"GALL BLADDER WALL THICKNESS IN DENGUE AND ITS ASSOCIATION WITH THE DISEASE SEVERITY"

Dissertation submitted to

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CHENNAI

APRIL 2017

CERTIFICATE

This is to certify that the dissertation titled **"GALL BLADDER WALL THICKNESS IN DENGUE AND ITS ASSOCIATION WITH THE DISEASE SEVERITY"** is a bonafide work done **by Dr.RAMU KRISHNAN .U** , Post graduate student, Institute of Internal Medicine, Madras Medical College, Chennai-03, in partial fulfillment of the University Rules and Regulations for the award of Degree of MD General Medicine (Branch - I), Internal Medicine, under our guidance and supervision, during the academic year 2014 – 2017.

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DECLARATION

I solemnly declare that the dissertation entitled "**GALL BLADDER WALL THICKNESS IN DENGUE AND ITS ASSOCIATION WITH THE DISEASE SEVERITY"** is done by me at Madras Medical College, Chennai – 3 during April 2016 to September 2016 under the guidance and supervision of **Prof.K.SRINIVASAGALU M.D., & Prof.S.MAYILVAHANAN M.D.,** To be submitted to The Tamilnadu Dr. M.G.R Medical University towards the partial fulfillment of requirements for the award of **M.D. DEGREE IN GENERAL MEDICINE BRANCH – I.**

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Last but not the least, I wish to thank all the patients without whom the study would have been impossible.

ABBREVIATIONS

DENV	-	Dengue Virus
DHF	-	Dengue hemorrhagic Fever
DSS	-	Dengue Shock Syndrome
DF	-	Dengue Fever
WHO	-	World Health Organisation
CDC	-	Centre for Disease Control
SAARC	-	South Asian association for regional cooperation
BP	-	Blood Pressure
GBWT	-	Gall bladder Wall thickness
SGPT	-	Serum glutamate – Pyruvate trans aminase.
SGOT	-	Serum glutamate – Oxalo Acetate trans aminase
HCT	-	Haematocrit
PCV	-	Packed cell volume
GIT	-	Gastro intestinal system
CNS	-	Central Nervous System
CVS	-	Cardio vascular System
RS	-	Respiratory System
MODS	-	Multi Organ Dysfunction Syndrome

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MASTER CHART

INTRODUCTION

One of the greatest tragedies in modern world is the rise in the viral infections causing epidemics and pandemics claiming thousands of lives. Adding to the problem is the lack of specific treatment in most of these diseases. So the only option that leaves is the accurate and early diagnosis of these diseases.

One such disease is the Dengue fever caused by Dengue virus. Came into limelight just about 5o years back, the disease is now prevalent in more than 100 countries causing mortality and morbidity year after year[1]. The incidence of dengue in endemic countries is around 50 million annually[2]. At any given time about 40% of the world's population is at risk of acquiring dengue infection. In 2005 the world health assembly revised the international health regulations adding dengue to the list of disease of public health emergencies due to the rapid spread of the disease.

Dengue fever produces a wide spectrum of disease manifestations ranging from mild febrile illness to severe forms like dengue hemorrhagic fever and dengue shock syndrome. So the main challenge a physician faces in an epidemic of dengue is monitoring of patients to look for early signs of deterioration. It has been

possible by means of an array of laboratory investigations. Plasma leakage is the most common internal abnormality associated with dengue infection and most complications are directly proportional to the severity of plasma leakage. There are several methods to assess plasma leakage. One of them is the increase in gall bladder wall thickness which has direct correlation with severity of plasma leakage according to many studies done elsewhere. The best advantage of this is method is that it is a cheap and quick method and also it can be done as a routine bed-side test. The procedure is a painless and non-invasive method and it can also look into other organs like pleura for pleural effusion and kidneys for peri-nephric collection all adding to better prognostification of the disease and better patient care.

AIMS AND OBJECTIVES

1. To evaluate the role of increase in gall bladder thickness in dengue fever.

2. To correlate the increased gall bladder thickness with dengue severity and prognosis.

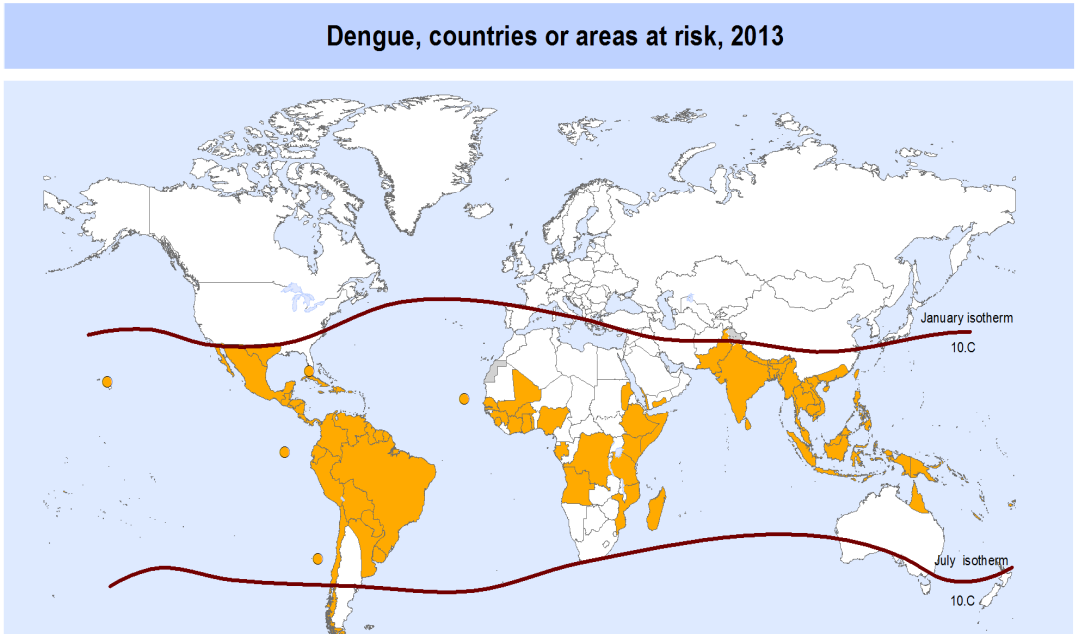
REVIEW OF LITERATURE

History of dengue

Dengue is an age old disease. There has been hieroglyphics from ancient Egypt of 2000 yrs mentioning of dengue like illness spread by mosquitoes as curse of Gods. Chinese manuscripts of the 4th century mentions about the "water disease" associated with flying and biting insects causing fever and joint pains and bleeding manifestations[3]. This is perhaps the first record of dengue. The first outbreak of dengue in the new world took place in the French West Indies and Panama in the 17th century. As the exploration by sea became common mosquitoes and human carriers helped to carry the disease to different parts of the world. The word dengue came from the word Ka-dingapepo called the disease of the devil. It was called as breakbone fever by Benjamin Rush who first reported the disease by clinical methods and he called it so because of the severe arthralgia and myalgia associated with the disease.

Beyond origins and geography the disease has now become a pandemic and is a great threat to health care. The first pandemic of dengue occurred in south east Asia and since regular outbreaks are happening year by year. [4]The first case of dengue in India was

reported in 1946 in Calcutta and the first epidemic occurred in 1963-1964.



Dengue- Global scenario

It is now an established fact that dengue is a worldwide concern, but south east Asia is the hot spot of the disease. The disease which was previously limited to few countries is now endemic in 110 countries. Cases in Americas, SE Asia, and western pacific exceeded 1.2 million in 2008 and in 2013 it is over 3 million[5]. Now outbreaks of Dengue exists even in European countries. About 500,000 cases of severe

dengue are reported each year of which 2.5% die, the major proportion of them being children[6].

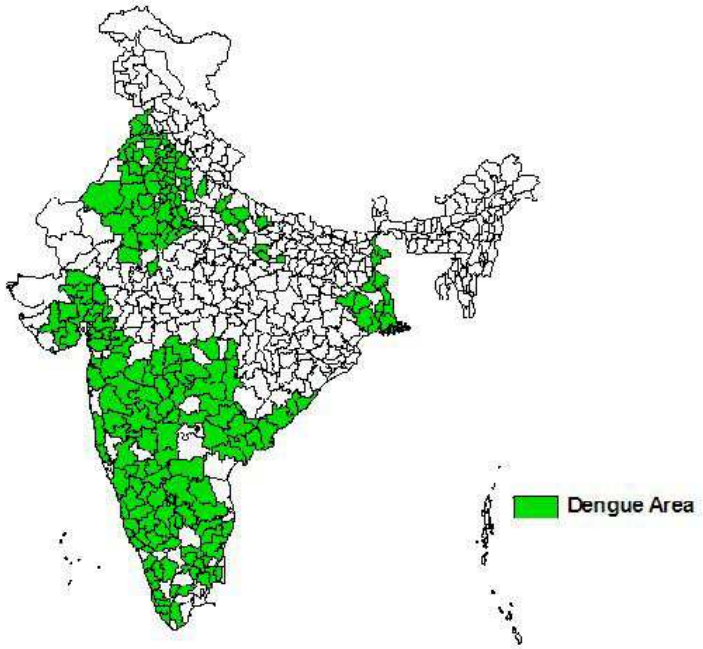
Dengue-Indian Scenario

The first case of dengue was reported in Chennai in 1780 and the virus was isolated in Kolkata in 1944 in US soldiers[6]. The dengue hemorrhagic fever started showing up in 1988 and first epidemic in 1996. Since there has been recurrent outbreaks in India. Highest outbreak occurred in 2015 with reported cases of 90,000 and deaths of 180[7].

Year wise Dengue cases in India

Year	Cases	Death
2009	15500	96
2010	28300	110
2011	18860	160
2012	50200	240
2013	75800	195
2014	40570	140
2015	90040	180

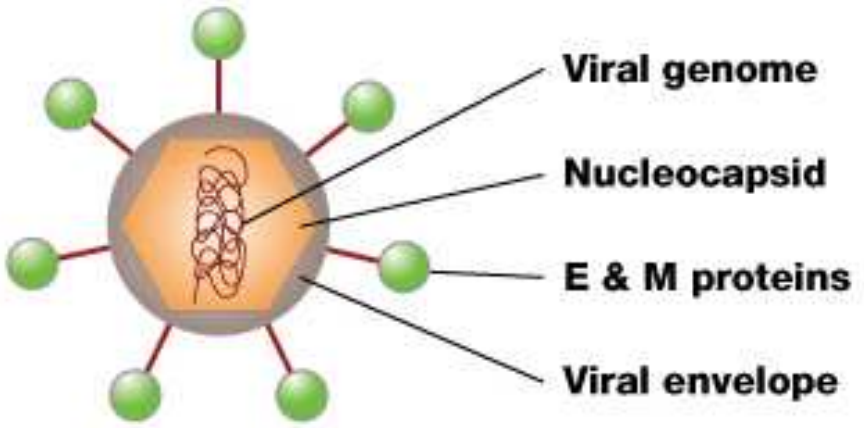
Distribution of dengue in India[8]



The virus

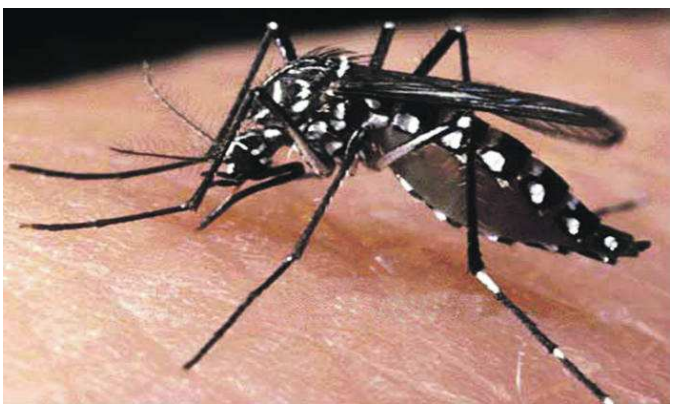
The virus is an Arbovirus belonging to genus Flaviviridae[9]. It is a single stranded RNA virus. It has 4 serotypes DENV-1,2,3 and4.

Serotype 2 is associated with severe form of dengue infection. All 4 types are prevalent in India. Infection with 1 serotype does not confer immunity against another. A dengue re-infection is attributed with more severe form of dengue.



The vector

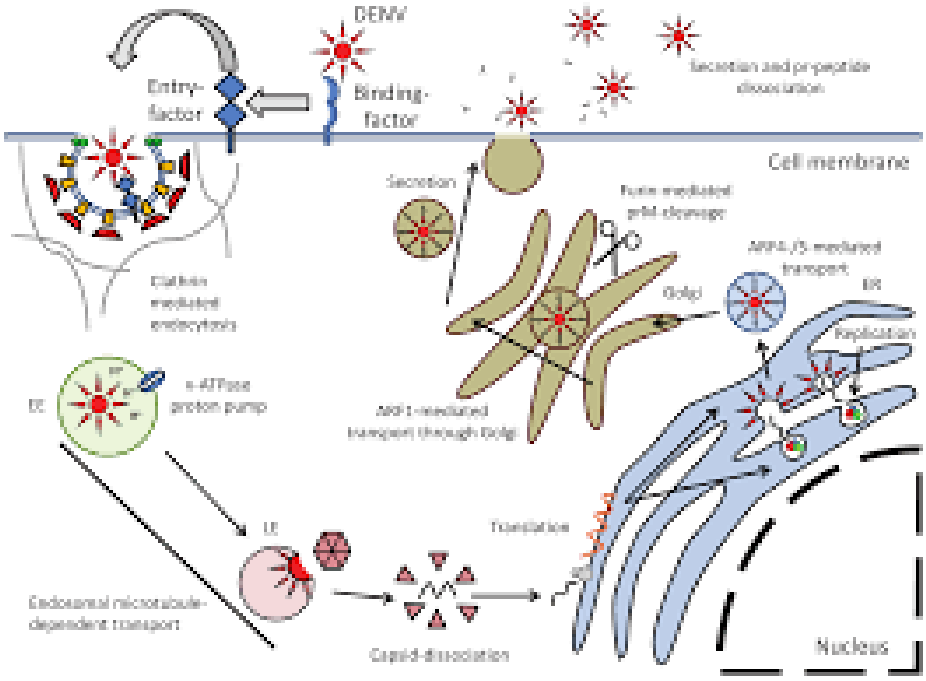
Aedes Aegypti is the main vector of dengue virus. Dengue infection is maintained through a human-mosquito-human cycle where human is the amplifying host. [10]After biting a carrier human there is an extrinsic incubation period of 8-12 days after which the mosquito can remain infective throughout its life. There is also supportive evidence of transovarian transmission of virus in mosquitoes.



