RELATIONSHIP BETWEEN ABO BLOOD GROUPS AND SEVERITY OF MALARIA

Submitted By

DR.TANMAY.R.BHAT

Dissertation submitted to

Rajiv Gandhi University of Health Sciences,

Karnataka, Bangalore.

In partial fulfillment of the

Requirements for the degree of

MD

in

General Medicine

Under the guidance of

DR M.S.MULIMANI **MD**

PROFESSOR OF MEDICINE

DEPARTMENT OF MEDICINE

B. L. D. E. A'S
SHRI B. M. PATIL MEDICAL COLLEGE, HOSPITAL & RESEARCH CENTRE, BIJAPUR.

2010

DECLARATION BY THE CANDIDATE

I hereby declare that this dissertation entitled **"RELATIONSHIP BETWEEN ABO BLOOD GROUPS AND SEVERITY OF MALARIA"** is a bonafide and genuine research work carried out by me under the guidance of Dr.M.S.MULIMANI $_{MD}$ Professor of Medicine.

Date:

Place: Bijapur.

Dr. TANMAY.R.BHAT

CERTIFICATE BY THE GUIDE

This is to certify that the dissertation entitled **"RELATIONSHIP BETWEEN ABO BLOOD GROUPS AND SEVERITY OF MALARIA"** is bonafide research work done by **Dr.TANMAY.R.BHAT** in partial fulfillment of the requirement for the degree of MD in General Medicine.

Dr.M.S.Mulimani **MD**
Professor of Medicine
BLDEA's Shri. B. M. Patil
Medical College, Hospital
and Research Centre, Bijapur

Date:
Place: Bijapur.

ENDORSEMENT BY THE HOD

This is to certify that the dissertation entitled **"RELATIONSHIP BETWEEN ABO BLOOD GROUPS AND SEVERITY OF MALARIA"** is a bonafide research work done by **Dr.TANMAY.R.BHAT** under the guidance of **Dr.M.S.MULIMANI**$_{\textbf{M.D}}$ Professor of Medicine.

Dr.M.S.Biradar $_{\textbf{MD}}$
Professor and Head
Department of Medicine
BLDEA's Shri. B. M. Patil
Medical College, Hospital
and Research Centre, Bijapur

Date:

Place: Bijapur.

ENDORSEMENT BY THE PRINCIPAL

This is to certify that the dissertation entitled **"RELATIONSHIP BETWEEN ABO BLOOD GROUPS AND SEVERITY OF MALARIA"** is a bonafide research work done by **Dr.TANMAY.R.BHAT** under the guidance of **Dr.M.S.MULIMANI** $_{\textbf{M.D}}$ Professor of Medicine.

Dr.M.S.Biradar $_{\textbf{MD}}$
Incharge principal
BLDEA's Shri. B. M. Patil
Medical College, Hospital
and Research Centre, Bijapur

Date :

Place : Bijapur

COPYRIGHT

Declaration by the candidate

I hereby declare that the Rajiv Gandhi University of Health Science Karnataka, Bangalore, shall have the rights to preserve, use and disseminate this dissertation / thesis in print or electronic format for academic / research purpose.

Date:

Place: Bijapur **Dr. TANMAY.R.BHAT**

ACKNOWLEDGEMENT

On completion of this contribution of scientific document it gives me deep pleasure to acknowledge the guidance provided by my distinguished mentors.

With privilege and respect I like to express my gratitude and indebtedness to my Guide M.S.MULIMANI $_{M.D}$*, Professor and Unit III chief. Sri.B.M.Patil Medical College, Bijapur, for his constant inspiration, extensive encouragement and support, which he rendered in pursuit of my post-graduate studies and in preparing this dissertation.*

I express sincere gratitude to Dr.M.S.BIRADAR$_{M.D}$*., Professor and Head, Department of Medicine for his advise valuable suggestions, encouragement and support.*

I am forever grateful to Dr.S S Devaramani Prof, Dr S R Badiger Prof, Dr L S Patil Prof, Dr R M Honnutagi Assoc. Prof, Dr R B Jakareddy Assoc Prof, Dr R M Madraki Assoc Prof , Dr A P Ambali Assoc Prof , Dr V G Warad Assoc prof , Dr P G Mantur Asst prof, Dr S M Biradar Asst prof, Dr G S Mahishale Asst prof, Dr Javed Patel Asst prof , Dr S B Bhagawati Asst Prof , Dr. S.G.Balaganur Asst Prof, Dr Sanjay Patil Asst Prof, Dr Sidray hanjagi, for their valuable help and guidance during my study.

I am extremely thankful to Dr.R.C.Bidri, Principal of B.L.D.E.A'S Shri B. M.Patil Medical College Hospital and Research Centre, Bijapur, for permitting me to utilize resources in completion of my work.

I would like to express my gratitude to the statistician who helped me in my dissertation work Mrs. Vijaya Sorganvi and Mr. Madagi

My thanks to one and all in the Library Staff, Medicine Dept Staff and all Hospital Staff for their co-operation in my study.

I am thankful to my friend Dr.Raghavendra in KMC mngalore, my seniors Dr Preetham, Dr Shrinivas, Dr.sandeep, Dr.Ravi , my classmates Dr Asna, Dr Utkarsha, Dr Jagdeesan, Dr Amit, and my juniors Dr Chandrakanth, Dr Sachin, Dr Abhishek, Dr Aveg Dr Sandeep for their suggestions and advice.

I am deeply indebted to my parents Mrs. Ganga and Mr.Ramachandra whose constant encouragement, patience and support helped me to complete this dissertation.

Last but not the least; I convey my heartfelt gratitude to all the patients, without whose co-operation, this study would be incomplete.

My special thanks to Mr. Kalyan Kumar, Asif of 'PREETI NET ZONE' and Sai internet Bijapur for computerizing my dissertation work in a right format. I sincerely appreciate his skills and recommend him for my junior colleagues.

Date:

Place: Bijapur **DR.TANMAY.R.BHAT**

LIST OF ABBREVIATIONS

ADAMTS13 – a disintegrin and metalloproteinase with a thrombospondin type 1 motif, member 13

AIDS – Acquired immunodeficiency syndrome

API – Annual parasitic index

BC – Before Christ

DBL - Duffy binding-like

DDT – Dichloro diphenyl trichloroethane

DNA – Deoxyribonucleic acid

EMCP – Enhanced Malaria Control Project

G6PD – Glucose -6-phosphate dehydrogenase

IgG – Immunoglobulin G

MPO – Modified plan of operation

NMCP – National Malaria Control Programme

PCR – Polymerase chain reaction

PfEMP-1 - Plasmodium falciparum erythrocyte membrane protein-1

PfHRP2 – Plasmodium falciparum histidine rich protein 2

PMA – Pan-malarial plasmodium aldolase

QBC – Quantitative buffy coat

RBC – Red blood cell

SE – South east

UV – Ultraviolet

vWF - von Willebrand factor

ABSTRACT

BACKGROUND :. The ABO blood group system is arguably the best known, and yet the most functionally mysterious, genetic polymorphism in humans. In the century since their discovery, ABO antigen associations with infections and other diseases have been the subject of hundreds of publications. Much new information has emerged since a relationship between ABO and malaria was first suggested more than 40 years ago. There is hypothesis that *Plasmodium falciparum* malaria has shaped the distribution of ABO blood groups in humans. We aim to study the relationship between ABO blood groups and severity of malaria.

MATERIAL AND METHODS: The present study was done in 100 patients with history of fever, peripheral smear study & QBC test positive for malarial parasite admitted to B.L.D.E.A's Shri B.M.Patil Medical College, Bijapur, from November 2007 to September 2009. Quantitative buffy coat study was done to confirm the presence of malarial parasite. ABO blood grouping was done using the slide agglutination method at the time of admission and relationship between ABO blood groups and malaria (both complicated and uncomplicated) was studied. Complications of malaria were studied with respect to various ABO blood groups and to look whether complications occurred with increased and decreased frequency in any particular blood group.

OBSERVATION: Of the 100 malaria cases, 30 cases belonged to blood group A, out of which 15 patients (50%) had complications and 15 (50%) with no complications. Out of total 24 O blood group cases, 10(41.66%) had complications and 14(58.33%) were in

uncomplicated group. Out of 33 cases which belonged to blood group B, 8 patients (24.24%) had complications and 25 patients (75.75%) had no complications. The association between blood group and malaria showed statistical significance. Thus blood group A patients had more complications compared to other blood groups. While blood group B had least complications.

CONCLUSION: Patients with blood group A are prone to develop malaria complications while blood group B individuals had had least complications when compared to other ABO blood groups.

CONTENTS

LIST OF TABLES

LIST OF GRAPHS

LIST OF FIGURES

INTRODUCTION

Malaria is probably one of the oldest diseases known to mankind that has had profound impact on our history. But for malaria, the outcomes of many a wars and destinies of many a kings would have been different. It has been responsible for the decline of nations and crushing military defeats, often having caused more casualties than the weapons themselves. For centuries it prevented any economic development in vast regions of the earth. It continues to be a huge social, economical and health problem, particularly in the tropical countries.

Every year 300 million to 500 million people suffer from this disease (90% of them in sub-Saharan Africa, two thirds of the remaining cases occur in six countries- India, Brazil, Sri Lanka, Vietnam, Colombia and Solomon Islands). About 1.5 million to 3 million people die of malaria every year. Malaria ranks third among the major infectious diseases in causing deaths- after pneumococcal acute respiratory infections and tuberculosis. It accounts for 2.6 percent of the total disease burden of the world. It is responsible for the loss of more than 35 million disability-adjusted life-years each year.

Malaria was nearly eradicated from most parts of the world by the early 60's, owing largely to concerted anti malarial campaigns world over under the guidance of the World Health Organization.

The following are some of the reasons for the resurgence of malaria:

Table no.1

Man made	Complacency and laxity in anti malarial campaigns; conflicts and wars; migrations; deteriorating health systems; poverty
Parasite	Drug Resistance
Vector	Insecticide Resistance and ? ban on DDT
Environment	Global Warming - increased breeding and life span of the insect vector
Jet Age	Shrinking World - spread of malaria from endemic areas to all other parts of the world

AIMS AND OBJECTIVES

- The aim of the study is to study the relationship between ABO blood groups and severity of malaria

REVIEW OF LITERATURE

HISTORICAL REVIEW

Malaria has infected humans for over 50,000 years, and may have been a human pathogen for the entire history of the species.[3] Close relatives of the human malaria parasites remain common in chimpanzees.[4] References to the unique periodic fevers of malaria are found throughout recorded history, beginning in 2700 BC in China.[5] The term malaria originates from Medieval Italian: *mala aria* — "bad air"; and the disease was formerly called **ague** or **marsh fever** due to its association with swamps and marshland.

In the *Susruta*, a Sanskrit medical treatise, the symptoms of malarial fever were described and attributed to the bites of certain insects. A number of Roman writers attributed malarial diseases to the swamps.

Charles Louis Alphonse Laveran, a French army surgeon stationed in Constantine, Algeria, was the first to notice parasites in the blood of a patient suffering from malaria. This occurred on the 6th of November 1880. For his discovery, Laveran was awarded the Nobel Prize in 1907.

Camillo Golgi, an Italian neurophysiologist, established that there were at least two forms of the disease, one with tertian periodicity (fever every other day) and one with quartan periodicity (fever every third day). He also observed that the forms produced differing numbers of merozoites (new parasites) upon maturity and that fever coincided with the rupture and release of merozoites into the blood stream. He was awarded a Nobel Prize in Medicine for his discoveries in neurophysiology in 1906 [2].

The Italian investigators Giovanni Batista Grassi and Raimondo Filetti first introduced the names *Plasmodium vivax* and *P. malariae* for two of the malaria parasites that affect humans in 1890.[1] Laveran had believed that there was only one species, *Oscillaria malariae*. An American, William H. Welch, reviewed the subject and, in 1897, he named the malignant tertian malaria parasite, *P. falciparum*. There were many arguments against the use of this name, however, the use was so extensive in the literature that a change back to the name given by Laveran was no longer thought possible. In 1922, John William Watson Stephens described the fourth human malaria parasite, *P. ovale*.

