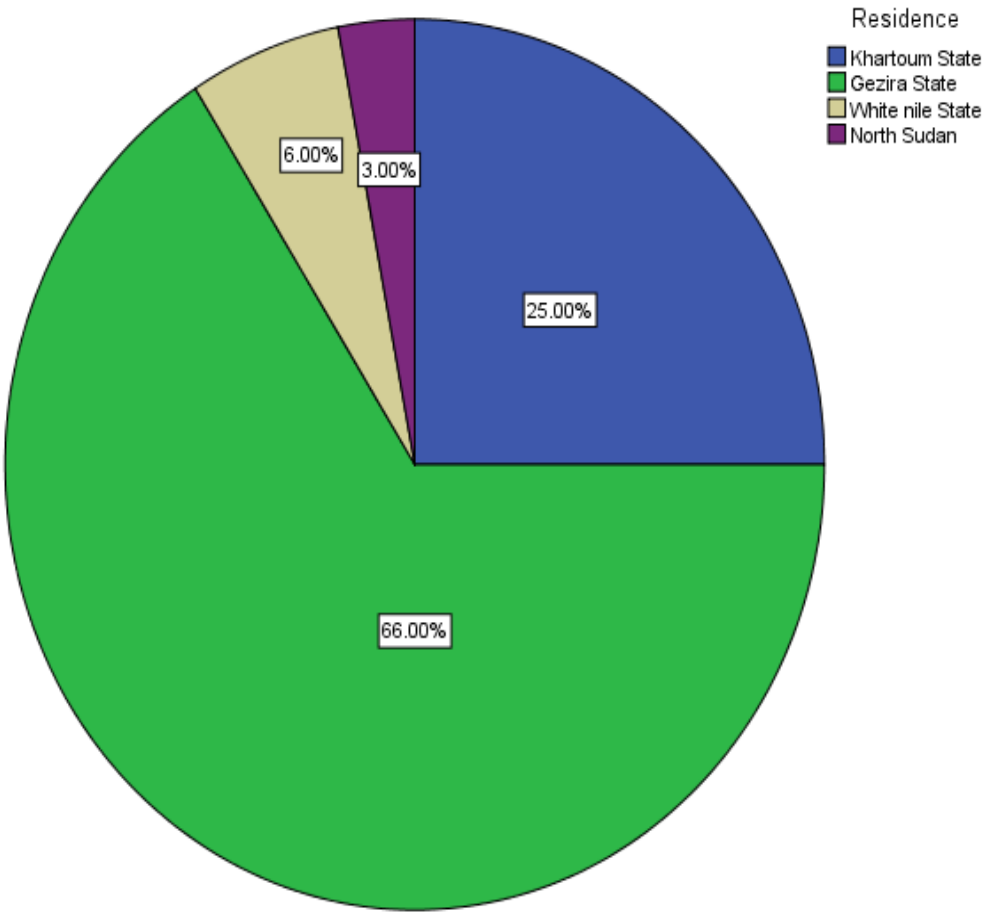

Figure (4.3) Distribution of the UGIB patients according to residence area

The majority of the population were married (87%) and only (13%) were single (Figure 4.4) .