The host

The incubation period is 4 to 10 days after which a wide spectrum of disease appears. The host immunity plays a major role in the pathogenesis of dengue fever. The disease has a more indolent course in children and young adults as plasma leakage is more severe in them. Infection with one serotype confers lifelong immunity to that serotype. Individual risk factors like secondary dengue, cardiac diseases, bronchial asthma, diabetes mellitus, sickle cell anaemia have higher morbidity and mortality.

Pathogenesis of dengue[11]



Replication of dengue and infection cycle[12]

Dengue virus attaches to the cell wall of the human being

Cell membrane folds around the virus a pouch is formed

Virus will be sealed.The pouch is called endosome

Viral particle will be released into cell cytoplasm

Nucleocapsid opens to uncoat the viral genome and viral RNA will

will be released

Viral RNA uses host cell machinery for its replication

Viral RNA uses host ribosomes present on the ER

It will be translated into viral RNA and viral polypeptide

The viral polypeptide is made into viral proteins

Viral RNA is coated by nucleocapsid containing C protein

Nucleocapsid enters into ER

Nucleocapsid will be surrounded by E and M protein

Immature viral particles are formed

Immature viruses are transmitted through golgi network

Immature virus becomes matured viruses and are released

These virus affects new host cells

Skewed T cell response

In some persons dengue infection causes an altered T cell response[13]. The heightened response is mediated through memory T cells especially in dengue re-infection. The alterd response causes a cytokine storm causing capillary leakage and severe dengue disease.

Factor affecting dengue severity

1) antibodies dependent enhancement

The most accepted theory for dengue infection is the Halstead hypothesis. According to this theory a patient suffering from a re-infection of dengue has higher risk of DHF and DSS. Pre-existing antibodies from previous infection recognizes the infective virus and forms antigen-antibody complex, which is binds to Fc receptor of immunoglobulins. This cause the mononuclear cells to release vasoactive mediators that in turn causes increased vascular permeability.

2) Compliment activation

Compliment activation also plays a major part in severe dengue as evidenced by an increased compliment C3a and C5a in DSS[14]. The NS1 antigen is primarily responsible for compliment activation..

3) Non structural 1(NS1)

It was first detected in dengue cell cultures and later was found to circulate as complexes wit thombin and prothrombin elevating aPTT. It also activates compliment pathway.

4) Cytotoxic factor

It is produced by CD4+T cells and it kills CD4+T cells and macrophages and cause immune suppression. It has been found that people with DHF have high concentratons of CF in serum. CF is specific for dengue virus and hence can be used in diagnosis.

5) Host genetic factors

Some host genetic factors have its role to play in dengue infection. G6PD infection is found to be associated with higher incidence if DHF. [15]Polymorphism in TNFα, CTLA-4, TGF-β, JAk1 genes all are associated with DHF/DSS. AB blood group has high resistance to dengue fever and DSS.

6) Influence of age

Children are more prone to severe forms of dengue. In infants even primary dengue can cause DSS/DHF.

7) Effects of malnutrition

Malnourishment either over or under nourishment is adversely affected in dengue.

8) Influence of race

More severe in Cuban, African, Caribbean, mongoloid races less in Caucasians.

9) Auto immunity cross reaction

Antibodies formed during dengue like anti NS1 antibody has been found it cross with cells of liver, endothelial cells, and platelets and in production of nitric oxide and IL-6 and may be responsible for plasma leakage.

10) Viral factors

Dengue severity has been shown to vary according to the serotypes of the virus. DENV type 2 is known to be associated with severe forms of the disease. DENV type 1 has low mortality but high morbidity. Sequential infection and time interval between primary infection and secondary are factors that play an important role in dengue severity.

Laboratory diagnosis of dengue virus infection

Dengue diagnosis can be performed through virus isolation, genome and antigen detection and serological studies. Since easily available and rather cheap with fair amount sensitivity and specificity serological studies are the most applied methods in treating hospitals. Virus isolation and genome studies are done in research institutes. Different diagnostic tests can only be done at a particular time frame of the disease.

Networking of laboratories in India

Since India is an endemic country for dengue and there has been recurrent breakouts a efficient network of specialized laboratories are required both detection during epidemics as well as for sentinel monitoring. For this the Government of India has setup a network of laboratories both sentinel surveillance hospitals and apex referral laboratories since 2007. ARLs have advanced diagnostic facilities for back support and serotonin of dengue samples and sends regularly to district level/ state level authorities for proper implementation of preventive measures.

For confirmation of dengue the government of India recommends ELISA based antigen detection test on first day and for ELISA antibody detection test for IgM after 5 days of the disease[16].

Serological diagnosis

The serological tests are done to detect either antigens or antibodies and ELISA is the most common applied test.

IgM based assays

The detection of dengue IgM is a useful diagnostic test. in primary infection the IgM antibodies are detected starting from the fifth day of the disease but can detected as early as 3rd day. IgM may appear earlier in

secondary dengue infection but titers will be lesser.[17] IgM ELISA tests have a sensitivity of 90% and specificity of 98% if taken 5 days after onset of illness. The dengue antigen used for antibody detection is the dengue protein E antigens of all 4 serotypes. Because the antibody is present in blood for atleast 3 months, its presence may not be diagnostic in current illness. For current infection a seroconversion of 4 fold or higher in paired sera is required.

Rapid diagnostic tests for IgM are now available which can be used as bedside tests. Most of these tests use recombinant antigens from all 4 serotypes and particle agglutination or lateral flow immunochromatographic strips. Results are available within 15 to 90 minutes. They have sensitivity of 21-99% and specificity of 77-98%.

IgG based assays

IgG based assays are mainly done to detect past infections. It is also done to differentiate from a primary and secondary infection of dengue. IgM/IgG ratio is a better index for detection primary infection where the ratio will be always greater than one whereas in a send art dengue the ratio will be less than one.

Neutralisation test

It is the most specific and sensitive serological test for dengue viruses and is used for determining the immune protection. The common protocol used is the serum dilution plaque neutralisation test. It is highly expensive and time consuming, hence not routinely done.

Virus detection

Dengue virus is present in blood 2 to 3 days prior to illness and 4 to 5 days after. Whole blood, serum or plasma can be used for virus extraction. Virus is heat labile and hence must be transported in 4 degree Celsius for short period or at -70 degrees for longer storage. Mosquito inoculation is the best sensitive method for dengue virus isolation but it requires great technical skill and special containment so cell culture is preferred. Commonly used cell cultures are Vero cells, LLCMK2, BHK21.

Antigen detection-NS1 based assays

NS1 is a non-structural protein and is required for virus viability. It is secreted in both membrane bound forms and secreted forms. It can be detected by using ELISA at an early part of the clinical illness. But in case of dengue secondary infection there will be high titre of IgG antibodies that will neutralise the NS1 antigen hence will give poor outcome.[18]Many rapid diagnostic test kits for NS1 have been developed

and has been judiciously I areas of dengue break out but the sensitivity of the test is only 66% .

Polymerase Chain Reaction

The advantage of PCR is than it can detect the virus from small samples. The procedure include extraction of nucleic acid, amplification of nucleic acid and finally detection of the amplified product. There are different types of PCR techniques like RT-PCR, nested RT-PCR, one-step multiplex RT-PCR, real time RT-PCR. These tests are good enough to detect all the serotypes of dengue. Real time RT-PCR is much better as it involves only one step and does not require electrophoresis as required by other PCR tests.

Clinical features

The incubation period is around 4 to 7 days. The disease spectrum varies from asymptomatic cases to mild febrile illness to severe forms with DHF or DSS and also MODS. The disease has three phases

1. Febrile phase
2. Critical phase
3. Recovery phase

The febrile phase starts with high grade fever with prodromal symptoms such as facial flushing, skin erythema, headache, myalgia, arthralgia, retro-orbital pain, sore throat, pharyngeal congestion, conjunctival redness, loss of appetite, nausea, vomiting. Mild haemorrhagic manifestations like petechiae, mucosal membrane bleeding from nose and gums. [19]Tourniquet test is positive during this time. Liver may be enlarged and tender.

The critical phase lasts for another 5 days where fever subsides. Increased capillary permeability is the hall mark of this stage. Seriousness of the illness depends upon the severity of the plasma leakage. Warning signs during the critical phase include abdominal pain and tenderness, persistent vomiting, serositis, mucosal bleeding, tiredness, hepatomegaly, increase in hematocrit with fall in platelet count. Blood work during this time also shows decreased total count, elevated liver enzymes, decreased protein and albumin.

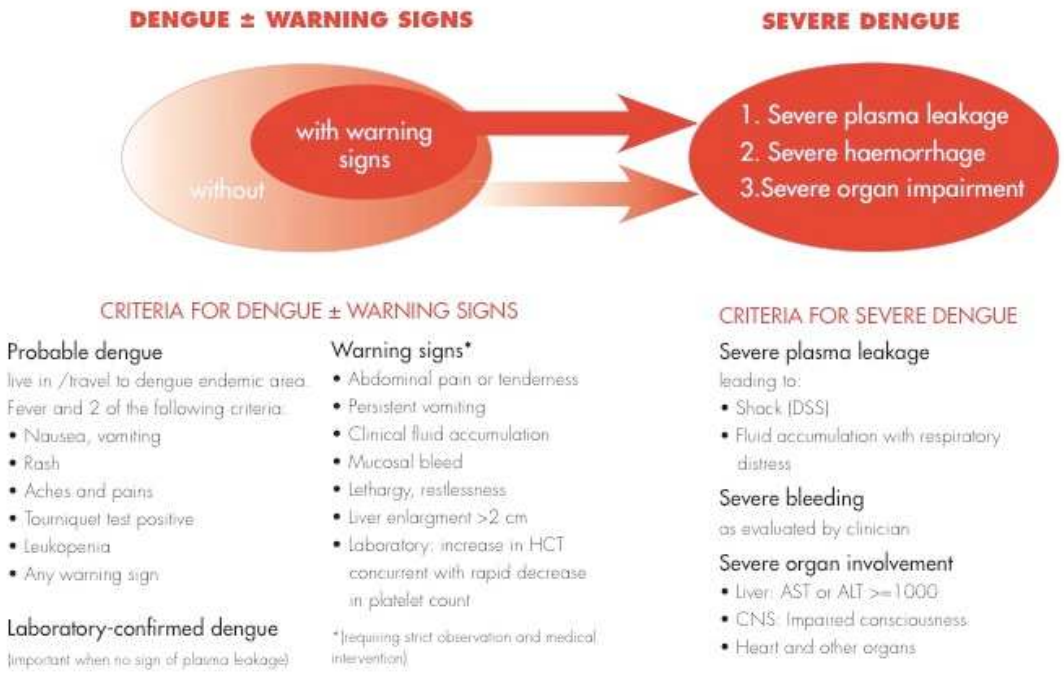
The recovery phase occurs usually 2 to 3 days of critical phase. The patient if gets better his general condition improves, there will be slow reabsorption. The appetite improves, hemodynamic status becomes normal. Bradycardia is common and some develop a petechiae rash and mild pruritus. WBC count improves and platelets also rises slowly.

The criteria for discharge includes no fever for more than 48 hrs, improvement in general well being, normal vital signs, platelets more than 50,000 and rising trend, no bleeding manifestations. Healthy nutritious diet must be followed the replenish the catabolic state that the body has gone through. They should also be advised to take part in active vector control program so as to curb the infection rate.

Classification of DHF by WHO[20]

	Grade	Sign and Symptomps	Laboratory
DF		DHF without plasma leakage	
DHF	I	Fever with non-specific constitutional symptoms; the only hemorrhagic manifestation is a positive tourniquet test &/or easy bruising evidence of plasma leakage	Thrombocytopenia (platelet count ≤ 100,000/µL)
	II	DHF grade I plus spontaneous bleeding	
	III	Circulatory failure manifested by a rapid, weak pulse, narrowing of pulse pressure, or hypotension, cold & clammy skin, restlessness	
	IV	Profound shock with undetectable blood pressure	

Assessing the severity of dengue



Dengue shock syndrome

It is a type of Hypovolemic shock seen in dengue due to vascular permeability and plasma leakage causing displacement of intravascular fluid to leak third space. It has different spectrum like compensated shock, Hypovolemic shock, hypotension shock and cardiac arrest.

Signs of DSS

1) coolness, pallor and delayed capillary refill time
2) CVS- low SBP, high DBP, and narrow pulse pressure
3) Kidneys- reduced urine output
4) GIT- vomiting and pain abdomen
5) CNS- altered sensorium, restlessness
6) RS- increased respiratory rate

Inadequate perfusion leads to tissue hypoxia and increased anaerobic glycolysis leading to production of lactic acidosis. The condition if not reversed at this stage will go on to refractory shock. Lactic acid is a myocardial depressant and will lead low cardiac output and cardiomyopathy. Other complications like DIC and MODS will ensue and death occurs by cardiac arrest.

Other Manifestations of Dengue

Dengue infection sometimes can have atypical presentations and may lead to misdiagnosis or delayed diagnosis.

1) GIT- hepatitis and liver cell failure, acalculous cholecystitis, pancreatitis, acute abdominal pain

2) CNS- Acute encephalitis, GBS

3) Haemophagocytic syndrome- Due to overt activation of T cells causing cytokine storm causing immense plasma leakage leading to cell death, progressive cytopenia and MODS.

4) Renal- asymptomatic proteinuria, nephrotic range proteinuria, acute renal failure.

Management of dengue

There is no specific treatment for dengue fever and fluid therapy is the best treatment for dengue. Symptomatic and supportive measures can prevent mortality and morbidity provided they are started at early stage.

Domiciliary management of dengue, which can be done in more than 80% of cases includes

1. Adequate bed rest
2. Tepid sponging
3. Antipyretics like paracetamol 500 mg q6
4. Oral rehydration solutions like WHO formulated ORS or fruit juices, maintain good hydration
5. Monitoring for any complications during the critical phase.
6. Taking adequate measures to prevent spread of dengue by using mosquito nets or repellents.

Most of the cases of dengue can be managed at home, but some require hospital admission and careful monitoring and accurate intravenous fluid management.

Criteria for admissions are:

1) DF with warning signs and symptoms
2) Significant bleeding from any site
3) Hypotension
4) Persistent high grade fever
5) Rapid fall of platelet count
6) Sudden drop in temperature
7) Evidence of organ involvement
8) High risk groups

High risk groups are

1) Infancy and pregnancy
2) Elderly or obesity
3) Peptic ulcer disease
4) G6PD deficiency/Thalassemia
5) Coronary artery disease

6) Chronic diseases such as COPD, bronchial asthma, diabetes, hypertension

7) Patients on steroids, anticoagulants , anti-platelets.