On August 20th, 1897, Ronald Ross, a British officer in the Indian Medical Service, was the first to demonstrate that malaria parasites could be transmitted from infected patients to mosquitoes. In further work with bird malaria, Ross showed that mosquitoes could transmit malaria parasites from bird to bird. This necessitated a sporogonic cycle (the time interval during which the parasite developed in the mosquito). Thus, the problem of malaria transmission was solved. For his discovery, Ross was awarded the Nobel Prize in 1902[1].

Malaria in India[6,7,9]

Malaria is one of the major public health problems in the developing countries. Recent estimates indicate that between 300-500 million clinical cases and between 1.5-2.7 million deaths due to it, occur world wide annually, 90% of which occur in tropical Africa. It is estimated that 1.2 billion people out of the 1.4 billion people of SE Region live in Malarious areas. In 1995, malaria cases in the region were estimated at 21.9

million, with almost 32,000 deaths. India accounts around 85% of the total reported cases in the region in the same year. During 1996 also, India contributed 83% of total malaria cases in SE Region. Thus around 80% of reported cases in the region are being contributed by India.

Malaria is a complex disease and various factors influenced by human activities and natural calamity like excessive rainfall, flood, drought and other disasters have great bearing on mosquitogenic conditions leading to increased potential for malaria transmission. Like any other disease, natural transmission of malaria depends on the presence of, and relationship between the three basic epidemiological factors : the agent, the host and the environment.

There are four species of human malaria parasites *Plasmodium vivax, falciparum, malariae* and *ovale*. In India 60 to 65 % of the infections are due to *P.vivax* and 35 to 40% due to *P. falciparum*. Only few cases of *P. malariae* have been reported from Orissa and Karnataka.

National Anti-Malaria Programme[5,6]

In April 1953, Govt. of India launched a National Malaria Control Programme (NMCP) with the following objectives:

- To bring down malaria transmission to a level at which it would cease to be a major public health problem; and
- Thereafter an achievement was to be maintained by each state to hold down the malaria transmission at low level indefinitely

Modified Plan of Operation (MPO) [4,5,6]

In 1977 attempts at malaria eradication were given up and under the review policy, a Modified Plan of Operation (MPO) was adopted.

Objectives

- Elimination of malaria deaths
- Reduction of malaria morbidity
- Maintenance of the gains achieved so far by reducing transmission of malaria

Enhanced Malaria Control Project (EMCP)

It was launched in April 1997 with the assistance of the World Bank.

Objectives of EMCP

- Effective control of malaria to bring reduction in malaria morbidity;
- Prevention of death due to malaria;
- Consolidation of the gain achieved so far.

Strategies

- Early case detection and prompt treatment;
- Vector control by indoor residual insecticide spray in rural areas with API of 2 per 100 and above in the preceding three years with appropriate insecticide and by recurrent anti-malaria in urban areas.
- Health Education and community participation.

Components of EMCP

- Early case detection and prompt treatment
- Selective Vector Control

- Legislative Measures
- Personal Protective Measures
- Epidemic Planning and Rapid Response and Intersectoral Coordination
- Institutional and Management capacities strengthening
- Operation Research
- Community Participation

Transmission of malaria

The female anopheles mosquito is the vector for human malaria. When this female mosquito bites the man for a blood meal, which it needs to nourish its eggs, it inoculates the sporozoites into human blood stream, thus spreading the infection. This type of transmission is occasionally referred to as anterior station transfer.[11]

Other modes of transmission:

1. *Blood transfusion (Transfusion malaria)*[10]
2. *Mother to the growing fetus (Congenital malaria)*
3. *Needle stick injury*

Transfusion malaria: This is fairly common in endemic areas. Most infections occur in cases of transfusion of blood stored for less than 5 days and it is rare in transfusions of blood stored for more than 2 weeks. Frozen plasma is not known to transmit malaria. The clinical features of transfusion malaria occur earlier and any patient who has received a transfusion three months prior to the febrile illness should be suspected to have malaria.

Donor blood can be tested with indirect fluorescent antibody test or ELISA, and direct examination of the blood for the parasite may not be helpful. In endemic areas, it is safe to administer full course of chloroquine to all recipients of blood transfusion.

In transfusion malaria, pre-erythrocytic schizogony does not occur and hence relapses due to dormant hepatic forms also does not occur. Therefore, treatment with primaquine for 5 (or14) days is not indicated

Life cycle of malaria [12,13,14]

Asexual phase in the human host

Tissue schizogony (Pre- erythrocytic schizogony) :

This phase starts with the inoculation of the parasite into the human blood by the bite of a female anopheles mosquito. Within half an hour, the sporozoites reach the liver and invade the liver cells. Once in the liver, these organisms differentiate to yield thousands of merozoites, which, following rupture of their host cells, escape into the blood and infect red blood cells, thus beginning the erythrocytic stage of the life cycle.[12] The parasite escapes from the liver undetected by wrapping itself in the cell membrane of the infected host liver cell.[13]

Within the liver cells, the trophozoites start their intracellular asexual division. At the completion of this phase, thousands of extra erythrocytic merozoites are released from each liver cell. The time taken for the completion of the tissue phase is variable, depending on the infecting species; *(8 - 25 days for P. falciparum, 8 - 27 days for P. vivax, 9 - 17 days for P. ovale, 15 - 30 days for P. malariae)* and this interval is called as *pre-patent period.*

In case of *P. vivax* and *P. ovale*, some sporozoites may go into hibernation - the *cryptobiotic phase*- in which they are called as *hypnozoites.*[14] They can lie dormant for months or years and on reactivation they cause clinical relapse.

Erythrocytic schizogony:

The merozoites released from the liver cells attach onto the red blood cell membrane and by a process of invagination, enter the red cell. Within the red blood cell, the asexual division starts and the parasites develop through the stages of rings, trophozoites, early schizonts and mature schizonts; each mature schizont consisting of thousands of erythrocytic merozoites. These merozoites are released by the lysis of the red blood cell and they immediately invade uninfected red cells. This repetitive cycle of invasion - multiplication - release - invasion continues. The intra erythrocytic cycle takes about 48 hours in *P. vivax*, *P. ovale* and *P. falciparum* infections and 72 hours in case of *P. malariae* infection. It occurs synchronously and the merozoites are released at approximately the same time of the day. The contents of the infected cell that are released with the lysis of the RBC stimulate Tumor Necrosis Factor and other cytokines, which results in the characteristic clinical manifestations of the disease.

A small proportion of the merozoites in the red blood cells undergo transformation into gametocytes - male and female. Mature gametocytes appear in the peripheral blood after a variable period and enter the mosquito when it bites an infected individual.

Sexual phase in the mosquito

Sporogony:

The gametocytes continue their development in the mosquito. The male and female gametes fuse and form into a zygote. This transforms into an ookinete which penetrates the gut wall and becomes an oocyst. The oocyst divides asexually into numerous sporozoites which reach the salivary gland of the mosquito. On biting a man, these sporozoites are inoculated into human blood stream. The sporogony in the mosquito takes about 10 - 20 days and thereafter the mosquito remains infective for 1 - 2 months.

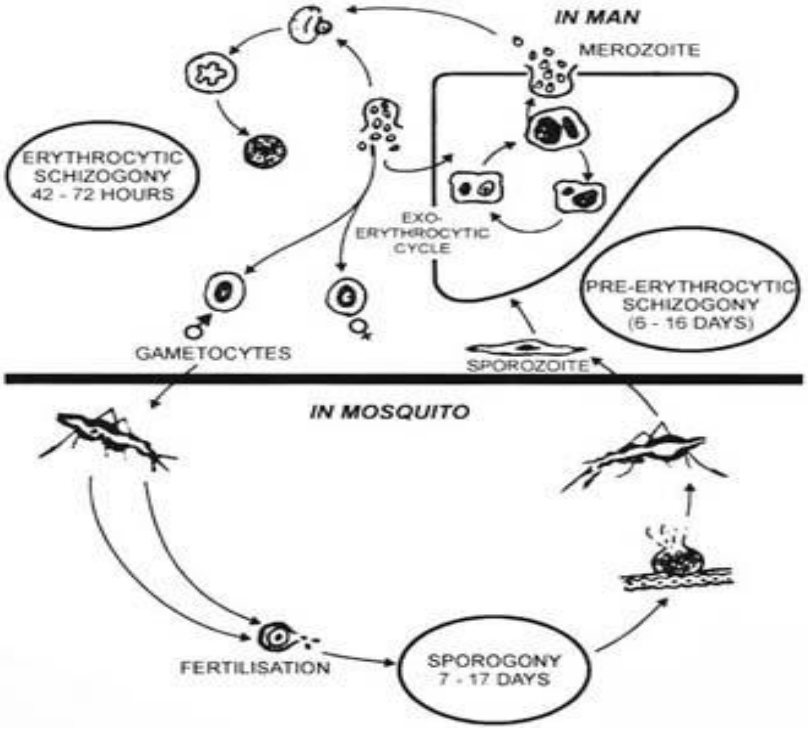


Fig. 1 : Life cylce of malarial parasite

Pathophysiology

All the clinical features of malaria are caused by the erythrocytic schizogony in the blood. The growing parasite progressively consumes and degrades intracellular proteins, principally hemoglobin, resulting in formation of the 'malarial pigment' and hemolysis of the infected red cell. The parasite is relatively protected from attack by the body's immune system because for most of its human life cycle it resides within the liver and blood cells and is relatively invisible to immune surveillance. However, circulating infected blood cells are destroyed in the spleen. To avoid this fate, the *P. falciparum* parasite displays adhesive proteins on the surface of the infected blood cells, causing the blood cells to stick to the walls of small blood vessels, thereby sequestering the parasite from passage through the general circulation and the spleen.[16] This "stickiness" is the main factor giving rise to hemorrhagic complications of malaria. High endothelial venules (the smallest branches of the circulatory system) can be blocked by the attachment of masses of these infected red blood cells. The blockage of these vessels causes symptoms such as in placental and cerebral malaria. In cerebral malaria the sequestrated red blood cells can breach the blood brain barrier possibly leading to coma.[15]

The rupture of red blood cells by merozoites releases certain factors and toxins (such as red cell membrane lipid, glycosyl phosphatidyl inositol anchor of a parasite membrane protein), which could directly induce the release of cytokines such as TNF and interleukin-1 from macrophages, resulting in chills and high grade fever. This occurs once in 48 hours, corresponding to the erythrocytic cycle.

Typical features: It includes three stages.

- Cold stage
- Hot stage
- Sweating stage

The febrile episode starts with shaking chills, usually at mid-day between 11 a.m. to 12 noon, and this lasts from 15 minutes to 1 hour (the cold stage), followed by high grade fever, even reaching above 106^0 F, which lasts 2 to 6 hours (the hot stage). This is followed by profuse sweating and the fever gradually subsides over 2-4 hours.

In vivax malaria, this typical pattern of fever recurs once every 48 hours and this is called as *Benign Tertian malaria.* Similar pattern may be seen in ovale malaria too *(Ovale tertian malaria).* In falciparum infection *(Malignant tertian malaria),* this pattern may not be seen often and the paroxysms tend to be more frequent *(Sub-tertian).* In *P. malariae* infection, the relapses occur once every 72 hours and it is called *Quartan malaria.* Other symptoms include, arthralgia, vomiting, anemia, hemoglobinuria, retinal damage,[17] and convulsions

Atypical features

Atypical features are more common in the following situations:

- Falciparum malaria
- Early infection
- Patients at extremes of age
- Patients who are immune-compromised (extremes of age, malnourished, AIDS, tuberculosis, cancers, on immunosuppressive therapy etc.)
- Patients on chemoprophylaxis for malaria
- Patients who have had recurrent attacks of malaria
- Patients with end stage organ failure
- Last but not the least, pregnancy.

1. Atypical fever
2. Headache
3. Body ache, back ache and joint pains
4. Dizziness, vertigo
5. Altered behaviour, acute psychosis
6. Altered sensorium
7. Convulsions, coma
8. Cough, Breathlessness, Chest pain
9. Acute abdomen
10. Pallor
11. Jaundice

Clinical features suggesting *P. falciparum* infection:

1. Presence of any of the complications of *P. falciparum* malaria viz. altered sensorium; convulsions; coma; jaundice; severe anemia; hypotension; prostration; hyperpyrexia; renal failure etc.
2. Atypical presentation.
3. Not responding to chloroquine therapy within 48 hours.
4. Recurrence within 2 weeks.