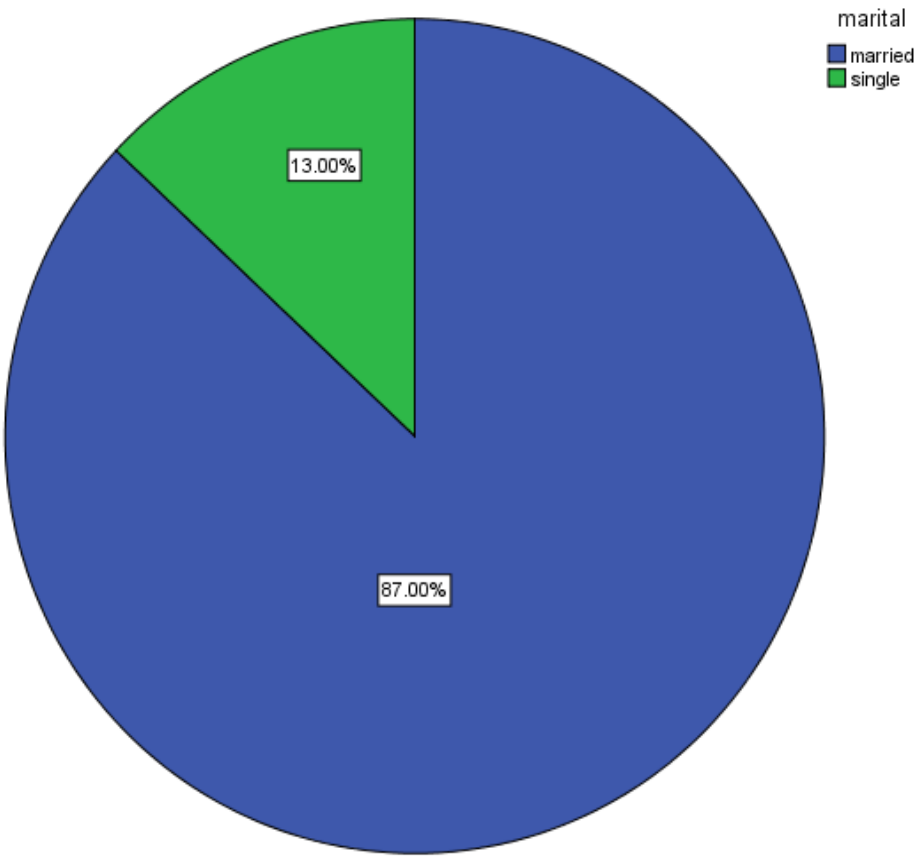

Figure (4.4) Distribution of the UGIB patients according to marital status

The primary education level among the studied population was found to be (64%) and only (3%) had higher education level(Figure 4.5).

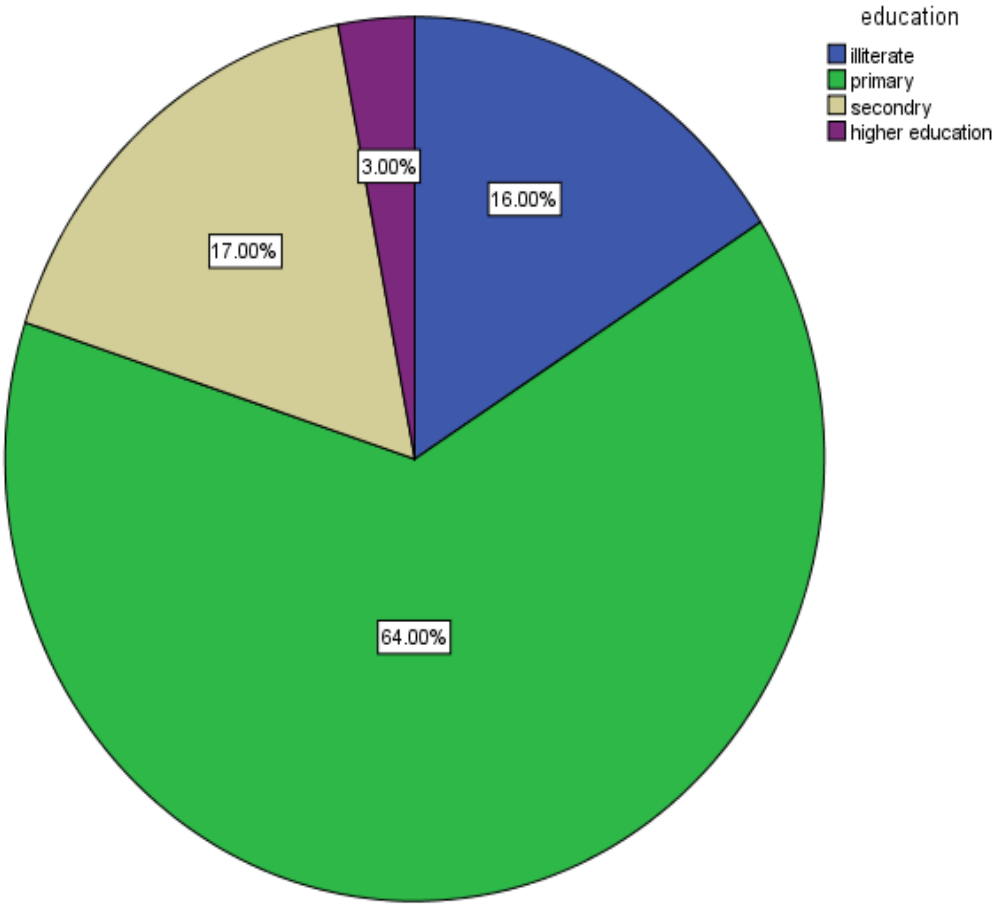

Figure (4.5) Distribution of the UGIB patients according to education level

Among the upper GI bleeding patients there is (3%) teacher , (18%) unemployed , (25%) free business and the majority of the patients are farmers (54%)(Figure 4.6).