8) Immunocompromised patients

Treatment of DHF

For DHF grade 1 and 2, close monitoring of vitals and hematocrit and platelets is needed along with adequate hydration using IV fluids, crystalloids are preferred.

Any sign of deterioration should be picked up early and hypotension or renal failure requires treatment similar to DHF 3/4.

Management of DHF grade 3 and 4

1. Vitals monitoring especially BP, HCT, and platelet count.
2. IV fluids with close monitoring of urine output and BP.
3. Colloids, of BP does not pick up even after 1 litre of fluid challenge of crystalloids.
4. Blood transfusion preferably whole blood, one in case of severe bleeding or in case of sudden drop of HCT. It is given at the rate of 10 ml/kg/hr.
5. O2 is found to be beneficial in all patients in shock even if they have no respiratory distress

6. Platelet transfusion if needed
7. Testing for other organ involvement like liver function test, renal function test.

Fluid requirement can be calculated by Holiday and Segar formula

Amount of fluid that should be given needs to be maintenance plus fluid lost by dehydration

Maintenance fluid for body weight

For less than 10 kg - 100ml per kg

For 10-20 kg - 1000ml + 50 ml/kg body weight exceeding 10 kg

More than 20 kg- 1500ml + 20ml/kg body weight exceeding 20 kg

Fluid lost by dehydration is taken as 5% or 50 ml / kg.

The fluid chosen for resuscitation is usually crystalloid and then colloids. Both have similar efficacy. Crystalloids, normal saline is the choice, but to prevent hyperchloremic acidosis Ringers' lactate is used as follow up.

When there is blood loss more than 10% of total volume or if there is refractory shock whole blood transfusion is indicated at the rate of 10ml/kg. Platelet transfusion is indicated irrespective of platelet count if

there is bleeding. It is indicated when the platelet count is less than 10,000 in absence of bleeding.

Prevention and control

Since dengue has become a major public health concern and has become a pandemic and there is no definite treatment other than supportive treatment, the golden rule of prevention is better than cure applies here.

Vector control

Aedes mosquitoes are the primary carries and amplifiers of dengue, to control the disease the strings should be pulled to reduce the vector load i.e. the mosquitoes. We have altered the environment and made it comfortable breeding grounds for mosquitoes. The Aedes mosquitoes lay eggs on fresh water sources and there plenty of man made sources to lay eggs and flourish.

Unless there is effective vector control the disease cannot be controlled. Destroying the breeding places should be done first. Insecticides are recommended for vector control during epidemics as well in endemic areas. Use of personal protective methods like long clothes

and use of mosquito repellents such as picaridin, DEET, IR3535 is also encouraged.

Dengue vaccine

Although not yet commercially available so many dengue vaccines are under trial and would be available in the near future. Some of them are Sarnoff Pasteur's CYD vaccine, DENVax, TV003/TV005, TDENV PIV, virus like particles using Pichia pastoris.

MATERIAL AND METHODS

The study was conducted at the department of Internal Medicine, Madras Medical College and Rajiv Gandhi Government General Hospital, Chennai 600003.

ETHICAL COMMITTEE APPROVAL

Obtained

PATIENT CONSENT

Obtained

DURATION OF STUDY

6 months

STUDY DESIGN

Observational study

SAMPLE SIZE

100 patients

INCLUSION CRITERIA

Patients

1) Age group 18-60 years

2) Diagnosed as Dengue fever by IgM Elisa

EXCLUSION CRITERIA

- Pregnant women
- Other causes of fever
- Acute calculous cholecystitis
- Chronic liver disease
- Chronic kidney disease
- Congestive cardiac failure
- Post cholecystectomy

DATA COLLECTION AND METHODS

Patients are subjected to detailed history taking and clinical examination and valid laboratory investigations.

Patients admitted with Dengue fever diagnosed by IgM Elisa - selected for clinical study as per inclusion / exclusion criteria are subjected to routine blood investigations like complete hemogram, renal function tests, liver function test and ultrasonogram of abdomen. Detailed history taking and clinical examination will be done. Patients with Dengue fever will be analyzed for following factors

-Age

-Sex

-Bleeding manifestations

-Pulse, Blood pressure

-Total count, Platelet count and Hematocrit

-Measurement of gallbladder thickness by ultrasound

-Presence of perinephric fluid collection

Patients diagnosed as Dengue fever by IgM Elisa will undergo ultrasound abdomen for the measurement of gallbladder wall thickness and it will be correlated with the severity of the disease.

STATISTICAL ANALYSIS

The results are analysed using SPSS software version 21. Association between variables was analysed using chi-square test.

The primary efficacy changes were the increase gall bladder thickness with severity of thrombocytopenia, bleeding manifestations, tachycardia, hypotension, deranged liver enzymes, renal failure all which would assess the severity of dengue and so a comparison was made between gall bladder wall thickness and disease severity.

Statistical significance is assumed with a p value of less than 0.005

SPONSORSHIP

No

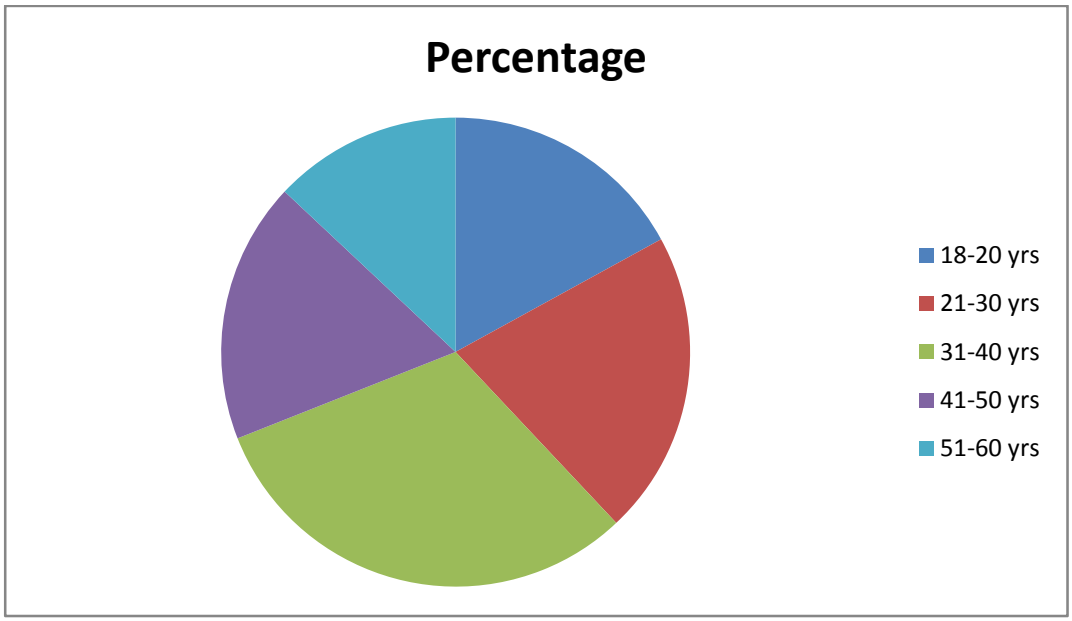
CONFLICT OF INTEREST

None

OBSERVATION AND RESULTS

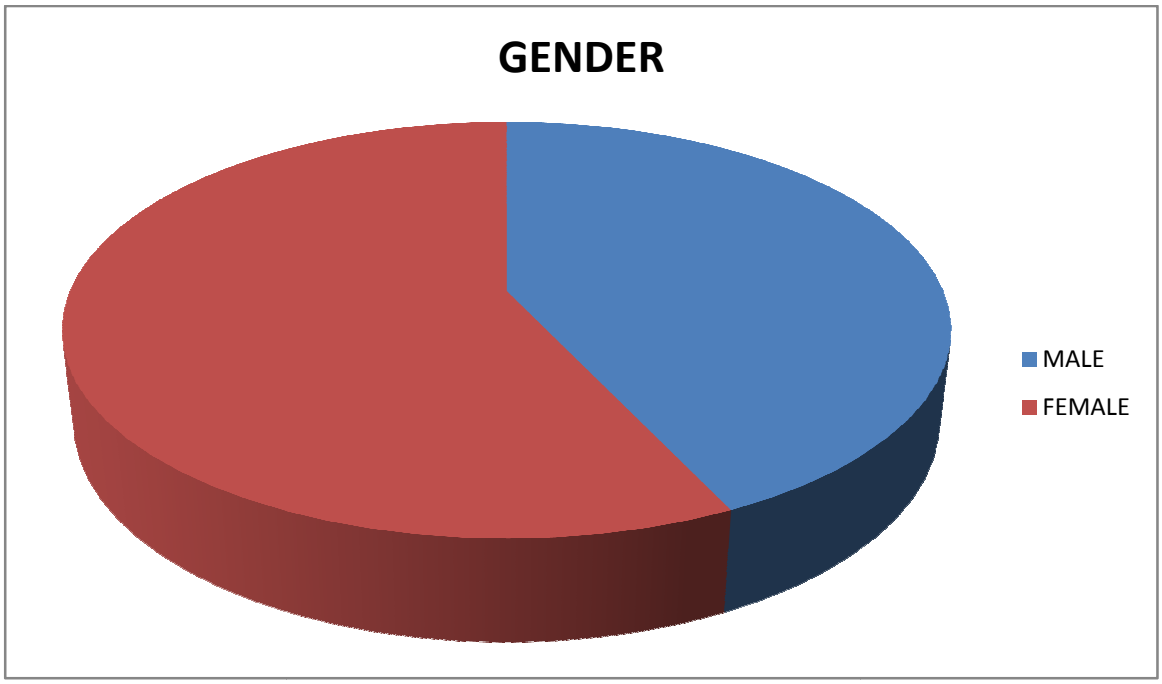
Age group in years

		Frequency	Percent	Valid Percent	Cumulative Percent
Valid	18-20	17	17.0	17.0	17.0
	21-30	21	21.0	21.0	38.0
	31-40	31	31.0	31.0	69.0
	41-50	18	18.0	18.0	87.0
	51-60	13	13.0	13.0	100.0
	Total	100	100.0	100.0	



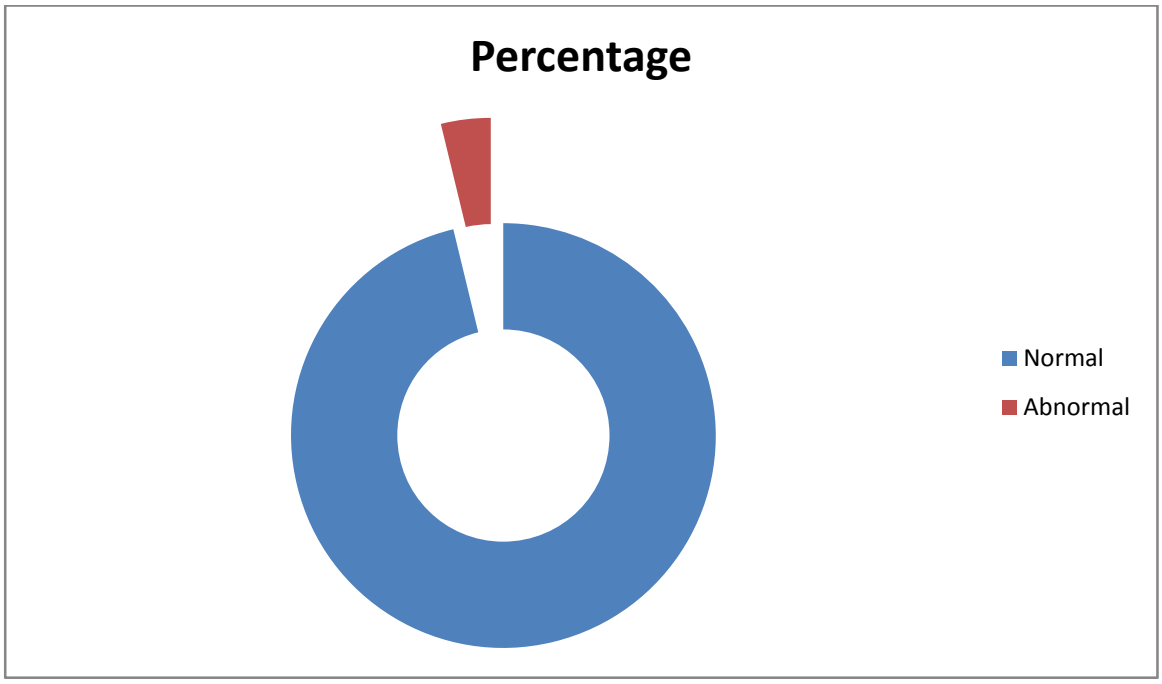
Gender

		Frequency	Percent	Valid Percent	Cumulative Percent
Valid	Male	43	43.0	43.0	43.0
	Female	57	57.0	57.0	100.0
	Total	100	100.0	100.0	



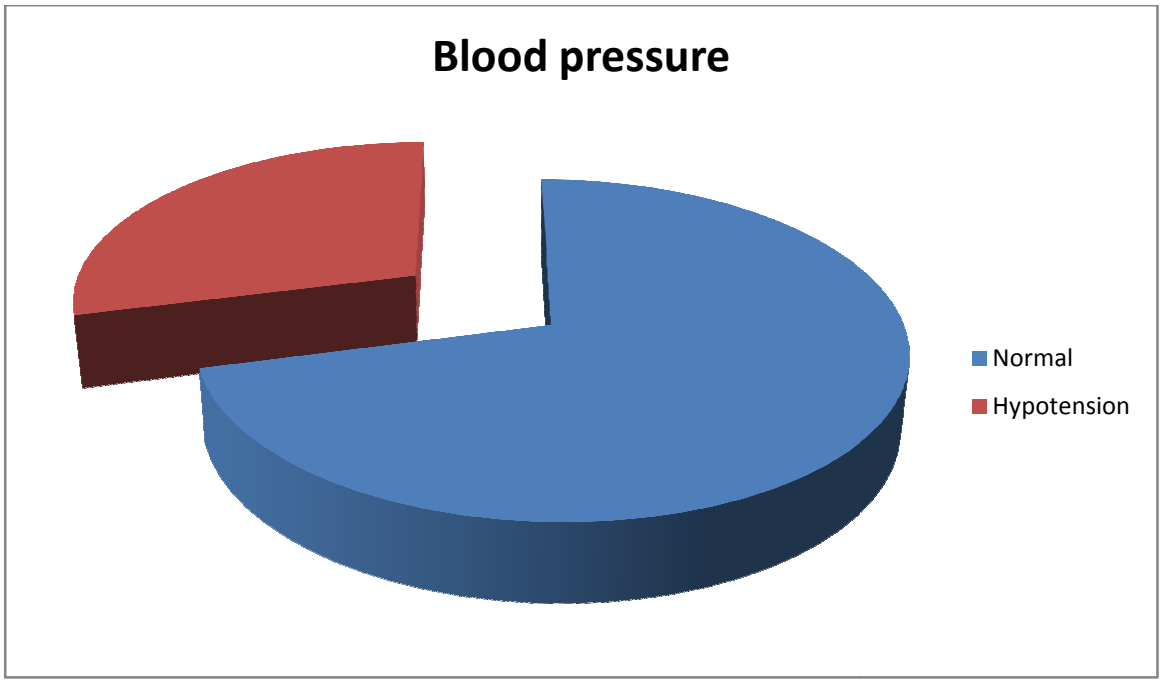
PULSE

Pulse		Frequency	Percent	Valid Percent	Cumulative Percent
Valid	Normal	81	81.0	81.0	81.0
	Abnormal	19	19.0	19.0	100.0
	Total	100	100.0	100.0	