Complications[30]

Severe malaria is almost exclusively caused by *P. falciparum* infection and usually arises 6–14 days after infection.[18] Severe malaria can progress extremely rapidly and cause death within hours or days.[18] In the most severe cases of the disease fatality rates can exceed 20%, even with intensive care and treatment.[19]

Cerebral malaria

Coma is a characteristic and ominous feature of falciparum malaria. Cerebral malaria manifests as diffuse symmetric encephalopathy; focal neurologic signs are unusual. Signs of meningeal irritation are lacking. The eyes may be divergent and a pout reflex is common, but other primitive reflexes are usually absent. The corneal reflexes are preserved, except in deep coma. Muscle tone may be either increased or decreased. The tendon reflexes are variable, and the plantar reflexes may be flexor or extensor; the abdominal and cremasteric reflexes are absent. Flexor or extensor posturing may be seen. Approximately 15% of patients have retinal hemorrhages; with pupillary dilatation and

indirect ophthalmoscopy, this figure increases to 30–40%. Other funduscopic abnormalities include discrete spots of retinal opacification (30–60%), papilledema (8% among children, rare among adults), cotton wool spots (<5%), and decolorization of a retinal vessel or segment of vessel (occasional cases). Convulsions, usually generalized and often repeated, occur in up to 50% of children with cerebral malaria. Whereas adults rarely (i.e., in <3% of cases) suffer neurologic sequelae, ~15% of children surviving cerebral malaria—especially those with hypoglycemia, severe anemia, repeated seizures, and deep coma—have some residual neurologic deficit when they regain consciousness; hemiplegia, cerebral palsy, cortical blindness, deafness, and impaired cognition and learning (all of varying duration) have been reported.[30]

Hematologic Abnormalities

Anemia results from accelerated RBC removal by the spleen, obligatory RBC destruction at parasite schizogony, and ineffective erythropoiesis. In severe malaria, both infected and uninfected RBCs show reduced deformability, which correlates with prognosis and development of anemia. Splenic clearance of all RBCs is increased. In nonimmune individuals and in areas with unstable transmission, anemia can develop rapidly and transfusion is often required. As a consequence of repeated malarial infections, children in many areas of Africa may develop severe anemia resulting from both shortened RBC survival and marked dyserythropoiesis. Anemia is a common consequence of antimalarial drug resistance, which results in repeated or continued infection.

Liver Dysfunction

Mild hemolytic jaundice is common in malaria. Severe jaundice is associated with *P. falciparum* infections; is more common among adults than among children; and results from hemolysis, hepatocyte injury, and cholestasis. When accompanied by other vital-organ dysfunction (often renal impairment), liver dysfunction carries a poor prognosis. Hepatic dysfunction contributes to hypoglycemia, lactic acidosis, and impaired drug metabolism. Occasional patients with falciparum malaria may develop deep jaundice (with hemolytic, hepatitic, and cholestatic components) without evidence of other vital-organ dysfunction.

Renal Impairment

Renal impairment is common among adults with severe falciparum malaria but rare among children. The pathogenesis of renal failure is unclear but may be related to erythrocyte sequestration interfering with renal microcirculatory flow and metabolism. Clinically and pathologically, this syndrome manifests as acute tubular necrosis, although renal cortical necrosis never develops. Acute renal failure may occur simultaneously with other vital-organ dysfunction (in which case the mortality risk is high) or may progress as other disease manifestations resolve. In survivors, urine flow resumes in a median of 4 days, and serum creatinine levels return to normal in a mean of 17 days. Early dialysis or hemofiltration considerably enhances the likelihood of a patient's survival, particularly in acute hypercatabolic renal failure.

Indicators of severe malaria and poor prognosis (Table no.2)

Manifestation	Features
Initial World Health Organization criteria from 1990 [53]	
Cerebral malaria	Unrousable coma not attributable to any other cause, with a Glasgow Coma Scale score ≤ 9. Coma should persist for at least 30 min after a generalized convulsion
Severe anemia	Hematocrit <15% or hemoglobin < 50 g/l in the presence of parasite count >10 000/μl
Renal failure	Urine output <400 ml/24 hours in adults (<12 ml/kg/24 hours in children) and a serum creatinine>265 μmol/l (> 3.0 mg/dl) despite adequate volume repletion
Pulmonary edema and acute respiratory distress syndrome	The acute lung injury score is calculated on the basis of radiographic densities, severity of hypoxemia, and positive end-expiratory pressure [54]
Hypoglycemia	Whole blood glucose concentration <2.2 mmol/l (<40 mg/dl)
Circulatory collapse (algid malaria)	Systolic blood pressure <70 mmHg in patients > 5 years of age (< 50 mmHg in children aged 1–5 years), with cold clammy skin or a core-skin temperature difference >10°C
Abnormal bleeding and/or disseminated intravascular coagulation	Spontaneous bleeding from gums, nose, gastrointestinal tract, or laboratory evidence of disseminated intravascular coagulation
Repeated generalized convulsions	≥ 3 convulsions observed within 24 hours
Acidemia/acidosis	Arterial pH <7.25 or acidosis (plasma bicarbonate <15 mmol/l)
Macroscopic hemoglobinuria	Hemolysis not secondary to glucose-6-phosphate dehydrogenase deficiency
Added World Health Organization criteria from 2000 [55]	
Impaired consciousness	Rousable mental condition
Prostration or weakness	
Hyperparasitemia	> 5% parasitized erythrocytes or > 250 000 parasites/μl (in nonimmune individuals)
Hyperpyrexia	Core body temperature >40°C
Hyperbilirubinemia	Total bilirubin >43 μmol/l (> 2.5 mg/dl)

Diagnosis

Peripheral smear examination for malarial parasite [21,22,23]

Peripheral smear examination for malarial parasite is the gold-standard in confirming the diagnosis of malaria. Thick and thin smears prepared from the peripheral blood are used for the purpose. The peripheral blood smear provides comprehensive information on the species, the stages, and the density of parasitemia with a sensitivity of 5 to 10 parasites/µL of blood for an experienced laboratory professional. The efficiency of the test depends on the quality of the equipment and reagents, the type and quality of the smear, skill of the technician, the parasite density, and the time spent on reading the smear

Thick smear: The thick smear of correct thickness is the one through which newsprint is barely visible. It is dried for 30 minutes and not fixed with methanol. This allows the red blood cells to be hemolyzed and leukocytes and any malaria parasites present will be the only detectable elements. However, due to the hemolysis and slow drying, the plasmodia morphology can get distorted, making differentiation of species difficult. Thick smears are therefore used to detect infection, and to estimate parasite concentration.

Infected erythrocytes are counted in relation to a predetermined number of WBCs and an average of 8000/µl is taken as standard. 200 leucocytes are counted in 100 fields (0.25 µl of blood). All parasite species and forms including both sexual and asexual forms are counted together.

Thin smear: Air dry the thin smear for 10 minutes. After drying, the thin smear should be fixed in methanol. This can be done by either dipping the thin smear into methanol for 5 seconds or by dabbing the thin smear with a methanol-soaked cotton ball. While fixing the thin smear, all care should be taken to avoid exposure of the thick smear to methanol.

Determining the percentage of parasitaemia will be essential for *P. falciparum*. The number of infected red cells (and not number of parasites) in 1000 RBCs is converted to percentage.

+ = 1–10 per 100 thick fields.

++ = 11-100 per 100 thick fields.

+++ = 1–10 per thick field.

++++ = >10 per thick field.

Staining: A number of Romanowsky stains like Field's, Giemsa's, Wright's and Leishman's are suitable for staining the smears.

Quantitative buffy coat test [24,25,26]

It involves staining of the centrifuged and compressed red cell layer with acridine orange and its examination under UV light source.

Method: The QBC tube is a high-precision glass hematocrit tube, pre-coated internally with acridine orange stain and potassium oxalate. It is filled with 55-65 microliters of blood from a finger, ear or heel puncture. A clear plastic closure is then attached. A precisely made cylindrical float, designed to be suspended in the packed red blood cells, is inserted. The tube is centrifuged at 12,000 rpm for 5 minutes. The components of the buffy coat separate according to their densities, forming discrete bands. Because the float occupies 90% of the internal lumen of the tube, the leukocyte and the thrombocyte cell band widths and the top-most area of red cells are enlarged to 10 times normal. The QBC tube is placed on the tube holder and examined using a standard white light microscope equipped with the UV microscope adapter, an epi-illuminated microscope objective. Fluorescing parasites are then observed at the red blood cell/white blood cell interface.

Red cells containing Plasmodia are less dense than normal ones and concentrate just below the leukocytes, at the top of the erythrocyte column. The float forces all the surrounding red cells into the 40 micron space between its outside circumference and the inside of the tube. Since the parasites contain DNA which takes up the acridine orange stain, they appear as bright specks of light among the non-fluorescing red cells.

Rapid diagnostic tests [27]

Immunochromatographic Tests for Malaria Antigens

Immunochromatographic tests are based on the capture of the parasite antigens from the peripheral blood using either monoclonal or polyclonal antibodies against the parasite antigen targets. Currently, immunochromatographic tests can target

1. The histidine-rich protein 2 of P. falciparum
2. A pan-malarial *Plasmodium* aldolase
3. Parasite specific lactate dehydrogenase

Sensitivity: Rapid diagnostic tests for the diagnosis of *P. falciparum* malaria generally achieve a sensitivity of >90% at densities above 100 parasites per µL blood and the sensitivity decreases markedly below that level of parasite density. For the diagnosis of *P. vivax* malaria, the PfHRP2/PMA test has a lower sensitivity compared to that for *P. falciparum* malaria; however, the pLDH test has an equal or better sensitivity for *P. vivax* malaria compared to *P. falciparum* malaria.

Other tests :

Polymerase Chain Reaction (PCR): Using the non-isotopically labelled probe following PCR amplification, it is possible to detect malaria parasites. The PCR test is reportedly 10-fold more sensitive than microscopy.

Treatment [28,29]

Antimalarials – Chloroquine : is the prototype anti malarial drug, most widely used to treat all types of malarial infections. It is also the cheapest, time tested and safe anti malarial agent.

Mechanism of action: Chloroquine inhibits the parasitic enzyme heme polymerase that converts the toxic heme into non-toxic hemazoin, thereby resulting in the accumulation of toxic heme within the parasite.

Anti malarial activity: It is highly effective against erythrocytic forms of *P. vivax*, *P. ovale* and *P. malariae*, sensitive strains of *P. falciparum* and gametocytes of *P. vivax.*

Adverse effects: dizziness, headache, diplopia, disturbed visual accomodation, dysphagia, nausea, malaise, and pruritus of palms, soles and scalp. It can also cause visual hallucinations, confusion, and occasionally frank psychosis.

Dose: Oral- 10mg/kg stat., then three doses of 5 mg/kg, over 36-48 hours

Dose of parenteral chloroquine: **(**Table no.3)

Intra venous infusion	10 mg / kg (max.600mg) in isotonic fluid, over 8 hours; followed by 15 mg / kg (max.900mg) over 24 hours.
Intra muscular or subcutaneous injections	3.5 mg of base/ kg (max.200 mg) every 6 hours or 2.5 mg of base/ kg (max.150mg) every 4 hours. (Intramuscular injection can cause fatal hypotension, especially in children).

Quinine : acts as a blood schizonticide although it also has gametocytocidal activity against *P. vivax* and *P. malariae*.

Dose: Oral- 10 mg/kg 8 hourly for 4 days and 5 mg/kg 8 hourly for 3 days.

Intra venous: 20 mg of salt/kg in 10 ml/kg isotonic saline or 5% dextrose over 4 hours, then 10 mg of salt/kg in saline or dextrose over 4 hours, every 8 hours until patient is able to take orally or for 5-7 days.

Intra muscular: 20 mg/kg stat, followed by 10 mg/kg 8 hourly by deep intra muscular injections for 5-7 days

Pyrimethamine/ Sulphadoxine

Dose**:** **(**Table no.4)

Age in years	**0-1**	**1-5**	**5-9**	**9-14**	**>14**
Dose of 25+500 mg tablet	1/4	1/2	1	2	3

Mefloquine

It is effective against the blood forms of falciparum malaria, including the chloroquine resistant types.