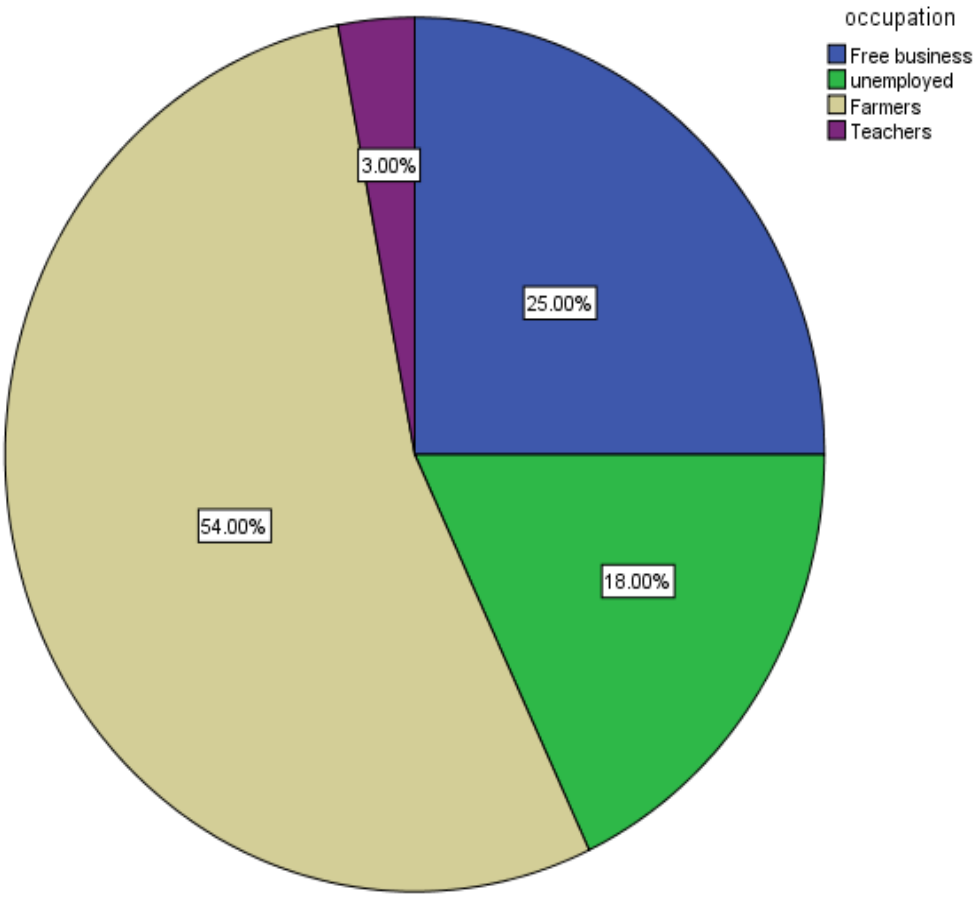

Figure (4.6) Distribution of the UGIB patients according to occupation

4.2 Distribution of UGIB patients according to some potential risk factors and ABO blood group

Among the UGIB patients 66 consume coffee of them 11 are group A ,13 are group B, four are group AB and 38 are group O.

Among the UGIB patients 27 were cigarette smokers of them three are group A,11 are group B,four are group AB and nine are group O. Among the UGIB patients 90 drink tea of them 15 are group A,18 are group B, five are group AB and 52 are group O.

Among the UGIB patients 31 use NSAID and their blood groups were found to be O(15) >A (nine) >B (five) >,AB(two) .

Among the UGIB patients 28 consume Alcohol of them four are group A,10 are group B, three are group AB and 11are group O.

Among the UGIB patients 39 had *H.pylori* infection of them nine are group A, four are group B, four are group AB and 22 are group O. Among the UGIB patients 88 take spicy food of them 14 are group A,18 are group B, five are group AB and 51 are group O.

Among the UGIB patients 61 had Bilharzia infection of them eight are group A,15 are group B, five are group AB and 33 are group O.