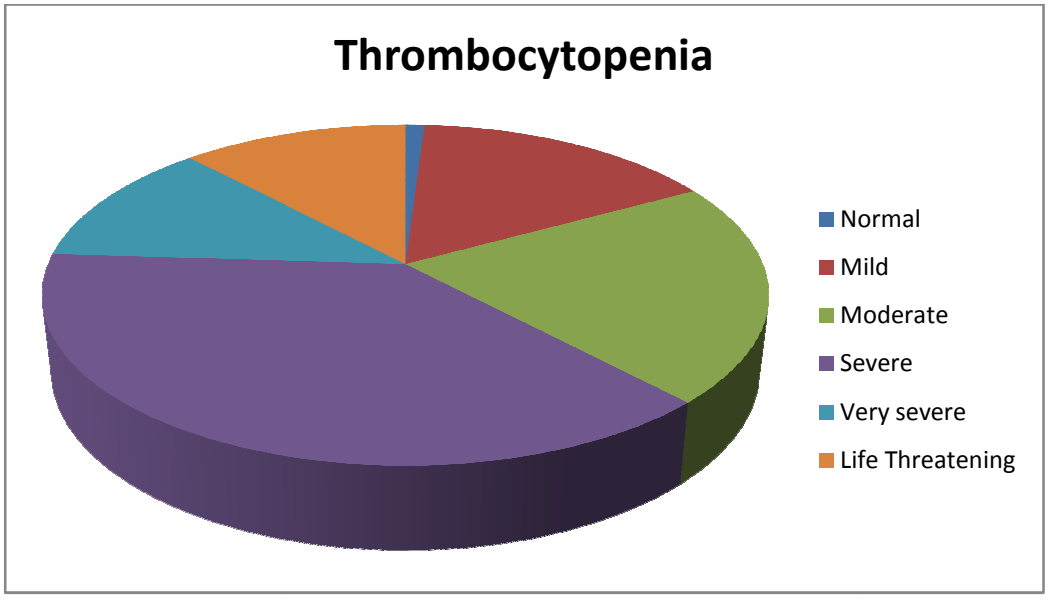
BLOOD PRESSURE

BP	Frequency	Percent	Valid Percent	Cumulative Percent
Normal	71	71.0	71.0	71.0
Hypotension	29	29.0	29.0	100.0
Total	100	100.0	100.0	



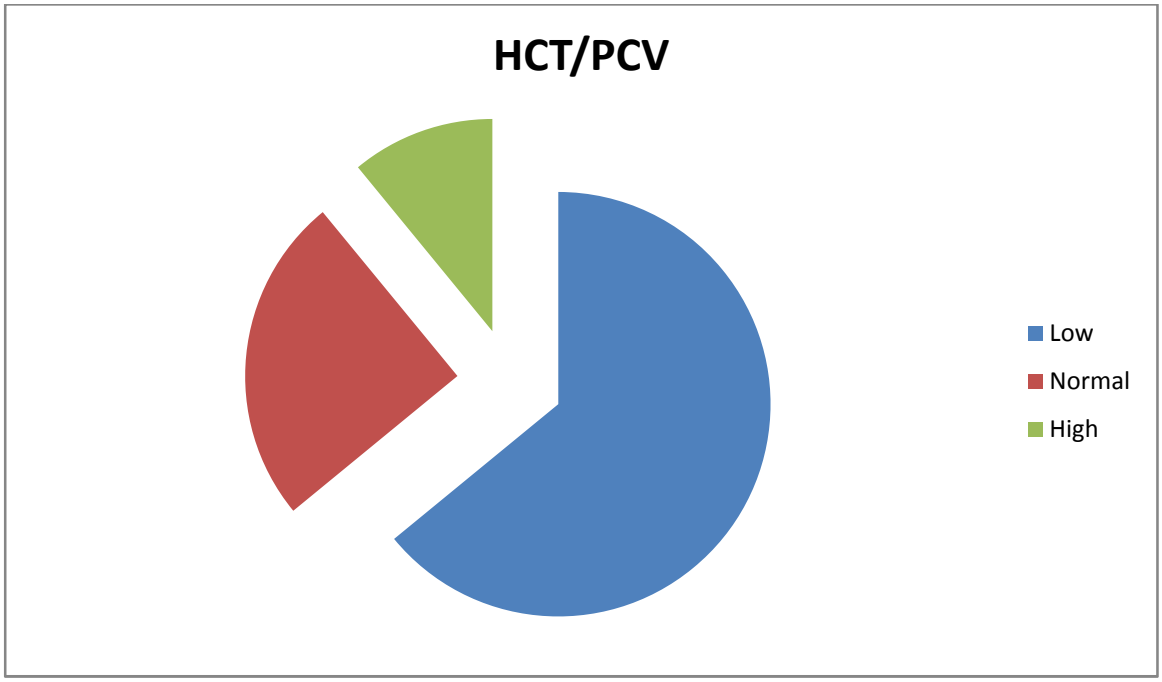
THROMBOCYTOPENIA

Thrombocytopenia		Frequency	Percent	Valid Percent	Cumulative Percent
Valid	Normal	1	1.0	1.0	1.0
	Mild	16	16.0	16.0	17.0
	Moderate	21	21.0	21.0	38.0
	Severe	38	38.0	38.0	76.0
	Very Severe	12	12.0	12.0	88.0
	Life Threatening	12	12.0	12.0	100.0
	Total	100	100.0	100.0	



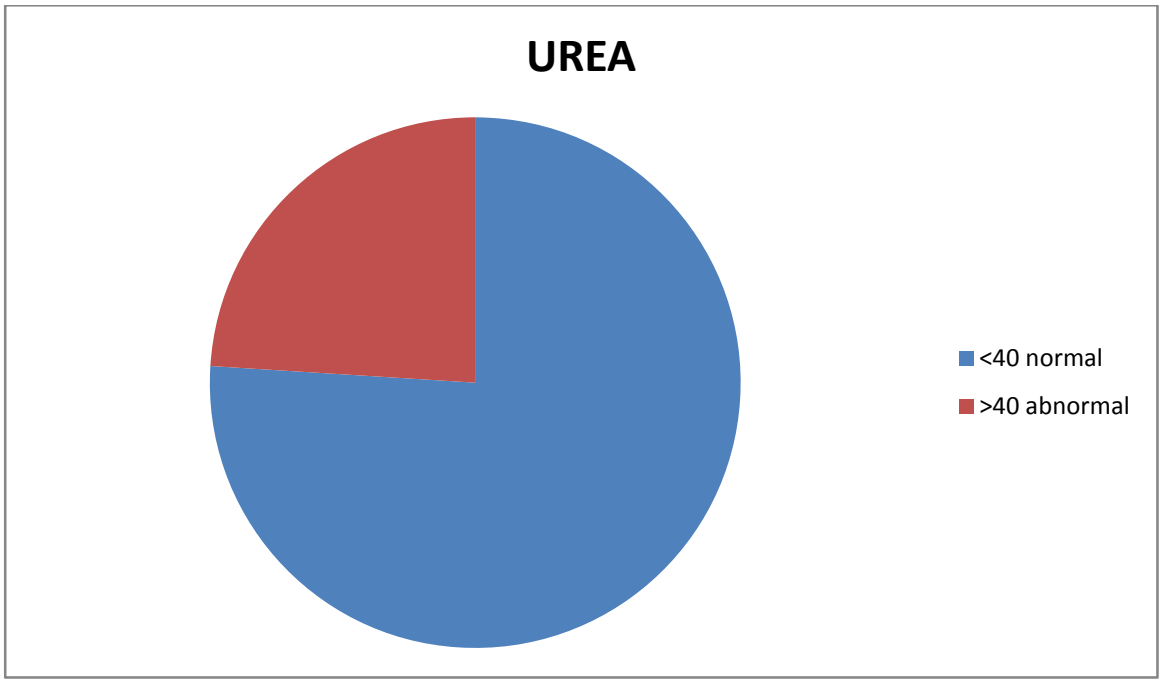
Hematocrit/ PCV

HCT/PCV		Frequency	Percent	Valid Percent	Cumulative Percent
Valid	Low	47	47.0	47.0	47.0
	Normal	47	47.0	47.0	94.0
	High	6	6.0	6.0	100.0
	Total	100	100.0	100.0	



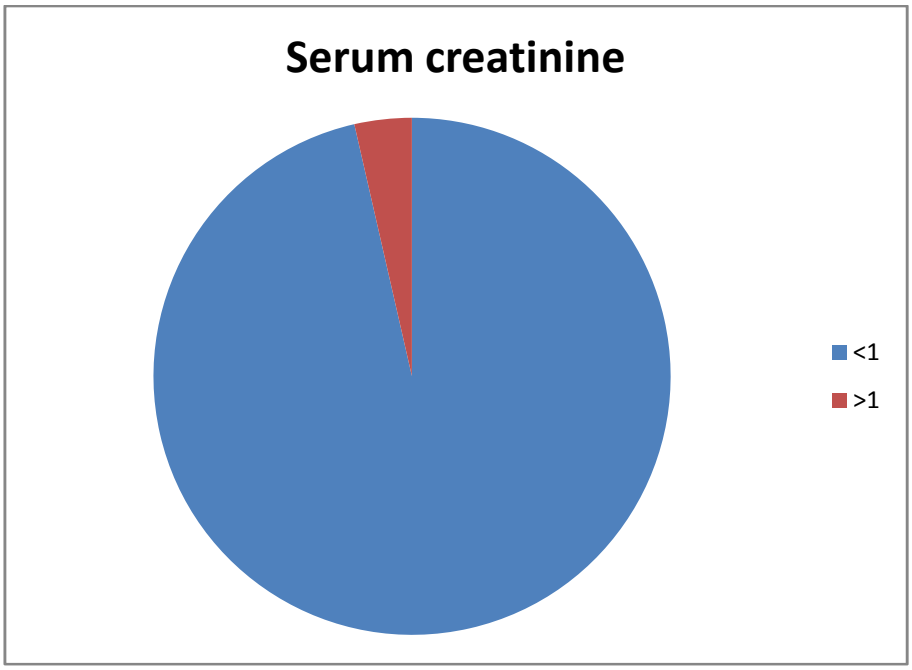
BLOOD UREA

Blood Urea		Frequency	Percent	Valid Percent	Cumulative Percent
Valid	< 40	76	76.0	76.0	76.0
	> 40	24	24.0	24.0	100.0
	Total	100	100.0	100.0	



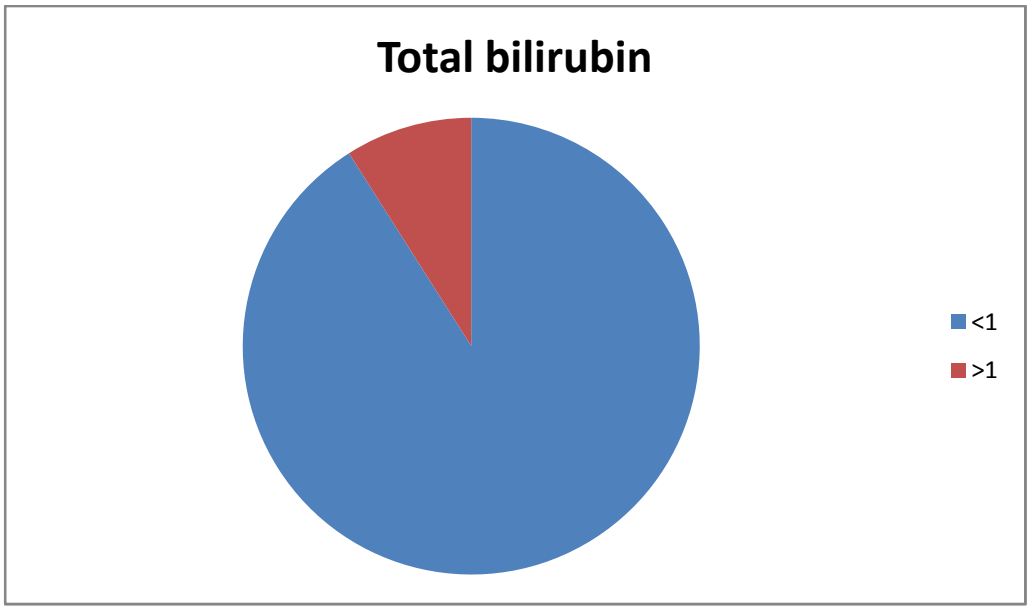
SERUM CREATININE

		Frequency	Percent	Valid Percent	Cumulative Percent
Valid	< 1	86	86.0	86.0	86.0
	> 1	14	14.0	14.0	100.0
	Total	100	100.0	100.0	