Dose: 15 mg/kg in a single dose. If the dose exceeds 1000 mg, the second dose can be given after 4-8 hours to minimise gastric irritation. Total dose should not exceed 1500 mg.

Halofantrine

It is used in the treatment of chloroquine resistant and multi-drug resistant, uncomplicated *P. falciparum* malaria.

Dose: For adults, three tablets of 500 mg each, 6 hours apart. For children, three doses of 8 mg/kg of the salt 6 hours apart. Treatment should be repeated after 7 days

Artemisinin Derivatives

It is the fastest acting anti malarial available. It inhibits the development of the trophozoites and thus prevents progression of the disease. Young circulating parasites are killed before they sequester in the deep microvasculature. These drugs starts acting within 12 hours.

These drugs prevent the gametocyte development by their action on the ring stages and on the early (stage I-III) gametocytes

Dose:

Artemether - Injection: 3.2 mg/kg intra muscularly as a loading dose, followed by 1.6 mg/kg daily until oral therapy or a maximum of 7 days.

Artesunate – Parenteral: Loading dose of 2.4 mg/kg followed by 2.4mg/kg after 12 hours, 24 hours and once daily thereafter for maximum of 7 days. For children, the recommended dose is 1.2 mg/kg/day for 5-7 days.

Primaquine

It is the essential co-drug with chloroquine in treating all cases of malaria. It is highly effective against the gametocytes of all plasmodia and thereby prevents spread of the disease to the mosquito from the patient. It is also effective against the dormant tissue forms of *P. vivax* and *P. ovale* malaria, and thereby offers radical cure and prevents relapses. It has insignificant activity against the asexual blood forms of the parasite and

therefore it is always used in conjunction with a blood schizonticide and never as a single agent.

Dose: 0.25mg/kg/day (once a day) for 14 days in *P. vivax*; 0.75 mg/kg as single dose in *P. falciparum*

Tetracyclines

It is useful in the treatment of drug resistant *P. falciparum* malaria. They act relatively slowly and hence should always be combined with a faster acting drug like quinine.

Dose: Tetracycline is given at a dose of 250 mg every 6 hours for 7-10 days. Dose of doxycycline is 100 mg twice daily for 7-10 days.

Drug Resistance

It is the ability of the parasite species to survive and/or multiply despite the administration and absorption of a drug given in doses equal to or higher than those usually recommended but within the limit of tolerance. The important factors that are associated with resistance are:

- Longer half-life
- Single mutation for resistance
- Poor compliance
- Host immunity
- Number of people using these drugs

Degree of resistance:

WHO has developed a simple scheme for estimating the degree of resistance that involves studying the parasitemia over 28 days.Smears on day 2, 7 and 28 are done to grade the resistance as R1 to R3. In a case of normal response parasite count to fall to 25% of pre-treatment value by 48 hours and smear should be negative by 7 days

RI, Delayed Recrudescence: The asexual parasitemia reduces to < 25% of pre-treatment level in 48 hours, but reappears between 2-4 weeks.

RI, Early Recrudescence: The asexual parasitemia reduces to < 25% of pre-treatment level in 48 hours, but reappears earlier.

RII Resistance: Marked reduction in asexual parasitemia (decrease >25% but <75%) in 48 hours, without complete clearance in 7 days.

RIII Resistance: Minimal reduction in asexual parasitemia, (decrease <25%) or an increase in parasitemia after 48 hours

Malaria control

Man's Role in Malaria Control: Man is the most important link in the malaria control chain. He can be made to understand the problem and he can help in breaking the chain at multiple points. Therefore great emphasis should be laid on educating the people about malaria and its control, so that common people can effectively contribute in controlling this disease. This includes education of doctors about the need for early diagnosis and prompt treatment of malaria.

1. Early diagnosis and treatment - treat early to reduce parasite load, hence spread; prevent deaths
2. Treat completely to prevent spread and relapse
3. Ensure compliance with complete treatment
4. Personal Protection- prevent malaria by using bed nets, insecticide sprays etc., and by chemoprophylaxis.
5. Seek his help in mosquito control

ABO Blood group system

History of discoveries

The ABO blood group system is widely credited to have been discovered by the Austrian scientist Karl Landsteiner, who found three different blood types in 1900.[31] He was awarded the Nobel Prize in Physiology or Medicine in 1930 for his work. Landsteiner described A, B, and O; Decastrello and Sturli discovered the fourth type, AB, in 1902. Ludwik Hirszfeld and E. von Dungern discovered the heritability of ABO blood groups in 1910–11, with Felix Bernstein demonstrating the correct blood group inheritance pattern of multiple alleles at one locus in 1924.[32]

The **ABO blood group system** is the most important blood type system (or blood group system) in human blood transfusion. The associated anti-A antibodies and anti-B antibodies are usually IgM antibodies, which are usually produced in the first years of life by sensitization to environmental substances such as food, bacteria and viruses.

Biochemical and Genetic Considerations[33]

Structure of A, B and H antigens

A, B, and H antigens have a basic structure that is formed on oligosaccharide chains. These chains are attached to proteins or lipid molecules on the red cell surface. Each chain is made of 4 sugar molecules that are linked in one straight line or branched. Immunodominant sugars present at the terminal ends of the chains confer ABO antigen specificity.

~ A antigen has N-acetylgalactosamine

~ B antigen has D-galactose

~ H antigen has L-fucose

~ O has no additional sugar (H structure)

The inheritance of at least one of the H genes is required for normal ABO expression. Group O individuals (genotype OO) will only have the H antigen on their surface.

Genes

A gene (A, B, O, or H) is a protein that codes for an enzyme that adds a sugar to the precursor substance. These enzymes are known as **transferases** which are responsible for attaching sugars to the precursor substance. There are a few loci that interact with each other: the H locus (chromosome 19), secretor locus (Se) linked to H, and the ABO locus on chromosome 9.[34]

H/h genes:

The two major alleles at the H locus are H and h. The H gene product (L-fucosyltransferase) adds L-fucose to the precursor substance. The h gene is an amorph and results in little or no production of L-fucosyltransferase. If both h genes are inherited (hh), the **Bombay phenotype** (Oh) occurs. Bombay is a rare blood type originally found in India, but has been found elsewhere in the world.

ABO genes:

There are four basic ABO alleles: A_1, A_2, B, and O. Each gene produces a transferase:

~ A gene produces N-acetylgalactosaminyl-transferase

~ B gene produces galactosyl transferase

~ O gene is an amorph

If fucose has been added to the terminal galactose (H antigen), then A and B transferases can add their respective sugars (N-acetylgalactosamine and D-galactose). Remember, H has to be present before A and B antigens can form. When both A and B are inherited, there is competition for the H substrate resulting in a depresses expression of the A antigen.

Secretor (Se/se) genes:

Secretor genes act on cells involved in watery secretions such as saliva, tears, amniotic fluid, digestive fluids, etc. enabling them to secrete glycoproteins with blood group activity. The majority (80%) of the population are secretors (SeSe or sese). Secretor status is determined by a neutralization procedure.[34]

ABO Antigens

ABO antigens can be detected on the red cells of embryos at 5-6 weeks though they are not fully developed at birth. By age 2-4 years, the antigens are developed and remain constand through life.

Subgroups

A_1 and A_2

These are two principle subgroups of A. Both subgroups of A are not dinstinguished very well with routine anti-A, however, they can be serologically dinstinguished based on the reactivity with anti-A_1 (*Dolichos biflorus* or human anti-A_1). When anti-A_1 is added,

- A_1 cells will agglutinate
- A_2 cells will not agglutinate

The majority (80%) of the A and AB population are A_1 or A_1B; the remaining 20% are A_2 or A_2B. Unlike the A_1 gene, the A_2 gene produces a transferase that doesn't convert the H substance into the A antigen very well. As a result, an A_2 individual has significantly fewer antigen sites (75% less) than an A_1 individual. Individuals who are are A_2 or A_2B may produce anti-A_1. Of course, this occurence is small. Anti-A_1 is found in 1-8% of A_2 individuals and 22-30% of A_2B individuals

ABO Antibodies

Development:

Sugar linkages of A, B, and H antigens also occur in other biologic material such as bacteria, dust, food, and other widely distributed agents constituting powerful and continuous antigenic stimuli. Healthy individuals react to those stimuli by producing antibodies against those antigens foreign to their own system. ABO antibodies are actually not "naturally occurring", they should instead be termed "non-red blood cell stimulated".[35]

- Group A serum contains anti-B
- Group B serum contains anti-A
- Group AB serum contains no antibodies
- Group O serum contains anti-A, anti-B, and anti A,B

Anti-H

There are two types of anti-H: cold reacting and the Bombay type.

Cold reacting agglutinin – found occasionally in the serum of an A_1 or A_1B (most of the H has been converted to A and/or B antigens. The following shows a decreasing order of H substance: $O>A_2>B>A_2B>A_1>A_1B$. Commercial anti-H lectin (a seed extract from *Ulex europaeus*) closely parallels the reaction of anti-H in the body.

Bombay anti-H – has a wide thermal range (4-37°C) and can bind complement to cause hemolysis

Anti-A,B

This antibody is found in the serum of group O individuals. It reacts with A, B, and AB cells. It is predominately IgG, with small portions being IgM. Anti-A,B is one antibody, it is not a mixture of anti-A and anti-B antibodies.

Anti-A_1

Group O and B individuals contain anti-A in their serum. However, the anti-A can be separated into different components: anti-A and anti-A_1. Anti-A_1 only agglutinates the A_1 antigen, not the A_2 antigen. There is no anti-A_2.

Time of Appearance

Antibodies develop after birth (about 3-6 months) and reach a fairly stable level at 5-6 years of age and decline in old age. Newborns may have a passively acquired maternal IgG anti-A or anti-B (crosses placenta in utero).

Nature of ABO antibodies

Non-red cell stimulated

Anti-A and anti-B occur so regularly after environmental exposure, they are considered "naturally occurring". There is no recognizable immunizing agent (pregnancy or transfusion) that leads to their appearance. The majority are IgM, but small amounts are IgG.

Red cell stimulated

These types of antibodies have a known stimulus and are associated with pregnancy or transfusion. In pregnancy, there may be an ABO incompatibility with the fetus; with transfusion, there may be an ABO incompatibility with blood or plasma. Characteristics of these antibodies are:

- Usually IgG
- Active at 37°C
- Titer and avidity increase
- Difficult to inhibit
- More common in group O, but may occur in group A or B

Inheritance

Blood groups are inherited from both parents. The ABO blood type is controlled by a single gene with three alleles: *i*, I^A, and I^B. The gene encodes a glycosyltransferase—that is, an enzyme that modifies the carbohydrate content of the red blood cell antigens. The gene is located on the long arm of the ninth chromosome (9q34).

Bombay phenotype

Individuals with the rare Bombay phenotype (*hh*) do not express substance H on their red blood cells, and therefore do not bind A or B antigens. Instead, they produce antibodies to substance H (which is present on all red cells except those of hh genotype) as well as to both A and B antigens, and can therefore receive blood only from other *hh* donors (although they can donate as though they were type O).