Among the UGIB patients 56 toombak dipping of them eight are group A,13 are group B, four are group AB and 31 are group O. **table (4.1)**

Table(4. 1) Distribution of UGIB patients according to some potential risk factors and ABO blood group.

Potential risk factors	A	B	AB	O	Total
	Frequency/(%)	Frequency/(%)	Frequency/(%)	Frequency/(%)	
Coffee consumers	11(11%)	13(13%)	4(4%)	38(38%)	66(66%)
Non consumers	5(5%)	7(7%)	1(1%)	21(21%)	34(34%)
Smokers	3(3%)	11(11%)	4(4%)	9(9%)	27(27%)
Non smokers	13(13%)	9(9%)	1(1%)	50(50%)	73(73%)
Tea consumers	15(15%)	18(18%)	5(5%)	52(52%)	90(90%)
Non consumers	13(13%)	9(9%)	1(1%)	50(50%)	73(73%)
NSAID taking	9(9%)	5(5%)	2(2%)	15(15%)	31(31%)
Non taking	7(7%)	15(15%)	3(3%)	44(44%)	69(69%)
Alcohol consumers	4(4%)	10(10%)	3(3%)	11(11%)	28(28%)
Non consumers	12(12%)	10(10%)	2(2%)	48(48%)	72(72%)
H.pylori Infected	9(9%)	4(4%)	4(4%)	22(22%)	39(39%)
Non infected	7(7%)	16(16%)	1(1%)	37(37%)	61(61%)
Spicy food taking	14(14%)	18(18%)	5(5%)	51(51%)	88(88%)
Non taking	2(2%)	2(2%)	0(0%)	8(8%)	12(12%)
Bilharzia Infected	8(8%)	15(15%)	5(5%)	33(33%)	61(61%)
Non infected	8(8%)	5(5%)	0(0%)	26(26%)	39(39%)
Toombak dippers	8(8%)	13(13%)	4(4%)	31(31%)	56(56%)
Non toombak dippers	8(8%)	7(7%)	1(1%)	28(28%)	44(44%)

4.3 Association of ABO blood group with UGIB:

Among all the study population 42 are group A of them (26) were control and (16) were cases, 37 are group B of them (17) were control and (20) were cases, 12 are group AB of them (7) were control and (5) were cases and 109 are group O of them (50) were control and (59) were cases.No association was found between ABO and UGIB ($P \leq 0.29$).**table (4.2)**

Table(4.2) Association of ABO blood group with UGIB using the Chi-square test (X^2).

Blood group	Control	Case	Total	P.value
	Frequency/Percent	Frequency/Percent		
A	26 (61.9%)	16(38.1%)	42 (100%)	0.29
B	17 (45.9%)	20(54.1%)	37(100%)	
AB	7 (58.3%)	5(41.7%)	12(100%)	
O	50 (45.9%)	59(54.1%)	109(100%)	

Significance level at($P \leq 0.05$)

4.4 Association of Rhesus antigen with UGIB:

Among all the study population 189 are Rhesus positive of them (95) were control and (94) were cases , 11 are Rhesus negative of them (5) were control and (6) were cases. No association was found between Rhesus antigen and UGIB ($P \leq 0.75$).**table (4.3)**

Table (4.3) Association of Rhesus antigen with UGIB using the Chi-square test (X^2).

Rhesus antigen	control	case	Total	P.value
	Frequency/Percent	Frequency/Percent		
Positive	95 (50.3%)	94 (49.7%)	189(100%)	0.75
Negative	5 (45.5%)	6 (54.5%)	11 (100%)	

Significance level at($P \leq 0.05$)

4.5 Association of ABO blood group with the endoscopic findings of the UGIB patients

Sixteen of the UGI bleeding patients were blood group A of them two had esophageal varices, nine had duodenal ulcer, two had gastric ulcer, three had fundal varices, twenty were group B of them13 had esophageal varices, four had duodenal ulcer, and three had fundal varices ,five were group AB of them two had esophageal varices, three had duodenal ulcer, and 59 were group O of them 40 had esophageal varices, 12 had duodenal ulcer, four had gastric ulcer and three had fundal varices . There is a significant ($P \leq 0.009$) association between ABO blood group and the endoscopic findings. **Table (4.4)**

Table (4.4) Association of ABO blood group with the endoscopic findings of the UGIB patients using Chi-square test (X^2).