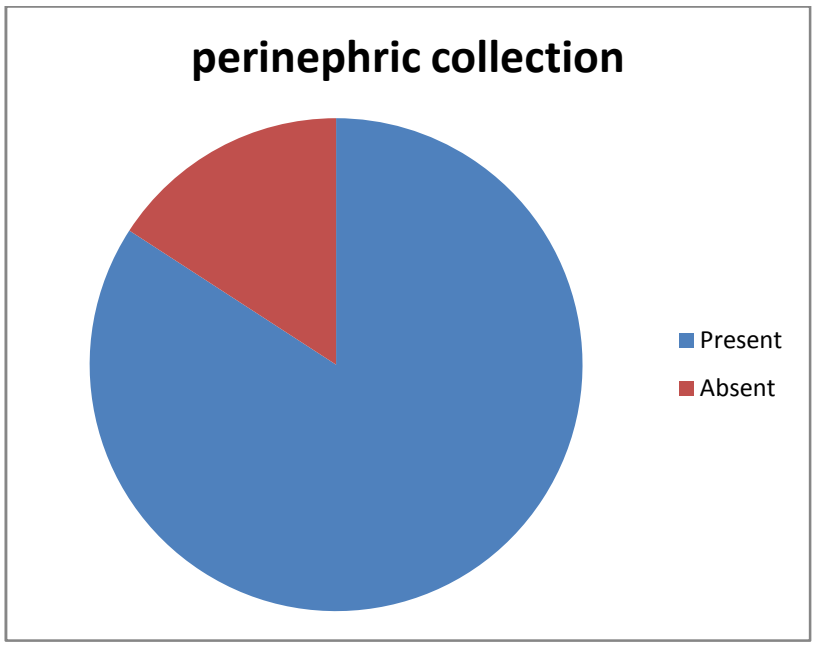
TOTAL BILIRUBIN

		Frequency	Percent	Valid Percent	Cumulative Percent
Valid	< 1	91	91.0	91.0	91.0
	> 1	9	9.0	9.0	100.0
	Total	100	100.0	100.0	



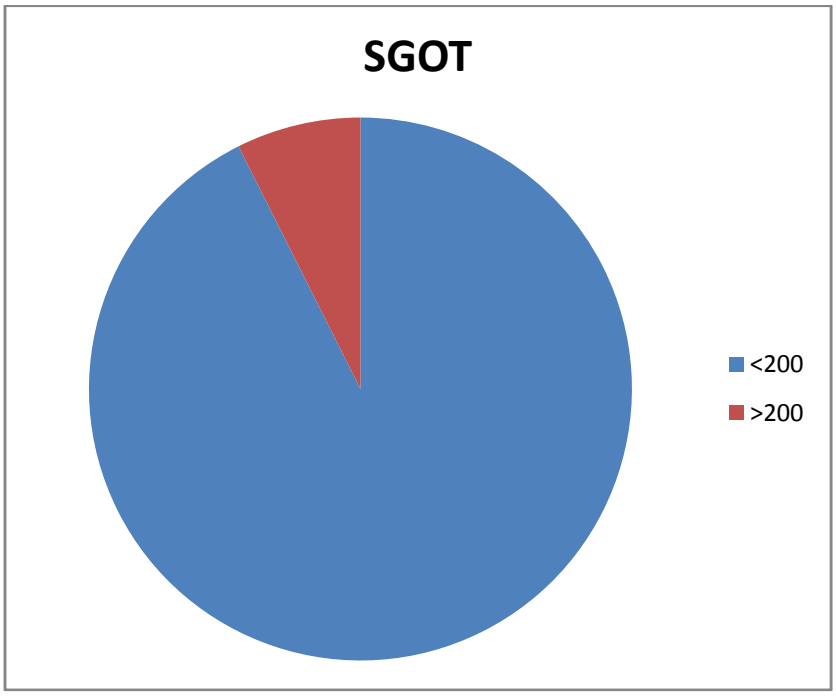
PERINEPHRIC COLLECTION

		Frequency	Percent	Valid Percent	Cumulative Percent
Valid	Present	17	17.0	17.0	17.0
	Absent	83	83.0	83.0	100.0
	Total	100	100.0	100.0	



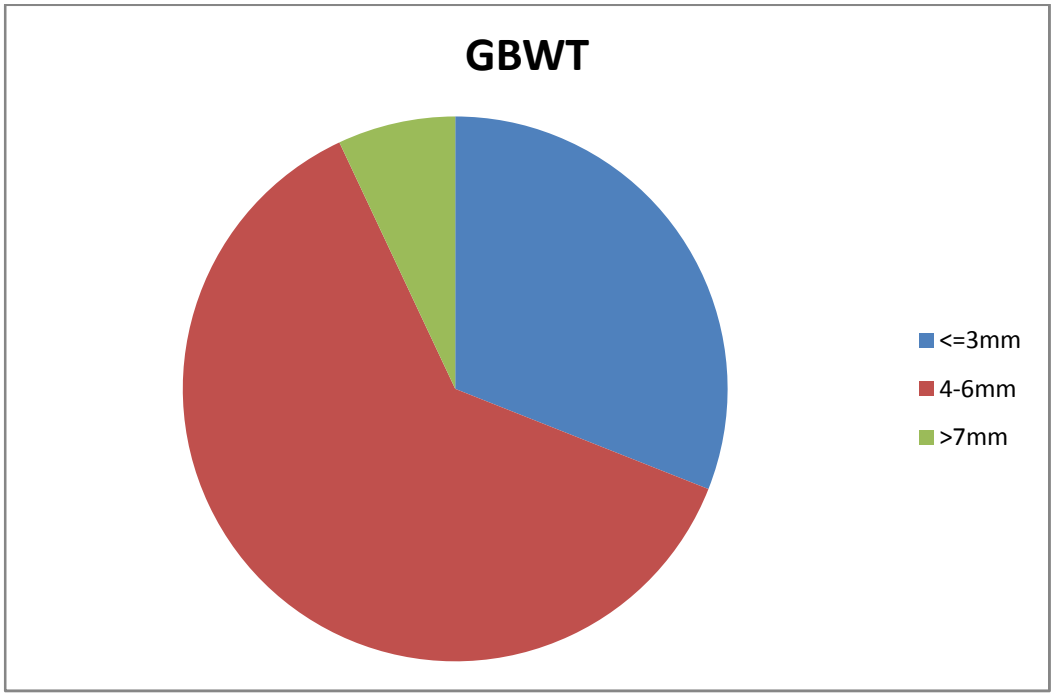
SGOT

		Frequency	Percent	Valid Percent	Cumulative Percent
Valid	< 200	40	40.0	40.0	40.0
	> 200	60	60.0	60.0	100.0
	Total	100	100.0	100.0	



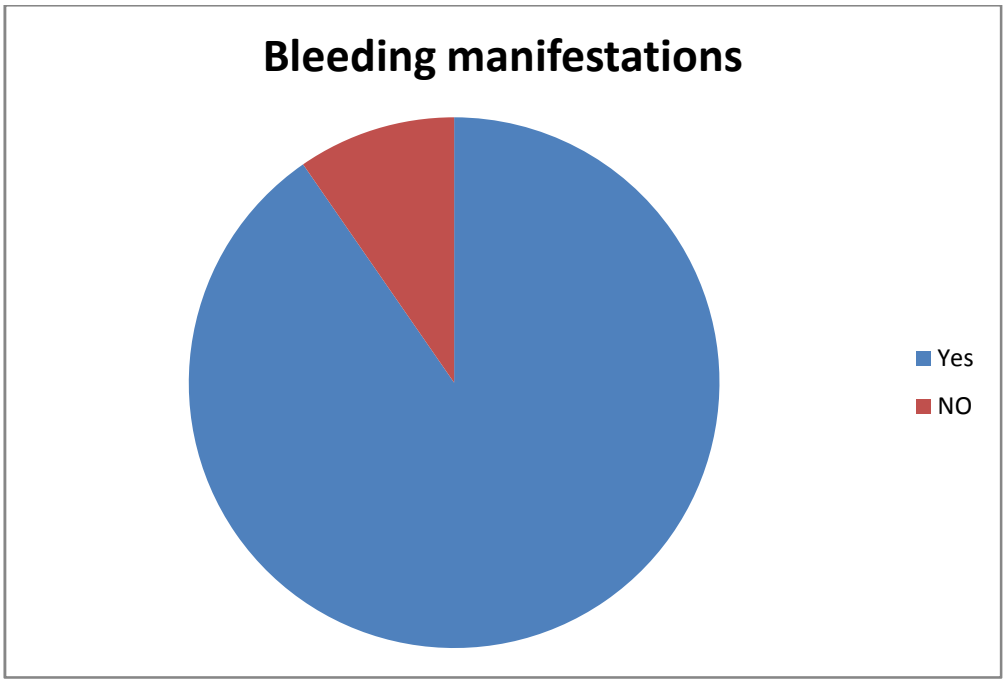
GALL BLADDER WALL THICKNESS

GBWT		Frequency	Percent	Valid Percent	Cumulative Percent
Valid	<= 3	31	31.0	31.0	31.0
	4-6	62	62.0	62.0	93.0
	>= 7	7	7.0	7.0	100.0
	Total	100	100.0	100.0	



BLEEDING MANIFESTATION

Bleeding		Frequency	Percent	Valid Percent	Cumulative Percent
Valid	Yes	30	30.0	30.0	30.0
	No	70	70.0	70.0	100.0
	Total	100	100.0	100.0	



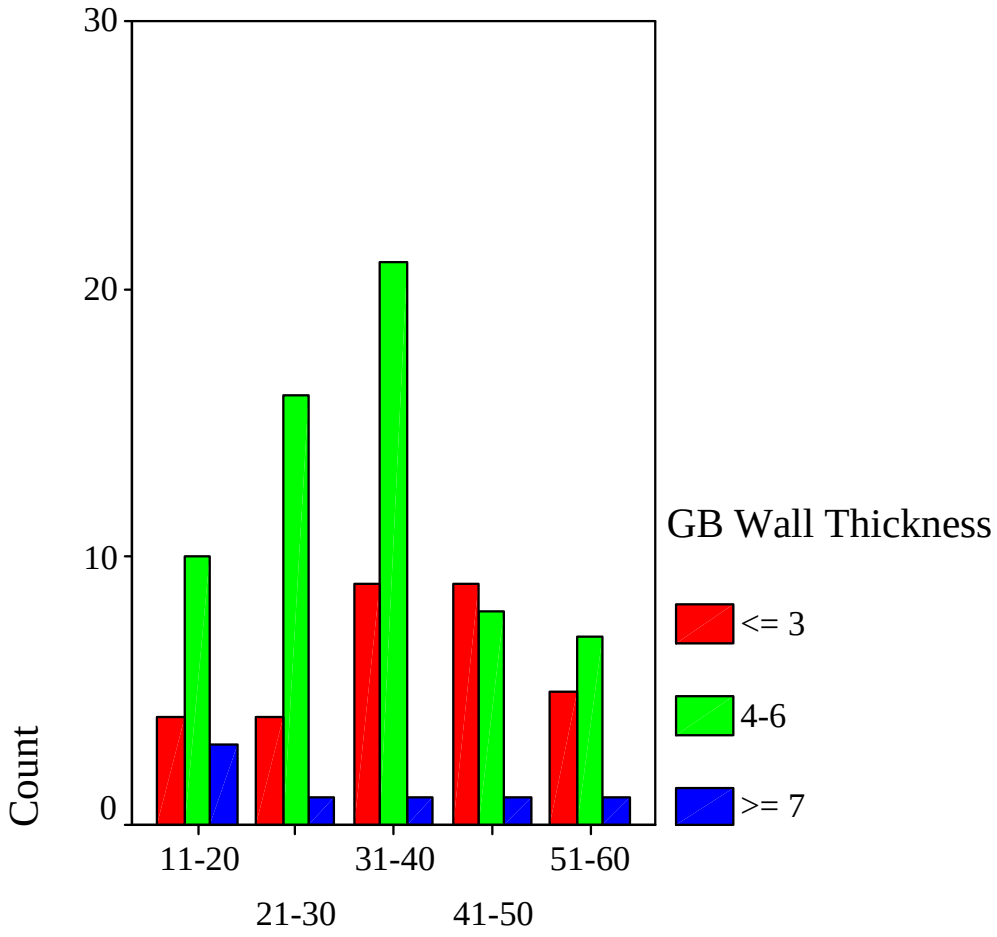
Comparison of Age groups and GBWT

Age Group in years		GB Wall Thickness			Total	P value
		<= 3	4-6	>= 7		
18-20	Count	4	10	3	17	0.33
	% within Age Group in years	23.5%	58.8%	17.6%	100.0%	
	% within GB Wall Thickness	12.9%	16.1%	42.9%	17.0%	
21-30	Count	4	16	1	21	
	% within Age	19.0%	76.2%	4.8%	100.0%	

	Group in years					
	% within GB Wall Thickness	12.9%	25.8%	14.3%	21.0%	
31-40	Count	9	21	1	31	
	% within Age Group in years	29.0%	67.7%	3.2%	100.0%	
	% within GB Wall Thickness	29.0%	33.9%	14.3%	31.0%	
	Count	9	8	1	18	

41-50	% within Age Group in years	50.0%	44.4%	5.6%	100.0%	
	% within GB Wall Thickness	29.0%	12.9%	14.3%	18.0%	
51-60	Count	5	7	1	13	
	% within Age Group in years	38.5%	53.8%	7.7%	100.0%	
	% within GB Wall	16.1%	11.3%	14.3%	13.0%	

	Thickness					
Total	Count	31	62	7	100	
	% within Age Group in years	31.0%	62.0%	7.0%	100.0%	
	% within GB Wall Thickness	100.0%	100.0%	100.0%	100.0%	

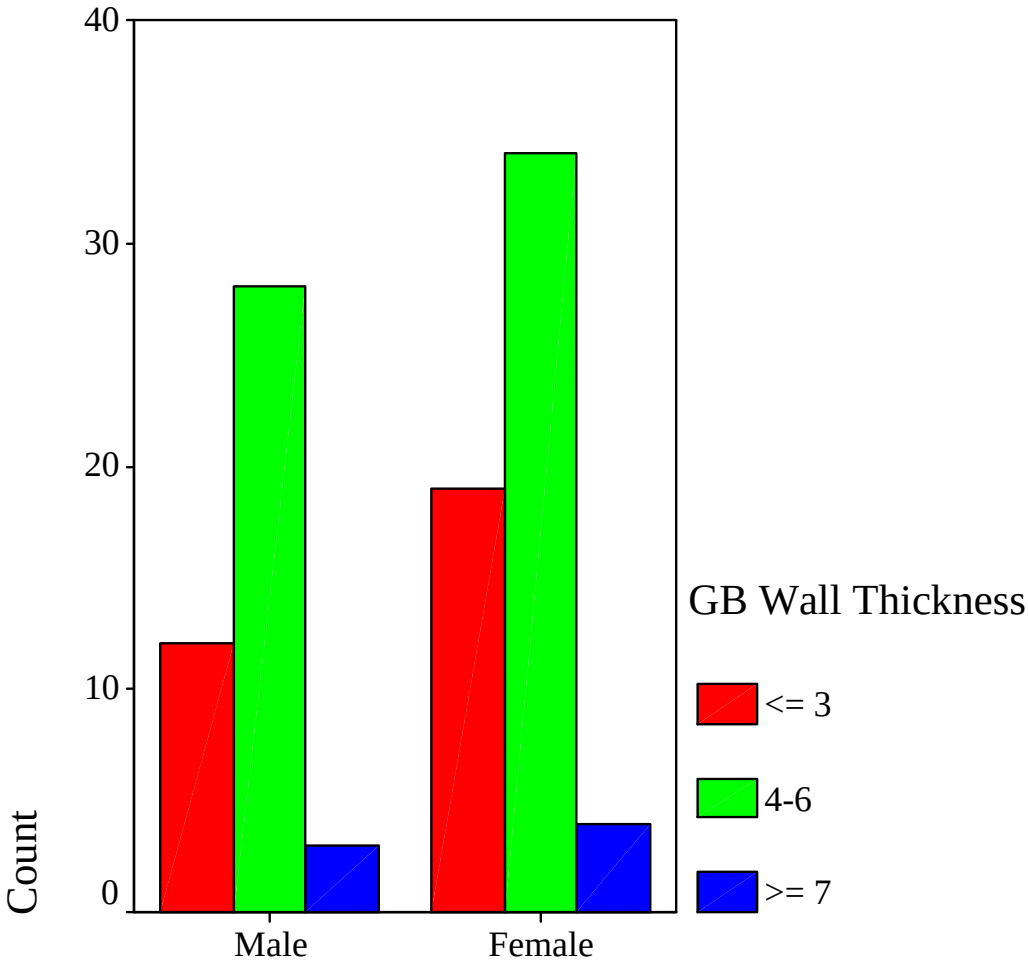


There was not much significance of comparison of GBWT with different age groups except in youngest age group were there is a slight high incidence of increase in gall bladder wall thickness.