Association with von Willebrand factor[36]

The ABO antigen is also expressed on the von Willebrand factor (vWF) glycoprotein, which participates in hemostasis (control of bleeding). In fact, having type O blood predisposes to bleeding, as 30% of the total genetic variation observed in plasma vWF is explained by the effect of the ABO blood group, and individuals with group O blood normally have significantly lower plasma levels of vWF (and Factor VIII) than do non-O individuals. In addition, vWF is degraded more rapidly due to the higher prevalence of blood group O with the Cys1584 variant of vWF (an amino acid polymorphism in VWF):the gene for ADAMTS13 (vWF-cleaving protease) maps to the ninth chromosome (9q34), the same locus as ABO blood type. Higher levels of vWF are more common amongst people who have had ischaemic stroke (from blood clotting) for the first time. The results of this study found that the occurrence was not affected by ADAMTS13 polymorphism, and the only significant genetic factor was the person's blood group.[36]

ABO blood group system and malaria

The ABO blood group system is arguably the best known, and yet the most functionally mysterious, genetic polymorphism in humans. In clinical practice, ABO is the most important system for blood group compatibility. In the century since their discovery, ABO antigen associations with infections and other diseases have been the subject of hundreds of publications.[37,38] Some reports found unexpected associations, such as the susceptibility of group A individuals to salivary or gastric cancers.[39] Much new information has emerged since a relationship between ABO and malaria was first suggested more than 40 years ago.[40] There is hypothesis that *Plasmodium falciparum* malaria has shaped the distribution of ABO blood groups in humans.[40]

During the period from 70 000 to 4000 years ago, multiple human erythrocyte mutations associated with a survival advantage in *P falciparum* infection are thought to have developed. These include structural and quantitative hemoglobinopathies , membrane mutations (spherocytosis, elliptocytosis, ovalocytosis), and enzymopathies (glucose-6-phosphate dehydrogenase [G6PD] deficiency).[41] The prevalence of these malaria-selected mutations, as well as the pressure *P falciparum* exerted on the distribution of blood groups, may have further increased 10 000 years ago when the death toll from *P falciparum* is thought to have increased substantially.[17] This increase in prevalence probably resulted from agriculture, forest-clearing, and animal domestication, all of which promoted success of the *Anopheles* mosquito. As a result, the most intense malarial selection pressures were effectively applied to the human genome in the

relatively compressed period of the past few millennia, coincident with the observed development of multiple adaptive erythrocyte mutations.[42]

Worldwide prevalence

The ratio of group O to A is higher in geographic regions where malaria is currently, or was previously, endemic.[43] An especially high prevalence of group O coupled with a low prevalence of group A is found throughout subSaharan Africa, where *P falciparum* persists to this day. In the Western hemisphere, the distribution of group A and group O generally matches malaria's tropical distribution. From the tropical regions of Central and South America southward, the indigenous peoples are almost exclusively group O. In Asia, the prevalence of group O rises among peoples who live closer to the equator. Group O is the most common blood group in Turkey and Persia.[43] In contrast, group A is the predominant blood group in the colder regions of the Earth, where malaria has not been endemic. Thus, if survival from malaria is associated with group O, and mortality is associated with group A, then the worldwide distribution of ABO groups is consistent with selective pressure from malaria.

Possible mechanisms

The adherence of parasitized RBCs to other cells is central to the pathophysiology of severe malaria syndromes including cerebral malaria, respiratory failure, multiorgan failure, and death.[44] Parasitized RBCs adhere to the vasculature through a process termed "sequestration," closely mimicking inflammatory leukocyte attachment.[45] Furthermore, half of infected RBC isolates form occlusive intravascular aggregates, which consist not

only of infected RBCs bound to each other ("autoagglutinates") but also of infected RBCs bound to uninfected RBCs ("homotypic RBC rosettes") and/or to platelets ("heterotypic RBC rosettes").[46] Sequestration and rosette formation impair blood flow, causing tissue ischemia and cell death.

P falciparum is unique among malaria species in that infected erythrocytes express an adhesive determinant, termed *P falciparum* erythrocyte membrane protein-1 (PfEMP-1). PfEMP-1 is encoded by the parasite genome and is expressed on the outer surface of infected RBCs. PfEMP-1 binds to a variety of target molecules found on RBCs, platelets, and vascular endothelial cells.[44] The structure of PfEMP-1 includes variable numbers of 2 types of adhesive binding domains: Duffy binding-like (DBL) regions and cysteine-rich interdomain regions.[47] DBL-1α demonstrates lectin-like properties, causing it to bind primarily to cells bearing A and B blood group oligosaccharides, and to other glycosylated targets, such as the glycoprotein CD35 (CR1), and heparan sulfate–like glycosaminoglycan.[48] Cysteine-rich interdomain region-1, however, binds principally to CD36 (platelet glycoprotein IV), thus targeting platelets and endothelium. Three lines of evidence suggest a direct role for group A or B antigens in cytoadherence as measured by rosette formation: (1) higher rosette rates and larger rosette sizes among non–group O compared with group O RBCs; (2) rosette disruption by soluble group A or group B oligosaccharides; and (3) correlation of rosette formation with transcription of the lectin-specific binding domain of PfEMP-1. ABO effects on the frequency, size, and strength of rosette formation in vitro were first reported in 1992.[49]

Malaria has been a major selective force on the human population, and several erythrocyte polymorphisms have evolved that confer resistance to severe malaria. *Plasmodium falciparum* rosetting, a parasite virulence phenotype associated with severe malaria, is reduced in blood group O erythrocytes compared with groups A, B, and AB, but the contribution of the ABO blood group system to protection against severe malaria has received little attention.

Human and *P falciparum* coevolution has shaped the proportions of ABO antigens observed in humans across geographic regions. However, the distribution of ABO has also been influenced by other events, including the migration of peoples with founder effects, population splitting from wars and famine, and other lethal pediatric diseases in which survival may be associated with a specific ABO antigen.[50] For example, the possibility that the isohemagglutinins found in group O individuals provide broader immunity against various pathogens has been previously suggested.[51] Review highlights the reduced cytoadherence of *P falciparum* among group O individuals, survival after infection is known to depend on a highly complex interaction between both host and parasite genes.[52] Indeed, the full extent of the selective pressure exerted by *P falciparum* on the human genome has yet to be realized, and new examples of host survival genes continue to be discovered.

METHODOLOGY

MATERIALS AND METHODS

In this study 100 patients with fever, peripheral smear & quantitative buffy coat positive for malarial parasite admitted to B.L.D.E.A's Shri B.M.Patil Medical College, Hospital and Research Center Bijapur, between November 2007 to September 2009 were selected.

Various complications of malaria were noted and were correlated with ABO blood groups and whether any particular complication occurred more frequently in any particular blood group.

Sample size :

As the prevalence of Malaria in India is 2 cases per 1000 population i.e. p=0.2% (Park text book of preventive and social medicine, 18th edition) at 95% level of confidence & with 1% margin of error, the calculated sample size is 76 using statistical formula :

$$n = \frac{(1.96)^2\ p \times (1-p)}{d^2}$$

Minimum sample size = 80

STATISTICAL METHOD

a) Diagrammatic representation

b) Proper statistical tests i.e. chi square test

METHOD OF COLLECTION OF DATA

INCLUSION CRITERIA

a) All patients with history of fever, peripheral smear study & QBC test positive for malarial parasite.

EXCLUSION CRITERIA

a) Cases who have undergone treatment before giving a blood sample

Study design

The study group consisted of 100 cases of malaria. Both thick and and thin smears were prepared and examined for malarial parasite. Quantitative buffy coat study will be done to confirm the presence of malarial parasite. ABO blood grouping to be done using the slide agglutination method at the time of admission and relationship between ABO blood groups and malaria (both complicated and uncomplicated) will be studied. Complications of malaria were studied with respect to various ABO blood groups and to look whether complications occurred with increased and decreased frequency in any particular blood group.

The patient will be regularly looked for signs & symptoms of uncomplicated and complicated malaria during the hospital stay .Patients will be followed up till the patient clinically improves & malarial parasites gets cleared off from the peripheral smear during the course of anti malarial treatment.

OBSERVATION AND RESULTS

Blood groups and complications in all patients

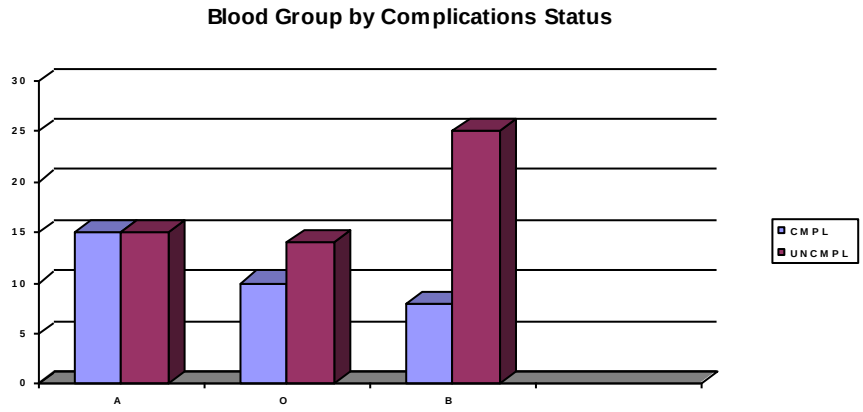
Table showing blood groups and complications in all patients

Table no.5

Blood Group	Complicated	Uncomplicated	Total
A	15	15	30
O	10	14	24
B	8	25	33
Total	33	54	100

Of the 100 malaria cases, 30 cases belonged to blood group A, out of which 15 patients (50%) had complications and 15(50%) with no complications. Out of total 24 O blood group cases, 10(41.66%) had complications and 14(58.33%) were in uncomplicated group. Out of 33 cases which belonged to blood group B, 8 patients (24.24%) had complications and 25 patients (75.75%) had no complications. The association between blood group and malaria has statistical significance.

Graph no.1



Conclusion : Since Chi Square calculated value is greater than tabled value (5.99) at 5% level of significance. That is an association between the said attributes.

Table showing Blood group and complications in falciparum positive patients

Table no.6

Blood Group	Complicated	Uncomplicated	Total	X^2	P Value
A	14	7	21	2.85	P>0.01 (Significant)
O	8	4	12		
B	5	8	13		
Total	27	19	46		

Of the 46 falciparum cases, 21 belonged to blood group A of which 14(66.66%) had complications and 7(33.33%) did not have any complications .Out of 13 patients with B blood group, 5(38.4%) had complications and 8(61.5%) did not have any complications. There was association between blood groups and complications in falciparum positive cases. It was statistically significant.

Graph no.2

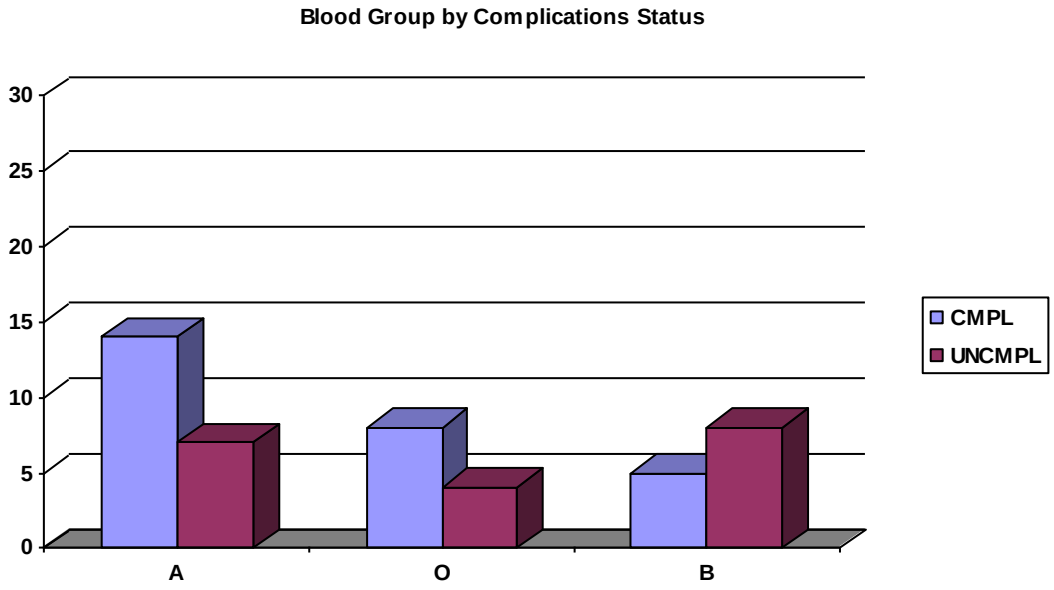


Table for association between blood group and type of complications

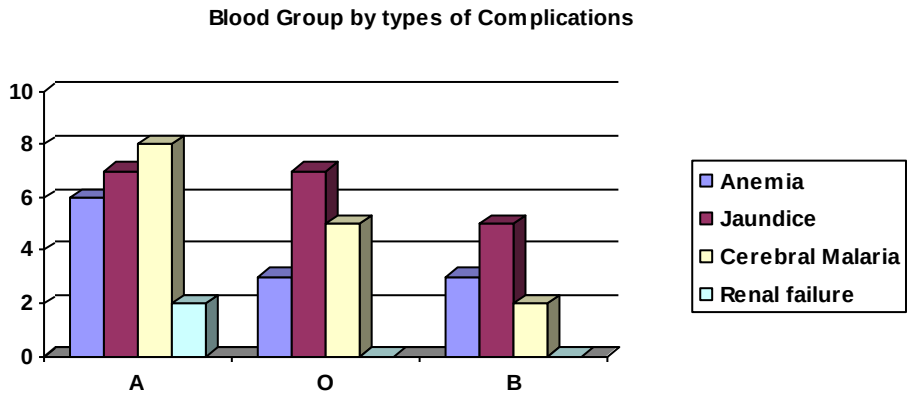
Table no.7

Blood Group	Anemia	Jaundice	Cerebral Malaria	Renal failure	Total
A	6	7	8	2	21
O	3	7	5	0	15
B	3	5	2	0	10
Total	12	19	15	2	47

33 complicated malaria patients were studied. Among patients with A blood group, 6 had severe anemia, 7 had jaundice and 8 had cerebral malaria. Among patients with O blood group 3 had severe anemia, 7 had jaundice and 5 had cerebral malaria. Among patients with B blood group, 3 had severe anemia, 5 had jaundice, 2 had cerebral malaria.