Blood Group	Esophageal Varices	Duodenal Ulcer	Gastric Ulcer	Fundal Varices	Total	P.value
	Frequency/(%)	Frequency/(%)	Frequency/(%)	Frequency/(%)		
A	2 (12.5%)	9 (56.2%)	2 (12.5%)	3 (18.8%)	16 (100%)	0.009
B	13 (65%)	4 (20%)	0 (0%)	3 (15%)	20 (100%)	
AB	2 (40%)	3 (60%)	0 (0%)	0 (0%)	5 (100%)	
O	40 (67.8%)	12 (20.3%)	4 (6.8%)	3 (5.1%)	59 (100%)	

Significance level at($P \leq 0.05$)

4.6 Association of endoscopic findings with some potential risk factors were displayed in table(4.5):

The total number of *H.pylori* infected UGI bleeding patients was 39 among them 17 had esophageal varices, 17 had duodenal ulcer, two had gastric ulcer and three had fundal varices. A significant association($P \leq 0.05$) was registered between endoscopic findings and *H.pylori*.

The number of UGI bleeding patients who take NSAID was 31 among them four had esophageal varices, 24 had duodenal ulcer,three had gastric ulcer .There is a significant ($P \leq 0.00$) association between endoscopic findings and NSAID.

The number of UGI bleeding patients who are toombak dippers was 56 among them twenty five had esophageal varices, 23 had duodenal ulcer, three had gastric ulcer and five had fundal varices.There is a significant association ($P \leq 0.01$) between endoscopic findings and toombak dipping.

The total number of UGI bleeding patients who are cigarette smoker was 27among them 13 had esophageal varices ,seven had duodenal ulcer,four had gastric ulcer and three had fundal varices.There is no association between endoscopic findings and smoking ($P \leq 0.13$)**.**

The number of UGI bleeding patients who drinks alcohol was 28 among them 13 had esophageal varices, 10 had duodenal ulcer, two had gastric ulcer and three had fundal varices. There is no association between endoscopic findings and alcohol consumption ($P \leq 0.61$).

The number of Bilharzia infected UGI bleeding patients was 61 among them 35 had esophageal varices, 14 had duodenal ulcer, five had gastric ulcer and seven had fundal varices.There is no association between endoscopic findings and bilharzias infection($P \leq 0.29$).

The number of UGI bleeding patients who drink coffee was 66 among them 39 had esophageal varices, 19 had duodenal ulcer, four had gastric ulcer and four had fundal varices.There is no association between endoscopic findings and coffee consumption ($P \leq 0.56$).

The number of UGI bleeding patients who drink tea was 90 among them 54 had esophageal varices, 22 had duodenal ulcer, six had gastric ulcer and eight had fundal varices.There is no association between endoscopic findings and tea consumption($P \leq 0.10$). The number of UGI bleeding patients who eat spicy food was 88 among them 54 had esophageal varices, 25 had duodenal ulcer, three had gastric ulcer and six had fundal varices. There is a significant ($P \leq 0.002$) association between endoscopic findings and spicy food.

Table (4.5) Association of endoscopic findings with some potential risk factors using Chi-square test (X^2).

	Esophageal varices	Duodenal ulcer	Gastric ulcer	Fundal varices	P.value
H.pylori infected **Non infected**	17(29.8%) 40(70.2%)	17(60.7%) 11(39.3%)	2(33.3%) 4(66.7%)	3(33.3%) 6(66.7%)	**0.05**
NSAID taking **Non NSAID taking**	4(7%) 53(93%)	24(85.7%) 4(14.3%)	3(50%) 3(50%)	0(0%) 9(100%)	**0.00**
Toombak dippers **Non dippers**	25(43.9%) 32(56.1%)	23(82.1%) 5(17.9%)	3(50%) 3(50%)	5(55.6%) 4(44.4%)	**0.01**
Smokers **Non smokers**	13(22.8%) 44(77.2%)	7(25%) 21(75%)	4(66.7%) 2(33.3%)	3(33.3%) 6(66.7%)	**0.13**
Alcohol drinkers **Non drinkers**	13(22.8%) 44(77.2%)	10(35.7%) 18(64.3%)	2(33.3%) 4(66.7%)	3(33.3%) 6(66.7%)	**0.61**
Bilharzia patients **Non bilharzia patients**	35(61.4%) 22(38.6%)	14(50%) 14(50%)	5(83.3%) 1(16.7%)	7(77.8%) 2(22.2%)	**0.29**
Coffee consumers **Non consumers**	39(68.4%) 18(31.6%)	19(67.9%) 9(32.1%)	4(66.7%) 2(33.3%)	4(44.4%) 5(55.6%)	**0.56**
Tea consumers **Non consumers**	54(94.7%) 3(5.3%)	22(78.6%) 6(21.4%)	6(100%) 0(0%)	8(88.9%) 1(11.1%)	**0.10**
Taking spicy food **Non taking**	54(94.7%) 3(5.3%)	25(89.3%) 3(10.7%)	3(50%) 3(50%)	6(66.7%) 3(33.3%)	**0.002**