Comparison of gender and GBWT

			GB Wall Thickness			Total	P value
			<= 3	4-6	>= 7		
Gender	Male	Count	12	28	3	43	
		% within Gender	27.9%	65.1%	7.0%	100.0%	
		% within GB Wall Thickness	38.7%	45.2%	42.9%	43.0%	
	Female	Count	19	34	4	57	
		% within Gender	33.3%	59.6%	7.0%	100.0%	
		% within GB Wall	61.3%	54.8%	57.1%	57.0%	0.89

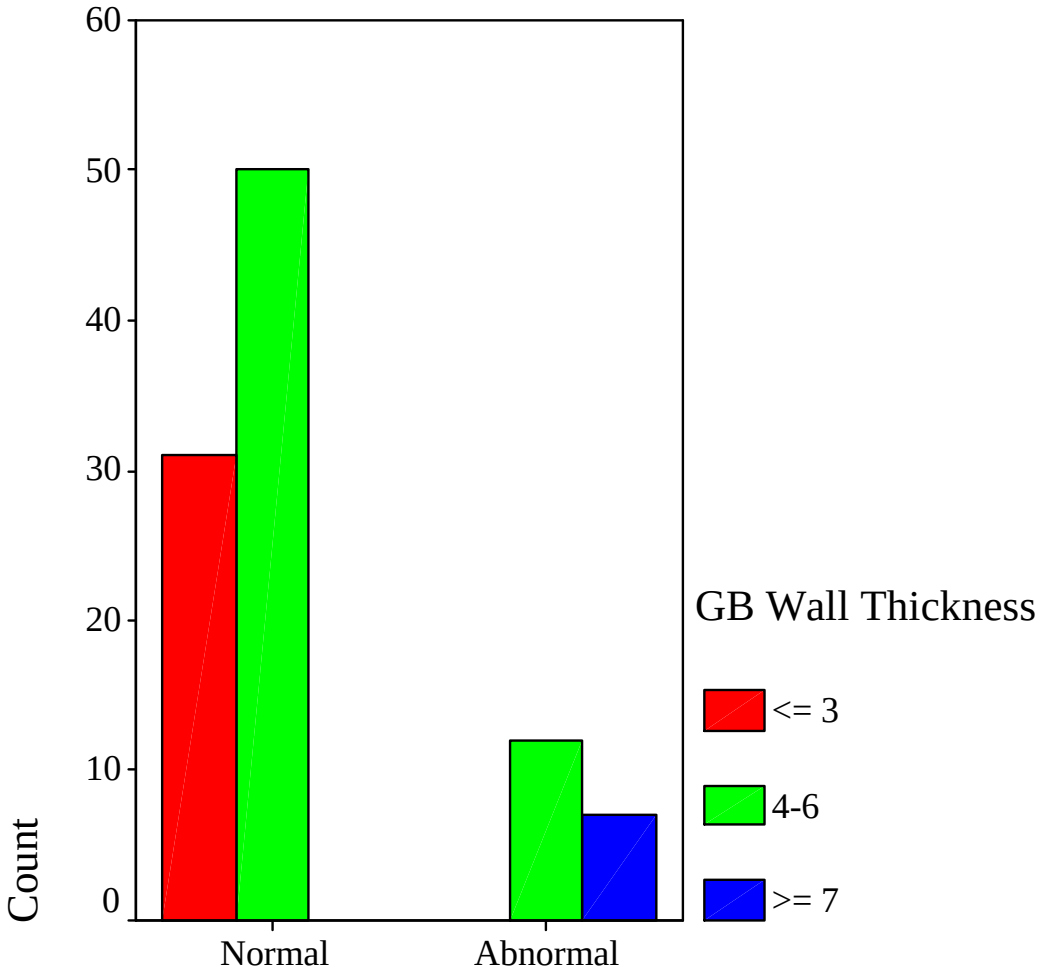
		Thickness					
Total		Count	31	62	7	100	
		% within Gender	31.0%	62.0%	7.0%	100.0%	
		% within GB Wall Thickness	100.0%	100.0%	100.0%	100.0%	



No significant association was found between gender and gall bladder thickness.

			GB Wall Thickness			Total	P value
			<= 3	4-6	>= 7		
Pulse	Normal	Count	31	50	0	81	Less than 0.001
		% within Pulse	38.3%	61.7%	.0%	100.0%	
		% within GB Wall Thickness	100.0%	80.6%	.0%	81.0%	
	Abnormal	Count	0	12	7	19	
		% within Pulse	.0%	63.2%	36.8%	100.0%	
		% within GB	.0%	19.4%	100.0%	19.0%	

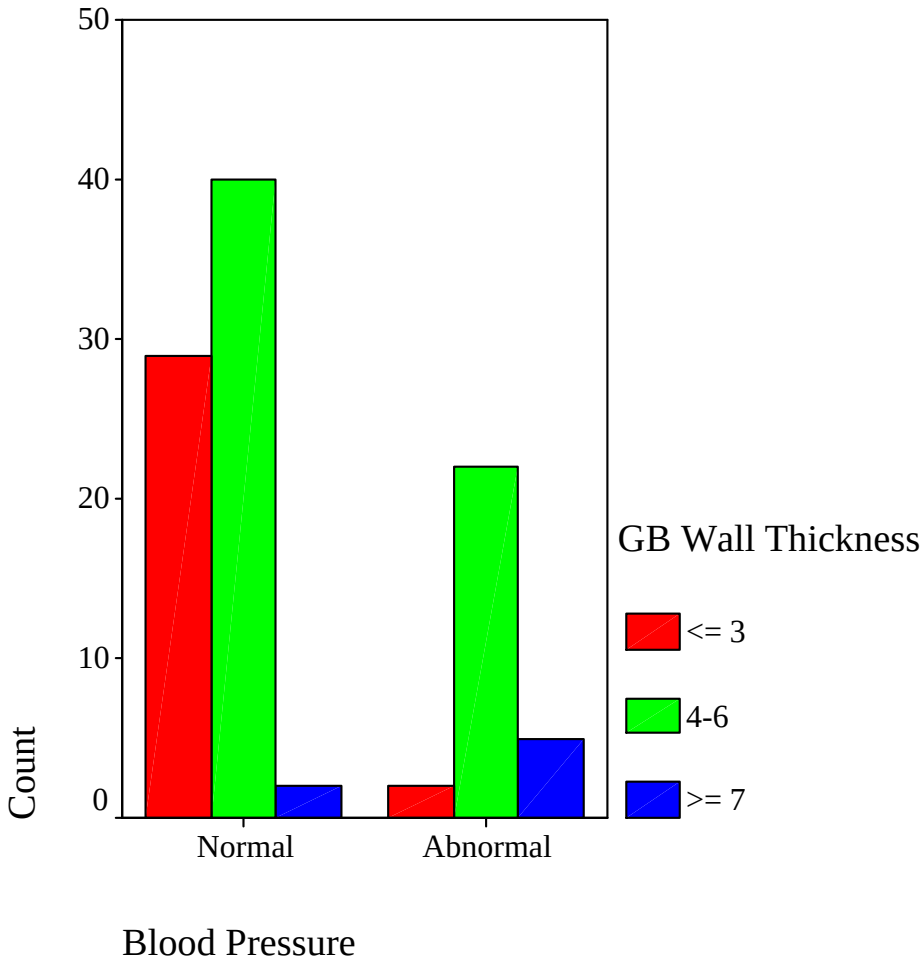
		Wall Thickness					
Total		Count	31	62	7	100	
		% within Pulse	31.0%	62.0%	7.0%	100.0%	
		% within GB Wall Thickness	100.0%	100.0%	100.0%	100.0%	



There was high significance between abnormal pulse i.e. tachycardia and GBWT. The pulse rate was more abnormal in patients with higher gall bladder thickness.

COMPARISON OF BLOOD PRESSURE AND GBWT

			GB Wall Thickness			Total	P value
			<= 3	4-6	>= 7		
Blood Pressure	Normal	Count	29	40	2	71	0.001
		% within Blood Pressure	40.8%	56.3%	2.8%	100.0%	
		% within GB Wall Thickness	93.5%	64.5%	28.6%	71.0%	
	Abnormal	Count	2	22	5	29	
		% within Blood Pressure	6.9%	75.9%	17.2%	100.0%	
		% within GB Wall Thickness	6.5%	35.5%	71.4%	29.0%	
	Total	Count	31	62	7	100	
		% within Blood Pressure	31.0%	62.0%	7.0%	100.0%	
		% within GB Wall Thickness	100.0%	100.0%	100.0%	100.0%	



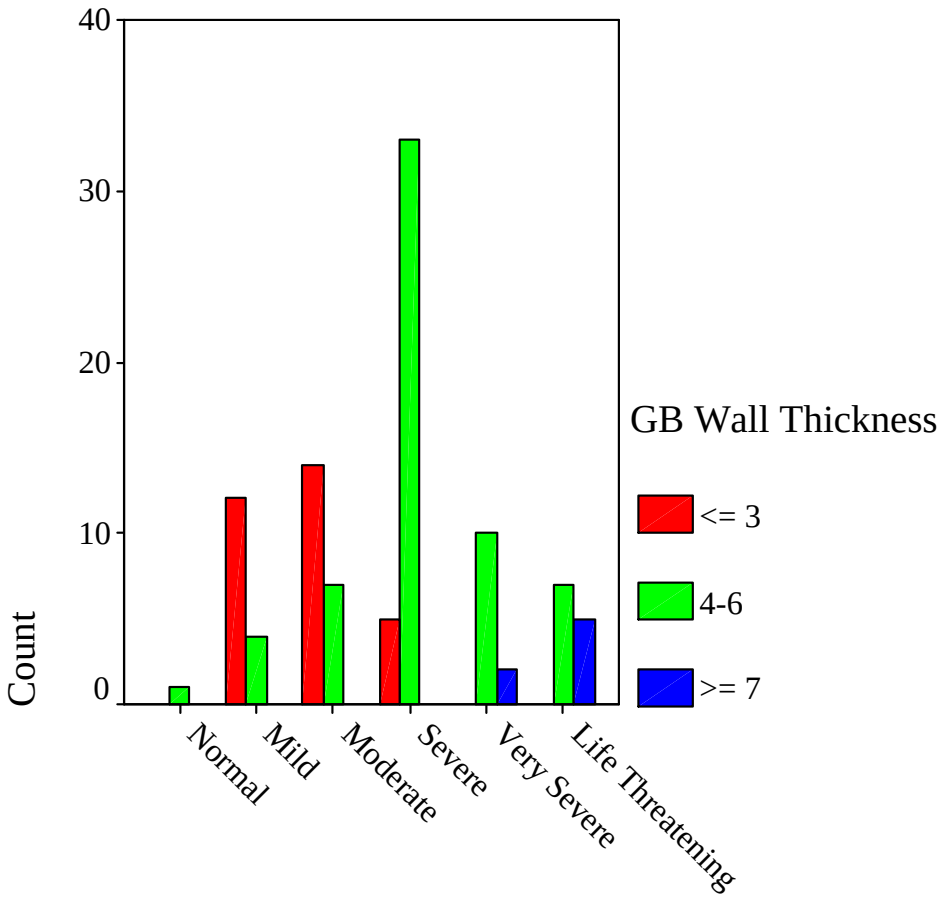
There was significant association which shows that as the gall bladder wall thickening increases there is chance to go into hypotension or shock.