Patients with A blood group had more complications when compared to other blood groups while patients with B blood group had least number of complications in all groups. But the association between blood groups and types of complications was not significant.

Graph no.3



Conclusion : Since Chi Square calculated value is smaller than tabled value (5.99) at 5% level of significance. That is no association between the said attributes.

Table showing relation between blood groups and complications in general

Table no.8

Blood Group	Number	Percent
A	15	45.4
O	10	30.2
B	8	24.4
AB	0	0
Total	33	100

Out of 33 complicated cases, 45.4% of patients belonged to blood group A, 30.2% of patients belonged to blood group O and 24.4% of them were of blood group B. Maximum number of complicated cases belonged to group A.

Graph no.4

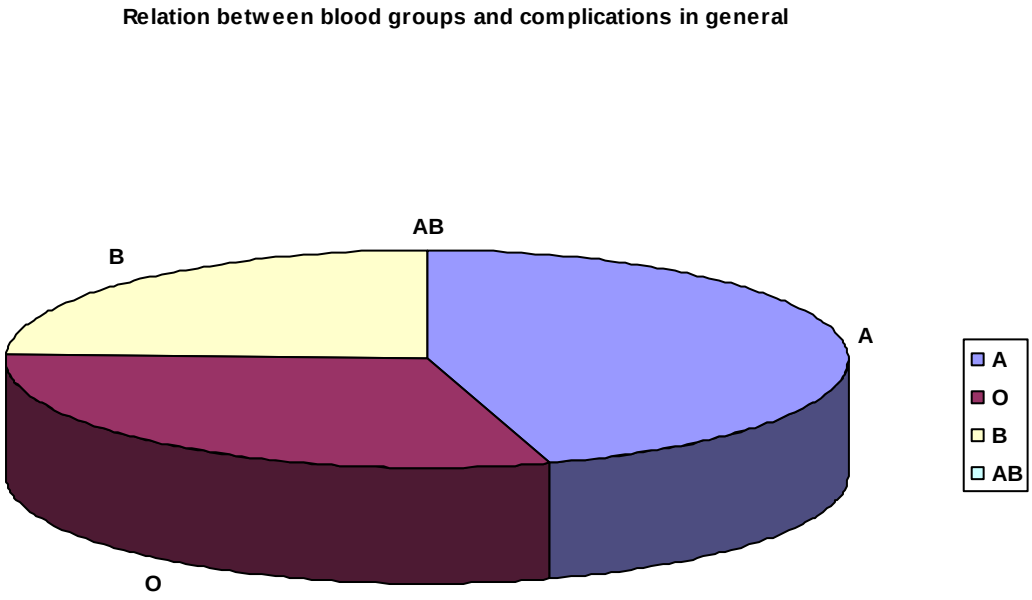


Table showing relation between severe anemia and blood groups

Table no.9

Blood Group	Severe anemia	Percent
A	6	50
O	3	25
B	3	25
Total	12	100

Out of 12 severe anemia cases , 50% of them belonged to A blood group, 25% of them were of O blood group and 25% were of B blood group. Maximum number of patients belonged to A blood group.

Graph no.5

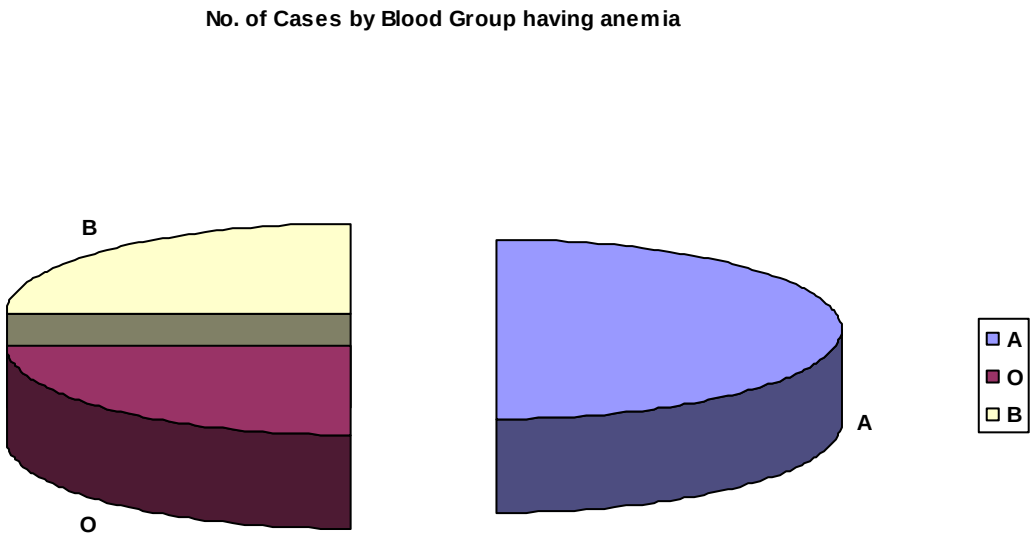


Table showing relation between jaundice and blood groups

Table no.10

Blood Group	Jaundice	Percent
A	7	37
O	7	37
B	5	26
Total	19	100

Out of total 19 jaundice patients, 37% of them were of A blood group, 37% belonged to O blood group and 26% of them belonged to B blood group. Least number of jaundice patients were in B blood group.

Graph no.6

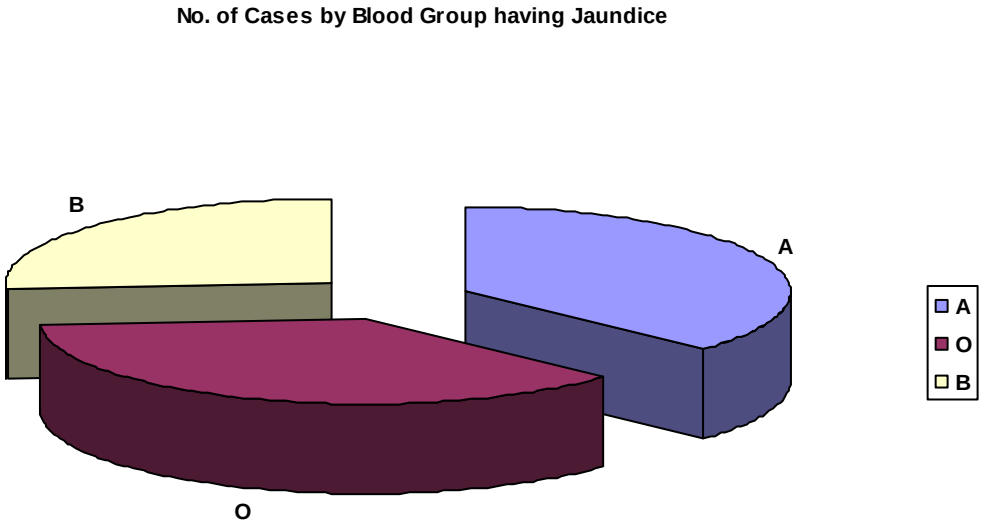


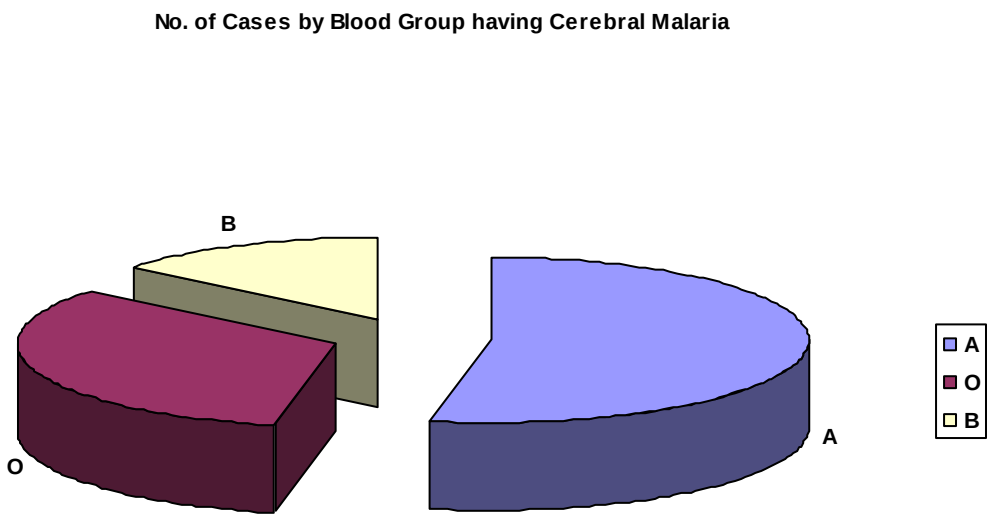
Table showing relation between cerebral malaria cases and blood groups

Table no. 11

Blood Group	Number	Percent
A	8	53
O	5	33
B	2	14
Total	15	100

Out of 15 total cerebral malaria cases, 53% of them belonged to A blood group, 33% were of O blood group and 14% were of B blood group. Maximum number of cases were seen in A blood group with least number in B blood group.

Graph no.7



DISCUSSION

Malaria has been emerging as a major national health problem with considerable morbidity and mortality and has long been eluding our efforts for effective control. Since blood groups are an expression of genetic constitution, it was decided to study their influence on susceptible to malaria.

Of the 100 malaria cases, 30 cases belonged to blood group A, out of which 15(50%) had complications and 15(50%) with no complications. Out of 33 cases which belonged to blood group B, 24% had complications and 76% had no complications. Similar results were obtained with falciparum cases as well.

Of the 46 falciparum cases, 21 belonged to blood group A of which 14 cases(67%) had complications and 7(33%) did not have any complications .Out of 13 patients with B blood group, 5(38.4%) had complications and 8(61.5%) did not have any complications.

In accordance with our study, Lell et al[57] studied complicated malaria cases and found that among all group A individuals, 71% had severe malaria and only 29% had uncomplicated malaria. In contrast to our study, among all group O cases 46% had severe malaria and 54% had uncomplicated malaria.

Pathirana et al[59] studied 243 malaria cases and found that the proportion of blood group A in uncomplicated cases was 25%, but was 33% in severe cases. The distribution of ABO groups was highly statistically different in severe malaria syndromes compared with uncomplicated malaria or the control population.

Since this association is statistically significant, our study shows blood group A patients are susceptible to develop complications of malaria in accordance with Lell et al[57] study.

Also our study shows a kind of protection for complications in blood group B patients suffering from malaria which is not in accordance with Fischer et al[60] who reported favourable outcomes for blood group O.

33 patients were having complicated malaria of which 45% belonged to A blood group. Rowe et al[56] in his study found similar results with 32% of complicated cases belonging to A blood group and 9% to AB blood group. This study again proved the fact that complications occur more frequently in blood group A individuals.

Our study showed maximum number of complications like severe anemia, jaundice, cerebral malaria and renal failure in blood group A individuals. But this association between blood groups and type of complications was not statistically significant.