4.7 Association of ABO blood group with the clinical outcomes of UGIB patients

Sixteen UGI bleeding patients are group A of them two with hematemesis, four with melena and 10 with both hematemesis and melena. Twenty are group B of them four had hematemesis, five with melena and 11 had both hematemesis and melena. Five are group AB and all of them had both hematemesis and melena. 59 are group O of them 21 had hematemesis only, three had melena and 35 had both hematemesis and melena. There is a significant ($P \leq 0.03$) association between ABO blood group and clinical outcomes of UGI bleeding patients. **table (4.6)**

Table (4.6) Association of ABO blood group with the Clinical outcomes of UGIB patients using Chi-square test (X^2).

Blood group	Hematemesis	Melena	Hematemesis And Melena	Total	P.value
	Frequency/ Percent	Frequency/ Percent	Frequency/ Percent		
A	2(12.5%)	4(25%)	10(62.5%)	16(100%)	0.03
B	4(20%)	5(25%)	11(55%)	20(100%)	
AB	0(0%)	0(0%)	5(100%)	5(100%)	
O	21(35.6%)	3(5.1%)	35(59.3%)	59(100%)	

Significance level at($P \leq 0.05$)

CHAPTER V

DISCUSSION, CONCLUSION, RECOMMENDATIONS

5.1 Discussion

This is a case control study conducted in Ibn Sina Hospital – Khartoum State during the period from March to June 2019.The study was undertaken to find the possible association between ABO blood group /Rhesus factors with upper gastrointestinal bleeding and potential risk factors.

In the present study no significant relationship was observed between ABO/Rh blood groups and upper gastrointestinal bleeding. This contradicts the findings of many researchers in this field that is Bayan, *et. al*.,(2009), Abdulridha, (2013) and Bahardoust, *et. al.*, (2018). Bayan, *et. al*.,(2009) found a positive correlation between group O and upper gastrointestinal bleeding and that blood group O have higher frequency in UGIB patients than in the control group. Abdulridha, (2013) fortified the findings of Bayan, *et. al*., (2009). They found the following order for the distribution of ABO/Rh in Iragi peptic ulcer patients O>A>B>AB which is on line with the findings of the current study. Bahardoust, *et. al*., (2018) investigated the association between ABO blood group and clinical outcomes in Iranian patients with gastrointestinal bleeding. Although blood group O was found to be the most frequent blood type in the Iranian population Bahardoust, *et. al*., (2018) reported that blood group O was significantly more common in patients with GI bleeding and especially UGIB patients in comparison to the healthy blood donors. They suggested that it is a prognostic genetic risk factor for bleeding tendency in these patients, especially in those with upper GI bleeding. The variation between the results of this work and the previous researchers may be due to the small size of the studied population in this study or due to both hereditary (ABO blood group) and environmental factors.

The main cause of upper GI bleeding according to the endoscopic findings in this study was esophageal varices (57%) this is on line with a previous study done in the Sudan by Salih, *et. al*.,(2009) who reported a higher percentage (90.3%) for the frequency of esophageal varices among acute upper GI bleeding. Salih, *et. al*.,*(*2009) attributed the high frequency of oesophageal varices to bilharzias ,which is an endemic disease in the Sudan.The frequency of peptic ulcer among UGIB patients in this study was 34 and of them 28 patients had duodenal ulcer and 6 patients had gastric ulcer. In Irag Abdulridha, (2013) investigated the possible association between peptic ulcer disease and ABO/blood