PLATELET COUNT AND GBWT

			GB Wall Thickness			Total	P value
			<= 3	4-6	>= 7		
Platelet Count	Normal	Count	0	1	0	1	
		% within Platelet Count	.0%	100.0%	.0%	100.0%	
		% within GB Wall Thickness	.0%	1.6%	.0%	1.0%	
	Mild	Count	12	4	0	16	<0.001
		% within Platelet Count	75.0%	25.0%	.0%	100.0%	
		% within GB Wall Thickness	38.7%	6.5%	.0%	16.0%	
	Moderate	Count	14	7	0	21	
		% within Platelet	66.7%	33.3%	.0%	100.0%	

	Count				
	% within GB Wall Thickness	45.2%	11.3%	.0%	21.0%
Severe	Count	5	33	0	38
	% within Platelet Count	13.2%	86.8%	.0%	100.0%
	% within GB Wall Thickness	16.1%	53.2%	.0%	38.0%
Very Severe	Count	0	10	2	12
	% within Platelet Count	.0%	83.3%	16.7%	100.0%
	% within GB Wall Thickness	.0%	16.1%	28.6%	12.0%
Life Threatening	Count	0	7	5	12
	% within	.0%	58.3%	41.7%	100.0%

	Platelet Count					
	% within GB Wall Thickness	.0%	11.3%	71.4%	12.0%	
Total	Count	31	62	7	100	
	% within Platelet Count	31.0%	62.0%	7.0%	100.0%	
	% within GB Wall Thickness	100.0%	100.0%	100.0%	100.0%	

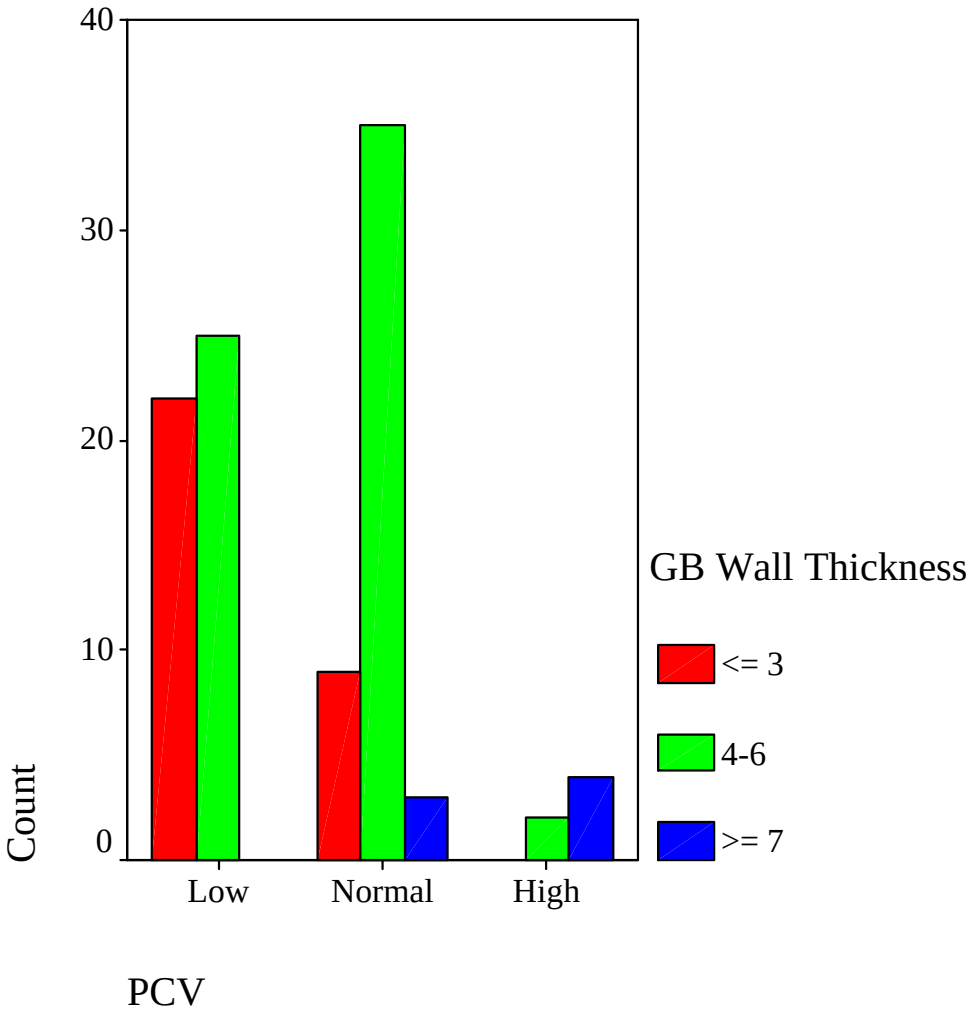


There was high significance in the association between the level of thrombocytopenia and the increase in GBWT. As the platelet count falls the gall bladder wall thickness increases. Gall bladder thickness is more than when there critical fall in level of platelets to life threatening level.

Haematocrit (PCV) and GBWT comparison

			GB Wall Thickness			Total	P value
			<= 3	4-6	>= 7		
PCV	Low	Count	22	25	0	47	<0.001
		% within PCV	46.8%	53.2%	.0%	100.0%	
		% within GB Wall Thickness	71.0%	40.3%	.0%	47.0%	
	Normal	Count	9	35	3	47	
		% within PCV	19.1%	74.5%	6.4%	100.0%	
		% within GB Wall Thickness	29.0%	56.5%	42.9%	47.0%	
	High	Count	0	2	4	6	
		% within PCV	.0%	33.3%	66.7%	100.0%	
		% within GB Wall	.0%	3.2%	57.1%	6.0%	

	Thickness					
Total	Count	31	62	7	100	
	% within PCV	31.0%	62.0%	7.0%	100.0 %	
	% within GB Wall Thickness	100.0 %	100.0 %	100.0 %	100.0 %	

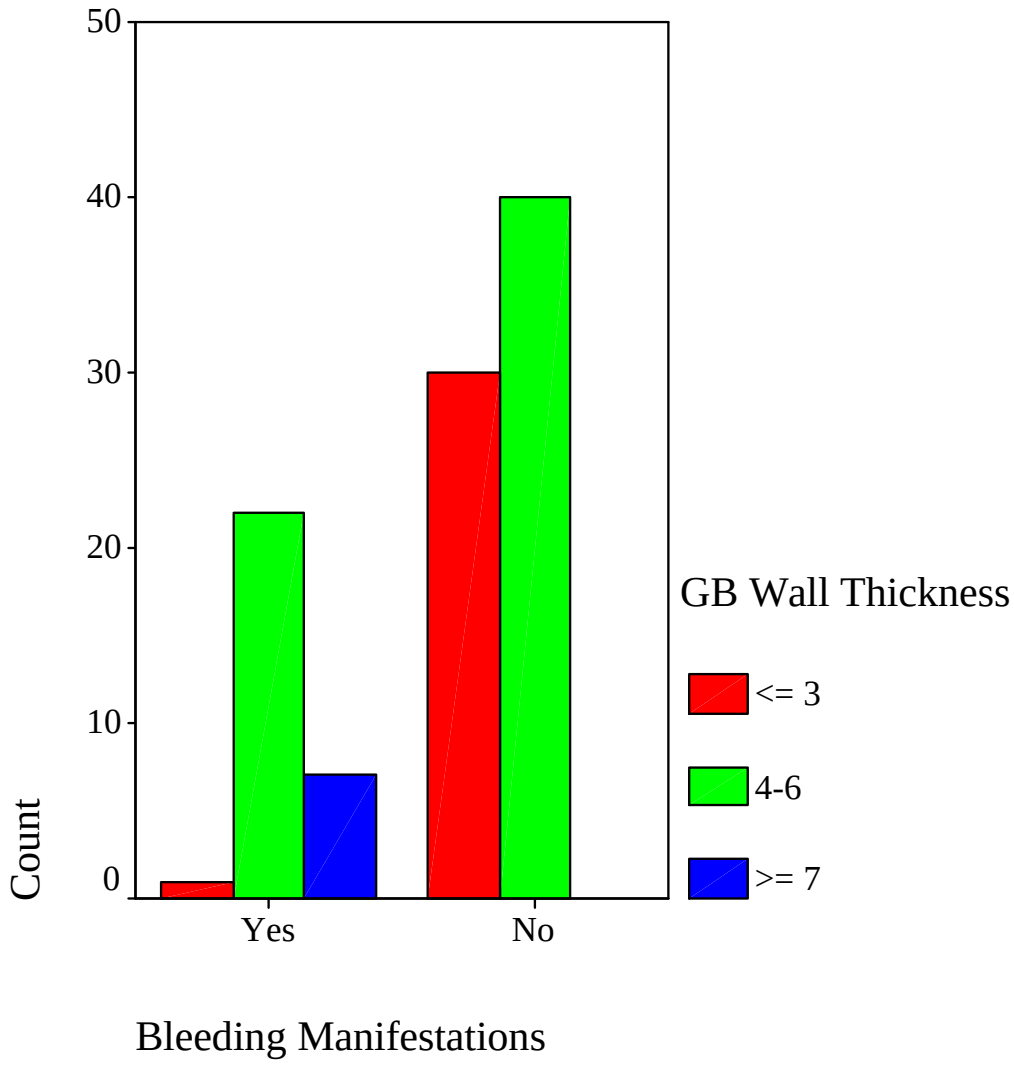


There was high significance statistically during comparison of HCT/PCV with GBWT, suggesting that there is higher plasma leakage with increasing GBWT causing elevated HCT levels.

COMPARISON OF BLEEDING MANIFESTATIONS AND GALL BLADDER WALL THICKNESS

			GB Wall Thickness			Total	P value
			<= 3	4-6	>= 7		
Bleeding Manifestations	Yes	Count	1	22	7	30	<0.001
		% within Bleeding Manifestations	3.3%	73.3%	23.3%	100.0%	
		% within GB Wall Thickness	3.2%	35.5%	100.0%	30.0%	
	No	Count	30	40	0	70	
		% within Bleeding Manifestations	42.9%	57.1%	.0%	100.0%	
		% within	96.8%	64.5%	.0%	70.0%	

	GB Wall Thickness					
Total	Count	31	62	7	100	
	% within Bleeding Manifestations	31.0%	62.0%	7.0%	100.0%	
	% within GB Wall Thickness	100.0%	100.0%	100.0%	100.0%	

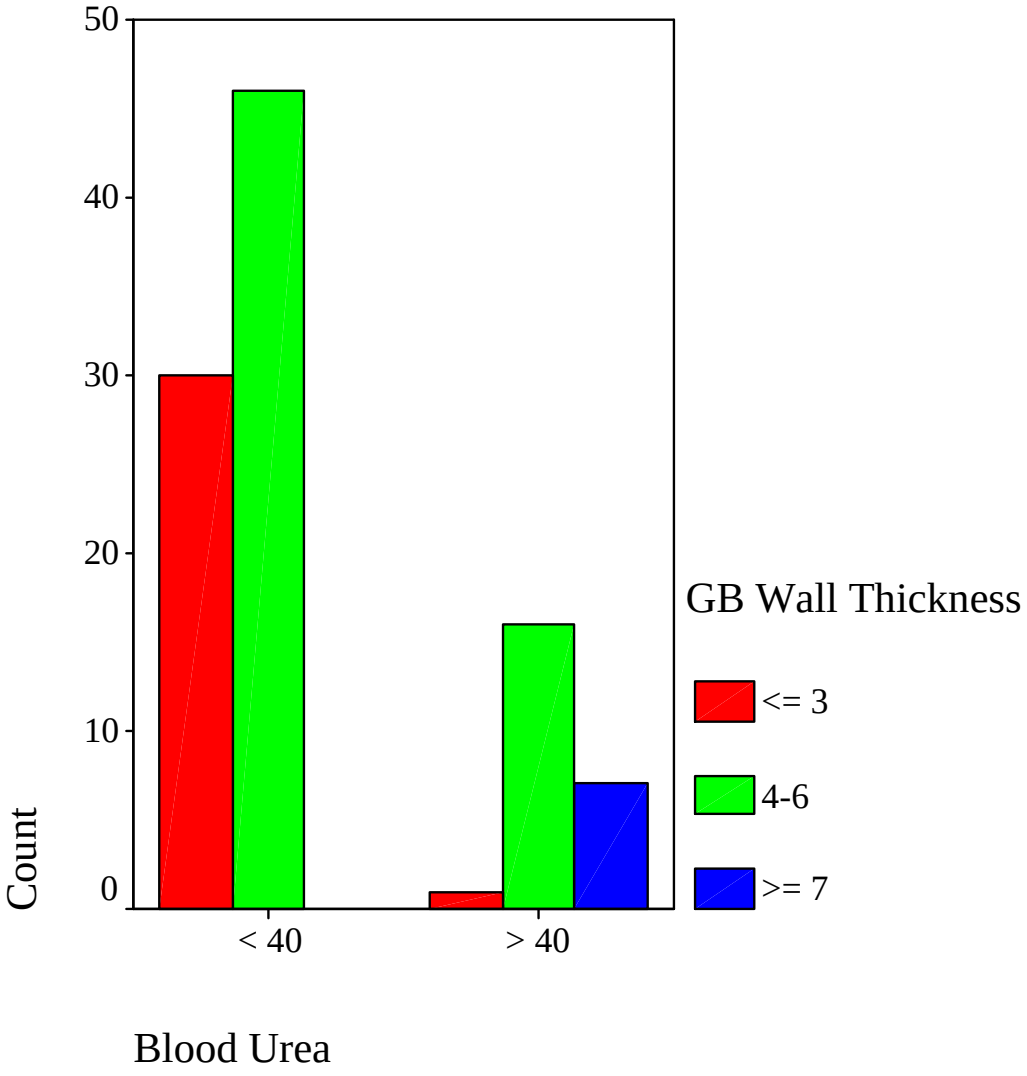


The comparison showed high statistical significance, meaning that there was high incidence of bleeding or DHF when the gall bladder thickness was more than or equal to 7mm.

COMPARISON OF SERUM UREA WITH GBWT

			GB Wall Thickness			Total	P value
			<= 3	4-6	>= 7		
Blood Urea	< 40	Count	30	46	0	76	
		% within Blood Urea	39.5%	60.5%	.0%	100.0%	
		% within GB Wall Thickness	96.8%	74.2%	.0%	76.0%	
	> 40	Count	1	16	7	24	
		% within Blood Urea	4.2%	66.7%	29.2%	100.0%	<0.001
		% within	3.2%	25.8%	100.0%	24.0%	

	GB Wall Thickness					
Total	Count	31	62	7	100	
	% within Blood Urea	31.0%	62.0%	7.0%	100.0%	
	% within GB Wall Thickness	100.0%	100.0%	100.0%	100.0%	

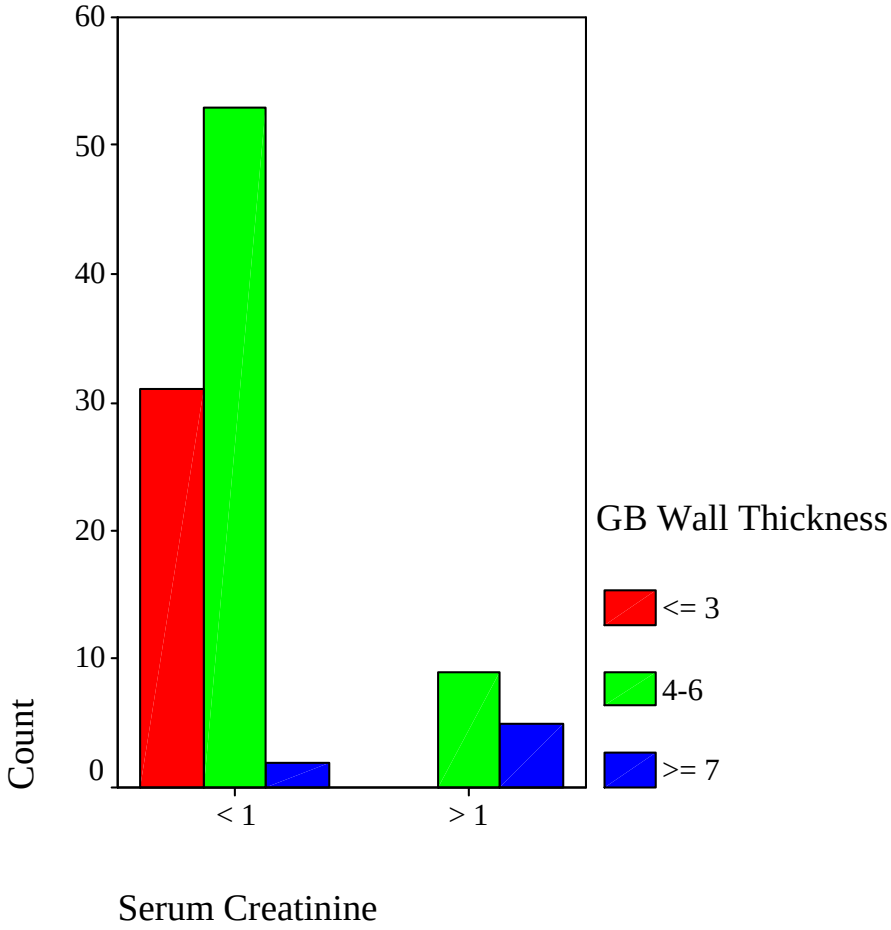


There was significant statistical outcome for the comparison, which suggests that the increased GBWT which is a measure of plasma leakage can cause renal failure as suggested by elevated urea levels.