Chowdhuri et al[58] in Bulletin of World Health Organisation has mentioned patients with blood group A were found to have more complications in the form of cerebral malaria, severe anemia, jaundice and renal failure.

The present study confirms the concept that blood group A individuals with malaria are susceptible to complications than other blood groups. Hence an association exists between ABO blood groups and complications of malaria in general. However an association between ABO blood groups and type of complications was not significant in our study.

CONCLUSION

The present study showed significant association between ABO blood groups and complications in malaria. Patients with blood group A were having more complications compared to the other blood groups. Hence the patients with blood group A may need stringent monitoring in hospital setup to avoid any overt complications.

Also our study shows a kind of resistance to complications in patients with B blood group. This might provide a survival advantage for patients with blood group B in malaria.

SUMMARY

Patients with blood group A had more complications of malaria then other blood groups. Thus blood group A is prone to develop complications while blood group B seems to offer a kind of protection for complications as least number of complications were seen in those individuals.

BIBILIOGRAPHY

1. Capanna E. Grassi versus Ross: who solved the riddle of malaria? Int. Microbiol. 2006;9(1)
2. The Hidden Structure: A Scientific Biography of Camillo Golgi. NEJM. 344 (14):1102.
3. Joy D, Feng X, Mu J, *et al* (2003). "Early origin and recent expansion of Plasmodium falciparum". *Science* **300** (5617): 318–21.
4. Escalante A, Freeland D, Collins W, Lal A (1998). "The evolution of primate malaria parasites based on the gene encoding cytochrome b from the linear mitochondrial genome". *Proc Natl Acad Sci USA* **95** (14): 8124–9.
5. Cox F (2002). "History of human parasitology". *Clin Microbiol Rev* **15** (4): 595–612.
6. A brochure for malaria medical officers : A.P. Ray, M.V.V.L. Narasimham, N.L. Kalra, Indian Society for malaria and other communicable diseases, New Delhi, July 1992.
7. Malaria Report of a scientific group of Indian College of Physicians N.P. Misra (ed); Technical Report Series II, Indian College of Physicians, Bombay 1996.
8. Severe and complicated malaria, World Health Organization malaria action programme, Transactions of the Royal Society of Tropical medicine and Hygiene, Vol. 80 Supplement 1986.
9. Malaria in Park's text book of preventive and social medicine, K. Park, Bhanarasidas Bhanot Publishers, Fifteenth Ed., 1997; pp 188-202

10. Marcucci C, Madjdpour C, Spahn D (2004). "Allogeneic blood transfusions: benefit, risks and clinical indications in countries with a low or high human development index". *Br Med Bull* **70**: 15–28.
11. Talman A, Domarle O, McKenzie F, Ariey F, Robert V (2004). "Gametocytogenesis: the puberty of Plasmodium falciparum". *Malar J* **3**: 24.
12. Bledsoe, G. H. (December 2005) "Malaria primer for clinicians in the United States" *Southern Medical Journal* 98(12): pp. 1197–204
13. Sturm A, Amino R, van de Sand C, Regen T, Retzlaff S, Rennenberg A, Krueger A, Pollok JM, Menard R, Heussler VT (2006). "Manipulation of host hepatocytes by the malaria parasite for delivery into liver sinusoids". *Science* **313**: 1287–1490.
14. Cogswell FB (January 1992). "The hypnozoite and relapse in primate malaria". *Clin. Microbiol. Rev.* **5** (1): 26–35.
15. Adams S, Brown H, Turner G (2002). "Breaking down the blood-brain barrier: signaling a path to cerebral malaria?". *Trends Parasitol* **18** (8): 360–6.
16. Chen Q, Schlichtherle M, Wahlgren M (July 2000). "Molecular aspects of severe malaria". *Clin. Microbiol. Rev.* **13** (3): 439–50.
17. Beare NA, Taylor TE, Harding SP, Lewallen S, Molyneux ME (November 2006). "Malarial retinopathy: a newly established diagnostic sign in severe malaria". *Am. J. Trop. Med. Hyg.* **75** (5): 790–7
18. Trampuz A, Jereb M, Muzlovic I, Prabhu R (2003). "Clinical review: Severe malaria". *Crit Care* **7** (4): 315–23.

19. Kain K, Harrington M, Tennyson S, Keystone J (1998). "Imported malaria: prospective analysis of problems in diagnosis and management". *Clin Infect Dis* **27** (1): 142–9.
20. Dilip R Karnad. Malaria. API textbook of internal medicine,2003;(7):104-109.
21. New Perspectives - Malaria Diagnosis : Report of a joint WHO/USAID informal consultation 25–27 october 1999 p 11
22. Castelli F, Carosi G. Diagnosis of malaria infection In Castelli F, Carosi G ed Handbook of malaria infection in the tropics. Organissazione per la cooperazione sanitaria internazionale 1997 pp 114
23. Warhurst DC, William J Laboratory diagnosis of malaria ACP Broadsheet No 148 J Clin Path 1996;49:533-8
24. Adeoye GO, Nga IC. Comparison of Quantitative Buffy Coat technique (QBC) with Giemsa-stained thick film (GTF) for diagnosis of malaria. *Parasitology International* 2007;56(4):308-312.
25. Cabezos J, Bada JL. The diagnosis of malaria by the thick film and the QBC: a comparative study of both technics *Med Clin (Barc)* 1993;101:91-4.
26. Pinto MJ, Rodrigues SR, Desouza R, Verenkar MP. Usefulness of quantitative buffy coat blood parasite detection system in diagnosis of malaria. Indian J Med Microbiol 2001;19:219-21.
27. Rapid Diagnosis of Malaria. *Lab Medicine.* 2003 Aug;8(34):602-608
28. The treatment of malaria: N.J. White, NEJM: 335:11:800-806: 12.9.1996.
29. Drugs used in the chemotherapy of protozoal infections, Malaria, James W. Tracy and Leslie T. Webster, Jr., in Goodman and Gilman's The pharmacological basis

of therapeutics, Joel G Hardman and Lee E. Limbird (ed-in-chief), Ninth edition, McGraw Hill, 1996; pp 965-985.

30. Nicholas J.White, Joel G. Breman. Malaria. Harrisons principles of Internal medicine. 2008;(7):1280-1285.
31. Landsteiner K (1900). "Zur Kenntnis der antifermentativen, lytischen und agglutinierenden Wirkungen des Blutserums und der Lymphe". *Zentralblatt Bakteriologie* **27**: 357–62.
32. Crow J (1993). "Felix Bernstein and the first human marker locus". *Genetics* **133** (1): 4–7.
33. Seltsam A, Hallensleben M, Kollmann A, Blasczyk R (2003). "The nature of diversity and diversification at the ABO locus". *Blood* **102** (8): 3035–42.
34. Ogasawara K, Bannai M, Saitou N, *et al* (1996). "Extensive polymorphism of ABO blood group gene: three major lineages of the alleles for the common ABO phenotypes". *Human Genetics* **97** (6): 777–83.
35. Calafell, Francesc; *et al* (September 2008). "Evolutionary dynamics of the human *ABO* gene". *Human Genetics* **124** (2): 123–135.
36. Gill, JC; Endres-Brooks J, Bauer PJ, Marks WJ, Montgomery RR (June 1987). "The effect of ABO blood group on the diagnosis of von Willebrand disease" (abstract). *Blood* **69** (6): 1691–5
37. Moulds JM and Moulds JJ. Blood group associations with parasites, bacteria, and viruses. Transfusion Med Rev 2000; 14:302–311.

38. Frattali A and Spitalnik S L. Blood Group Antigens as Receptors for Pathogens. In Blancher A, Klein J, Socha WW (Eds.). Molecular Biology and Evolution of Blood Group and MHC Antigens in Primates1997;Heidelberg Springer pp. 268–304.
39. Aird I, Bentall HH, Fraser Roberts JA. A relationship between cancer of the stomach and the ABO blood groups. Br Med J 1953; 1:799–801.
40. Athreya BH and Coriell LL. Relation of blood groups to infection: I A survey and review of data suggesting possible relationship between malaria and blood groups. Am J Epidemiol 1967; 86:292–304.
41. Kay AC, Kuhl W, Prchal J, Beutler E. The origin of glucose-6-phosphate-dehydrogenase (G6PD) polymorphisms in African-Americans. Am J Hum Genet 1992; 50:394–398.
42. Carter R and Mendis KN. Evolutionary and historical aspects of the burden of malaria. Clin Micro Rev 2002; 15:564–594.
43. Mourant AE, Kopec AC, Domaniewska-Sobczak K. The distribution of the human blood groups and other polymorphisms 2 nd ed. London Oxford University Press1976.
44. Sherman IW, Eda S, Winograd E. Cytoadherence and sequestration in Plasmodium falciparum: defining the ties that bind. Microbes Infect 2003; 5:897–909.
45. Ho M, Hickey MH, Murray AG, Andonegui G, Kubes P. Visualization of Plasmodium falciparum-endothelium interactions in human microvasculature: mimicry of leukocyte recruitment. J Exp Med 2000; 192:1205–1210.

46. Pain A, Ferguson DJP, Kai O, et al. Platelet-mediated clumping of Plasmodium falciparum-infected erythrocytes is a common adhesive phenotype and is associated with severe malaria. Proc Nat Acad Sci 2001; 98:1805–1810.
47. Smith JD, Gamain B, Baruch DI, Kyes S. Decoding the language of var genes and Plasmodium falciparum sequestration. Trends Parasitol 2001; 17:538–545.
48. Chen Q, Schlichtherle M, Wahlgren M. Molecular aspects of severe malaria. Clin Micro Rev 2000; 13:439–450.
49. Carlson J and Wahlgren M. Plasmodium falciparum erythrocyte rosetting is mediated by promiscuous lectin-like interactions. J Exp Med 1992; 176:1311–1317.
50. Mielke JH, Konigsberg LW, Relethford JH. Human Biological Variation. Oxford Oxford University Press2005.
51. Oliver-Gonzalez J and Torregrosa MR. A substance in animal parasites related to the human isoagglutinogens. J Infect Dis 1944; 74:173–177.
52. Williams TN. Human red blood cell polymorphisms and malaria. Curr Opin Microbiol 2006; 9:389–394
53. World Health Organization. Severe and complicated malaria. *Trans R Soc Trop Med Hyg.* 1990;**84**(suppl 2):S1–S65.
54. Gachot B, Wolff M, Nissack G, Veber B, Vachon F. Acute lung injury complicating imported *Plasmodium falciparum* malaria. *Chest.* 1995;**108**:746–749.
55. World Health Organization. Severe falciparum malaria. *Trans R Soc Trop Med Hyg.* 2000;**94**(suppl 1):S1–S90.

56. J. Alexandra Rowe **,** Ian G. Handel***,** Mahamadou A. Thera et al. Blood group O protects against severe *Plasmodium falciparum* malaria through the mechanism of reduced rosetting. PNAS. 2007;104:7471-17476.

57. Lell B, May J, Schmidt-Ott RJ, et al. The role of red blood cell polymorphisms in resistance and susceptibility to malaria. Clin Infect Dis 1999; 28:794–799.

58. Chowdhuri and gupta. Bulletin of the World Health Organisation. 1980;58(6):913-915

59. Pathirana SL, Alles HK, Bandara S, et al. ABO-blood-group types and protection against severe Plasmodium falciparum malaria. Ann Trop Med Parasitol 2005; 99:119–124.