group and recorded a significant higher percentage of patients with both gastric and duodenal ulcer disease are those holding blood group O+ compared to other blood group phenotypes (57.5%) and this may consider that ABO/Rh blood group (mainly blood group O+) an additional risk factor for peptic ulcer to the other known factors. She suggested that the functional significance of ABO blood group distribution might be associated with biological behavior of peptic ulcer disease. Also the present study accords with the findings Mohammed *et. al.,(*2015) ,who performed an oesophagogastrodudenoscopy in Gezira - Central Sudan, that the frequency of duodenal ulcers and gastric ulcers was 31 and 9 respectively.The order of ABO blood group distribution among the *H.pylori* infected patients was 22%, 9%, 4% and 4% for blood groups O, A, B and AB respectively and a significant association was registered between ABO blood group and *H.pylori*. Mohammed, *et. al*.,(2015) suggested that there can be a significant association between Rhesus positive group O and *H. pylori* infection. ABO blood group antigens have been hypothesized to influence the adherence of pathogenic organisms, specifically *Helicobacter pylori* (*H. pylori*), and levels of coagulation factors.

A significant association was found between UGIB and NSAID use which accords with the early report of Kuyvenhoven, (1999) and the results of Hreinsson, *et. al*., (2013) who suggested that NSAID use play an important role in UGIB occurrence. The present study found that there is a significant association between UGIB and toombak dipping no previous studies were found in this topic.

Smoking was not proven to be a risk factor for UGIB which agrees with the study of Strate, *et. al*.,(2016). No significant association was observed between UGIB and alcohol consumption in Sudanese UGIB patients which disagree with the work of Strate, *et. al*.,(2016) who found that alcohol consumption was associated with an increased risk for UGIB. This discrepancy may be due to differences in social cultures as most of the Sudanese alcoholics take alcoholic drinks after meals.

In the present study bilharzia was most frequent in patients with esophageal varices this agrees with the observation of Opio, *et. al*.,(2016) who investigated upper gastrointestinal bleeding among patients from rural Sub-Saharan Africa where schistosoma mansoni is common and reported that most of the participant who had esophageal varices were infected by bilharzias.

A significant association was found between UGIB and spicy food take which accords with the Albaqawi, *et. al* (2017) who reported that spicy food is a risk factor for peptic ulcer disease.

In the present study hematemesis and melena were more common in patients with blood group O (35%) which fortifies the results of Bahardoust, *et. al*.,(2018).

5.2 Conclusion

There is no association was found between ABO/Rh blood groups and UGIB.

A significant association between UGIB and potential risk factors such as *H.pylori***,** NSAID**,** toombak dipping and spicy food taking.

No association between UGIB and cigarette smoking, alcohol, bilharzias infection,coffee and tea.

5.3 Recommendations

Further large cross sectional studies ,all around Sudan, in more diverse populations should be done to evaluate the role of ABO/Rh blood group:

As an individual risk factor or as a co-founder with other risk factors (age ,sex and life style) for GI bleeding.

In the early diagnosis of UGI Bleeding.

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Appendixes

Appendix 1

Questionnaire

Sudan University of Science & Technology

Questionnaire about association of ABO blood group /Rhesus factor with upper gastrointestinal bleeding and potential risk factors

1/Name:……

2/Gender: Male ☐ Female ☐

3/Age:…… Year

Characteristic of the studied patient:

1/Education level:…….

2/Marital status: Married ☐ Single ☐

3/Residence:……

4/Occupation:……..

Potential risk factors:

1/Tea :	Consume	☐	Non consume	☐
2/Coffee:	Consume	☐	Non consume	☐
3/Alcohol:	Drinker	☐	Non drinker	☐
4/Smoking:	Smoker	☐	non smoker	☐
5/Spicy food:	Spicy	☐	Non spicy	☐
6/NSAID:	Take	☐	Non take	☐

7/*H.Pylori*: Infected ☐ Non infected ☐

8/Billharzia: Infected ☐ Non infected ☐

Type of diseases which exclude from the study and bone marrow transplant :

Malignancies: Yes ☐ No ☐

Autoimmune diseases: Yes ☐ No ☐

Bone marrow transplant: Yes ☐ No ☐

Appendix II

Laboratory Requirement

A. Reagents:

1.Antisera A

2.Antisera B

3.Antisera D

4.Coombs

B. Equipments:

1.Glass slides

2.Wooden stick

3.Water bath

4.Centrifuge

5.Normal saline(0.9%NaCl)

6.Test tubes

7. Pasteur pipettes

8.Gloves