60. Fischer PR and Boone P. Short report: Severe malaria associated with blood group. Am J Trop Med Hyg 1998; 58:122–123

BLDEA'S SHRI. B. M. PATIL MEDICAL COLLEGE HOSPITAL AND RESEARCH CENTRE, BIJAPUR

RELATIONSHIP BETWEEN ABO BLOOD GROUPS AND SEVERITY OF MALARIA

PROFORMA

Name:	IP. No:
Age:	Address:
Sex:	Date of Admission:
Occupation:	Date of Discharge:
Religion:	Status at Discharge:

PRESENTING COMPLAINTS:

HISTORY OF PRESENTING ILLNESS:

PAST HISTORY:

History of malaria in the past :

PERSONAL HISTORY:

FAMILY HISTORY:

GENERAL PHYSICAL EXAMINATION:

Pallor:

Icterus:

Cyanosis:

Clubbing:

Pedal edema:

Lymphadenopathy:

Vital Signs:

Pulse rate :

Blood pressure :

Temperature :

Respiratory rate :

GASTROINTESTINAL SYSTEM

Inspection :

Palpation :

Splenomegaly:

Hepatomegaly:

Percussion :

Auscultation :

CARDIOVASCULAR SYSTEM :

RESPIRATORY SYSTEM :

CENTRAL NERVOUS SYSTEM :

COMPLICATIONS OF MALARIA :

Impaired consciousness :

Prostration :

Jaundice :

Cerebral malaria :

Generalised convulsions :

Severe anemia :

Renal failure :

Hypoglycemia :

Fluid electrolyte, acid base disturbances :

Pulmonary oedema :

Algid malaria :

DIC :

Hyperpyrexia :

PROVISIONAL DIAGNOSIS :

INVESTIGATIONS

HAEMATOLOGY

Haemoglobin	gm/dl
TC	Cells/mm^3
DC	
Neutrophils	%
Lymphocytes	%
Eosinophils	%
Basophils	%
Monocytes	%
ESR	mm/1hr
Blood group	
Peripheral smear study for malarial parasite	
QBC test	
Follow up peripheral smear study for malarial parasite	

URINE

Albumin	
Sugar	
Microscopy	

RBS	mg/dl

RENAL FUNCTION TESTS

Urea	mg/dl
Creatinine	mg/dl
Sodium	meq/L
Potassium	meq/L

LIVER FUNCTION TESTS

Total bilirubin	mg/dl
Conjugated bilirubin	mg/dl
Unconjugated bilirubin	mg/dl
Total protein	gm/dl
Albumin	gm/dl
A/G ratio	
SGOT	IU/L
SGPT	IU/L
ALP	IU/L

DIAGNOSIS

SHRI B.M. PATIL MEDICAL COLLEGE, HOSPITAL AND RESEARCH CENTER, BIJAPUR – 586103.

CONSENT FORM

TITLE OF RESEARCH : RELATIONSHIP BETWEEN ABO BLOOD GROUPS AND SEVERITY OF MALARIA

GUIDE : DR. M.S. Mulimani

P.G. STUDENT : DR. Tanmay.R.Bhat

PURPOSE OF RESEARCH:

I have been informed that the purpose of this study is to evaluate the relationship between ABO blood groups and severity of malaria.

PROCEDURE:

I understand that I will undergo detailed history and clinical examination after which blood will be collected & sent to the laboratory for investigations.

RISKS AND DISCOMFORTS:

I understand that there is no risk involved and I may experience mild pain during the collection of blood.

BENEFITS:

I understand that my participation in this study will help in recognition of existence of relationship between ABO blood groups and malaria that will ultimately benefit my fellow beings.

CONFIDENTIALITY:

I understand that the medical information produced by the study will become a part of hospital record and will be subjected to confidentiality and privacy regulations of hospital. If the data is used for publications, the identity of the patient will not be revealed.

REQUEST FOR MORE INFORMATION:

I understand that I may ask for more information about the study at any time.

REFUSAL OR WITHDRAWAL OF PARTICIPATION:

I understand that my participation is voluntary and I may refuse to participate or withdraw for study at any time.

INJURY STATEMENT:

I understand in the unlikely event of injury to me during the study I will get medical treatment but no further compensations.

(Signature of Guardian) (Signature of patient)

(If the patient is conscious, well oriented and fully aware)

KEY TO MASTER CHART

Ane – Severe anemia

CM – Cerebral malaria

Compl – Complicated

IP – In patient

Jau – Jaundice

no. - Number

P – Present

Pf – Plasmodium falciparum

Pv – Plasmodium vivax

RF – Renal failure

Uncompl – Uncomplicated

+ve – Positive

-ve - Negative

Sl – Serial

MASTER CHART

Sl.no.	Name	Age	Sex	IP.no.	Bld.gp.	Parasite	Severity	Ane	Jau	CM	RF
1	Lalu	55	M	13238	B+ve	Pf	Compl		P		
2	Savitri	65	F	15041	A+ve	Pf	Uncompl				
3	Sugalawwa	45	F	15866	A+ve	Pf	Compl	P			
4	Mahanand	21	F	10937	O+ve	Pv	Uncompl				
5	Mamataz	24	F	10920	B+ve	Pv	Uncompl				
6	Shashikala	35	F	9450	A+ve	Pv	Compl	P			
7.	Sharanappa	49	M	3885	B+ve	Pf	Compl		P		
8.	Siddanagowda	20	M	10048	B+ve	Pv	Compl	P	P		
9.	Bapu	32	M	10418	B+ve	Pv	Uncompl				
10.	Mahadev	55	M	9770	AB+ve	Pf	Uncompl				
11.	Prakash	32	M	2528	B+ve	Pv	Uncompl				
12.	Sahebalal	55	M	9349	O+ve	Pf	Compl		P	P	
13.	Revanasidda	18	M	9713	A+ve	Pf	Compl	P			
14.	Siddu	25	M	555	AB+ve	Pf	Uncompl				
15.	Dasarewwa	55	F	12771	O+ve	Pf	Compl		P	P	
16.	Ammeena	55	F	11340	B+ve	Pf	Uncompl				
17.	Mynabai	55	F	987	O+ve	Pv	Uncompl				
18.	Usman	60	M	1105	A+ve	Pv	Uncompl				
19.	Suvarna	38	F	10411	A+ve	Pv&Pf	Uncompl				
20.	Bashasab	45	M	10833	A+ve	Pf	Compl		P		P
21.	Shankaramma	80	F	4811	B+ve	Pf	Uncompl				
22.	Mahadevappa	71	M	11531	A+ve	Pf	Uncompl				
23.	Shivalila	19	F	11891	AB+ve	Pv	Uncompl				
24.	Krishnaji	46	M	592	B+ve	Pv	Uncompl				
25.	Tippanna	45	M	13165	A+ve	Pf	Uncompl				
26.	Chandbasha	25	M	2428	B+ve	Pf	Compl		P	P	
27.	Chandappa	45	M	14466	O-ve	Pf	Compl		P		
28.	Siddayya	32	M	15844	B+ve	Pv	Uncompl				
29.	Yallawwa	80	F	10214	O+ve	Pv	Uncompl				
30.	Basappa	42	M	1920	A+ve	Pf	Uncompl				
31.	Shankarappa	60	M	7203	A+ve	Pf	Compl		P	P	
32.	Ramanagowda	25	M	262	A+ve	Pv	Uncompl				
33.	Basappa	23	M	14464	O+ve	Pf	Compl		P		
34.	Mallappa	27	M	1241	O+ve	Pv	Uncompl				
35.	Honnavva	26	F	13740	A+ve	Pv & Pf	Compl		P	P	

Sl.no.	Name	Age	Sex	IP.no.	Bld.gp.	Parasite	Severity	Ane	Jau	CM	RF
36.	Bhimasingh	42	M	13959	A+ve	Pf	Compl		P	P	
37.	Siddamma	40	F	13247	B+ve	Pv	Uncompl				
38.	Sabu	35	M	1528	A+ve	Pv & Pf	Uncompl				
39.	Prakash	32	M	2528	B+ve	Pv	Uncompl				
40.	Iranna	52	M	2999	O+ve	Pf	Uncompl				
41.	Shanta	59	F	2563	B+ve	Pv	Uncompl				
42.	Tayappa	38	M	16910	B+ve	Pf	Uncompl				
43.	Ambreesh	18	M	16161	O+ve	Pf	Uncompl				
44.	Somaraya	40	M	3094	B+ve	Pf	Uncompl				
45.	Meghabai	40	F	3178	AB+ve	Pf	Uncompl				
46.	Shreeshail	20	M	3028	O+ve	Pv	Compl	P			
47.	Santosh	20	M	11014	B-ve	Pv	Uncompl				
48.	Kavitabai	25	F	12372	O+ve	Pv & Pf	Uncompl				
49.	Palewwa	65	F	11830	B+ve	Pv	Uncompl				
50.	Mahadevi	35	F	11822	AB-ve	Pv	Uncompl				
51.	Sharanappa	55	M	11617	A+ve	Pf	Compl		P		
52.	Saddam	25	M	11191	B+ve	Pv	Uncompl				
53.	Siddappa	65	M	2321	O+ve	Pv	Uncompl				
54.	Sangappa	55	M	16165	AB+ve	Pf	Uncompl				
55.	Mahadevi	45	F	1341	B+ve	Pf	Uncompl				
56.	Sharanappa	60	M	1083	O+ve	Pv	Compl	P	P		
57.	Neelawwa	50	F	85	B+ve	Pf	Uncompl				
58.	Yallappa	30	M	30	A+ve	Pf	Compl	P			
59.	Revati	20	F	1702	A+ve	Pv	Uncompl				
60.	Mallappa	60	M	3138	O-ve	Pv	Uncompl				
61.	Gangadhar	47	M	4225	AB+ve	Pv	Uncompl				
62.	Renuka	34	F	2960	O+ve	Pf	Uncompl				
63.	Sanjeev	22	M	4305	AB+ve	Pv	Uncompl				
64.	Husensab	22	M	4768	A+ve	Pv	Uncompl				
65.	Ramesh	23	M	3866	B+ve	Pv	Uncompl				
66.	Shreeshail	30	M	411	O+ve	Pf	Compl		P	P	
67.	Chanabasappa	60	M	3260	O+ve	Pf	Compl		P		
68.	Chandamma	18	F	2428	A+ve	Pf	Compl			P	
69.	Channamma	67	F	676	B+ve	Pv	Compl			P	
70.	Usman	60	M	1105	A+ve	Pv	Uncompl				

Sl.no.	Name	Age	Sex	IP.no.	Bld.gp.	Parasite	Severity	Ane	Jau	CM	RF
71.	Swarika	20	F	4672	O+ve	Pv	Uncompl				
72.	Pooja	20	F	4661	A+ve	Pv	Uncompl				
73.	Arjun	34	M	4393	B+ve	Pf	Compl		P		
74.	Shankaramma	20	F	8707	B+ve	Pf	Compl	P			
75.	Devappa	24	M	8841	B+ve	Pv	Compl	P			
76.	Basavaraj	32	M	8935	A+ve	Pf	Compl			P	
77.	Balawwa	42	F	5361	A+ve	Pf	Compl	P		P	
78.	Sajjad	66	M	7006	A-ve	Pv	Uncompl				
79.	Mallappa	40	M	5468	A+ve	Pf	Compl		P	P	
80.	Renuka	35	F	10786	A+ve	Pf	Compl	P	P		P
81.	Mamata	30	F	11777	B+ve	Pv	Uncompl				
82.	Basavaraj	38	M	11877	A+ve	Pv	Uncompl				
83.	Savita	18	F	11977	O+ve	Pf	Compl	P		P	
84.	Shantawwa	44	F	11687	O+ve	Pv	Uncompl				
85.	Mahesh	45	M	11656	B+ve	Pv & Pf	Uncompl				
86.	Khajabee	45	F	11677	AB+ve	Pv	Uncompl				
87.	Nagamma	45	F	10842	B+ve	Pf	Uncompl				
88.	Basavaraj	32	M	11232	B+ve	Pv	Uncompl				
89.	Mahantesh	24	M	11642	A+ve	Pv	Uncompl				
90.	Siddamma	50	F	11436	O+ve	Pv	Uncompl				
91.	Savitri	41	F	11432	AB+ve	Pv	Uncompl				
92.	Manjula	34	F	11322	A-ve	Pf	Uncompl				
93.	Tukaram	32	M	11235	AB-ve	Pv	Uncompl				
94.	Malanabee	40	F	11384	AB-ve	Pv & Pf	Uncompl				
95.	Rajendra	44	F	10250	B+ve	Pv	Uncompl				
96.	Dasappa	39	M	10661	O+ve	Pv	Uncompl				
97.	Sanganagowda	30	M	10903	B+ve	Pv & Pf	Uncompl				
98.	Rajashekar	30	M	10749	O+ve	Pf	Compl			P	
99.	Bowrawwa	34	F	11670	AB+ve	Pv	Uncompl				
100.	Saidamma	18	F	12170	A+ve	Pf	Compl			P	