COMPARISON OF SERUM CREATININE WITH GBWT

			GB Wall Thickness			Total	P value
			<= 3	4-6	>= 7		
Serum Creatinine	< 1	Count	31	53	2	86	
		% within Serum Creatinine	36.0%	61.6%	2.3%	100.0%	
		% within GB Wall Thickness	100.0%	85.5%	28.6%	86.0%	
	> 1	Count	0	9	5	14	<0.001
		% within Serum Creatinine	.0%	64.3%	35.7%	100.0%	
		% within GB Wall Thickness	.0%	14.5%	71.4%	14.0%	
Total		Count	31	62	7	100	

% within Serum Creatinine	31.0%	62.0%	7.0%	100.0%	
% within GB Wall Thickness	100.0%	100.0%	100.0%	100.0%	

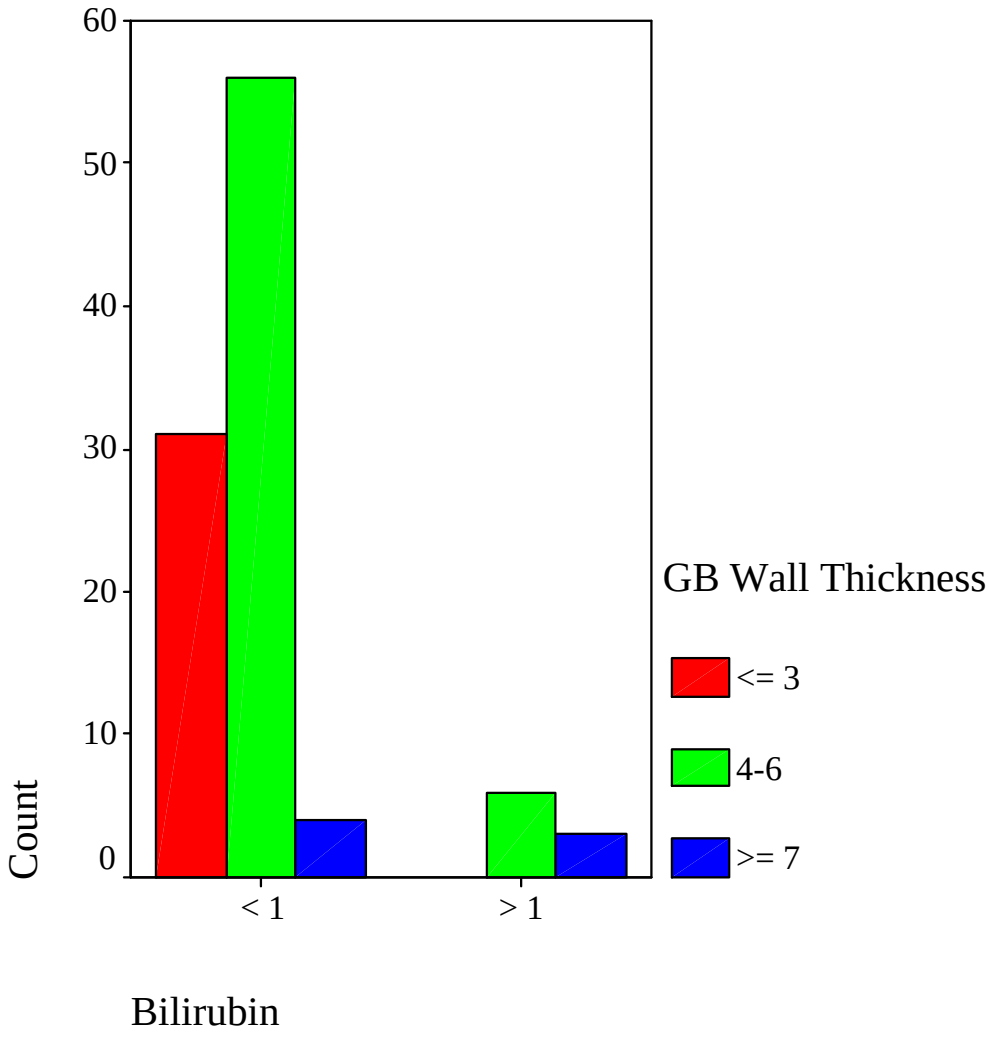


This comparative study showed high statistical significance, similar to the one with blood urea level, suggesting that increase in GBWT is associated with a high incidence in renal failure.

COMPARISON BETWEEN TOTAL BILIRUBIN AND GBWT

			GB Wall Thickness			Total	P value
			<= 3	4-6	>= 7		
Bilirubin	< 1	Count	31	56	4	91	
		% within Bilirubin	34.1%	61.5%	4.4%	100.0%	
		% within GB Wall Thickness	100.0%	90.3%	57.1%	91.0%	
	> 1	Count	0	6	3	9	
		% within Bilirubin	.0%	66.7%	33.3%	100.0%	0.002
		%	.0%	9.7%	42.9%	9.0%	

	within GB Wall Thickness					
Total	Count	31	62	7	100	
	% within Bilirubin	31.0%	62.0%	7.0%	100.0%	
	% within GB Wall Thickness	100.0%	100.0%	100.0%	100.0%	

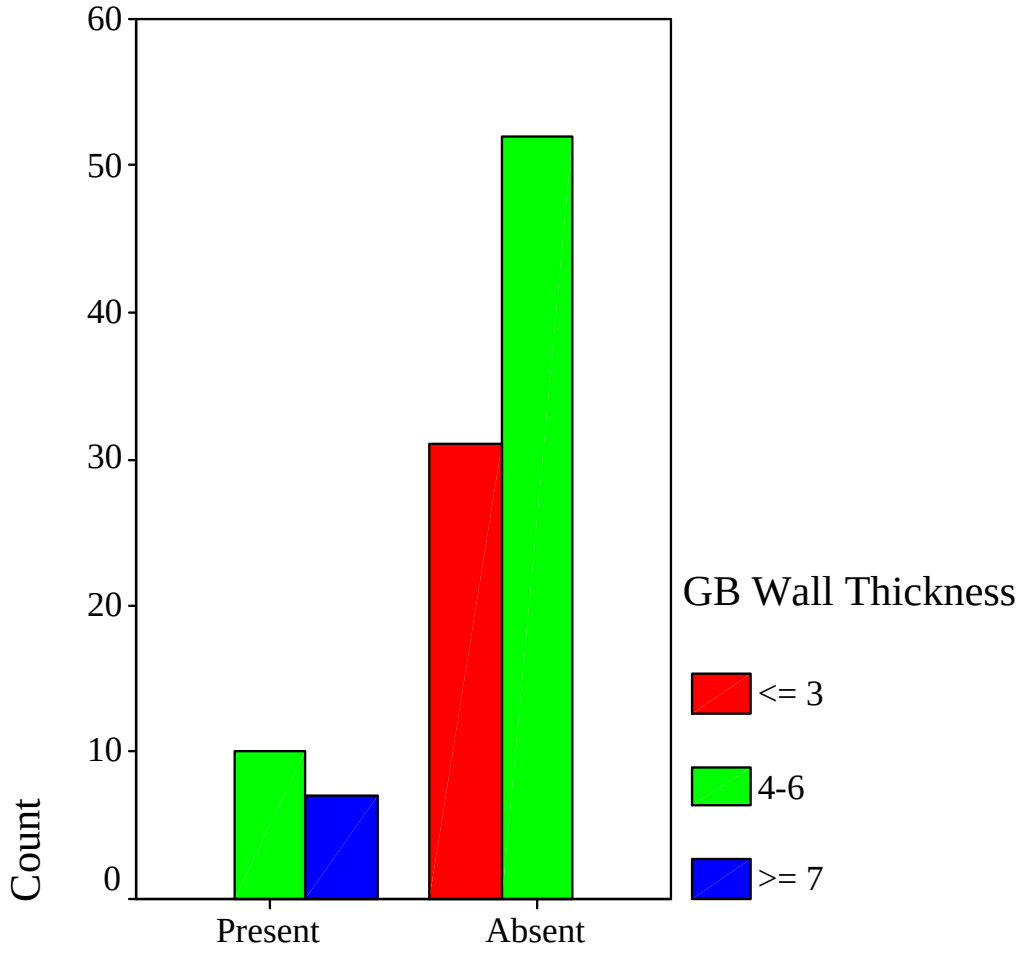


There is statistical significance with the comparison of GBWT with total bilirubin suggesting that there is high incidence of liver cell failure with increase in GBWT

COMPARISON OF GBWT AND PERINEPHRIC COLLECTION

			GB Wall Thickness			Total	P value
			<= 3	4-6	>= 7		
Perinephric Collection	Present	Count	0	10	7	17	
		% within Perinephric Collection	.0%	58.8%	41.2%	100.0%	
		% within GB Wall Thickness	.0%	16.1%	100.0%	17.0%	<0.001
	Absent	Count	31	52	0	83	
		% within Perinephric Collection	37.3%	62.7%	.0%	100.0%	
		% within GB Wall Thickness	100.0%	83.9%	.0%	83.0%	

Total	Count	31	62	7	100	
	% within Perinephric Collection	31.0%	62.0%	7.0%	100.0%	
	% within GB Wall Thickness	100.0%	100.0%	100.0%	100.0%	

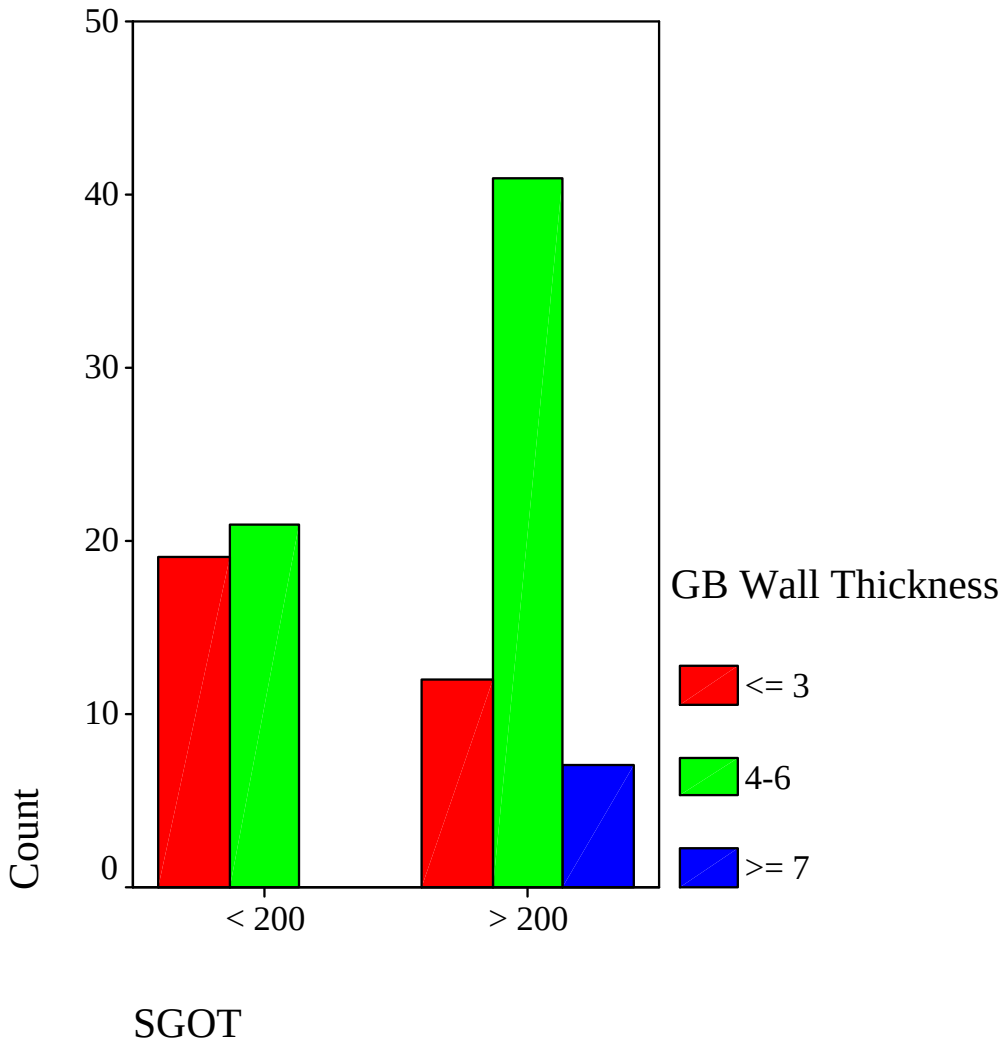


There is high statistical significance in the comparative data suggestive that increased GBWT is associated with severe plasma leakage as evidenced by perinephric collection.

COMPARISON OF GBWT AND SGOT

			GB Wall Thickness			Total	P value
			<= 3	4-6	>= 7		
SGOT	< 200	Count	19	21	0	40	
		% within SGOT	47.5%	52.5%	.0%	100.0%	
		% within GB Wall Thickness	61.3%	33.9%	.0%	40.0%	
	> 200	Count	12	41	7	60	
		% within SGOT	20.0%	68.3%	11.7%	100.0%	0.003
		% within GB Wall	38.7%	66.1%	100.0%	60.0%	

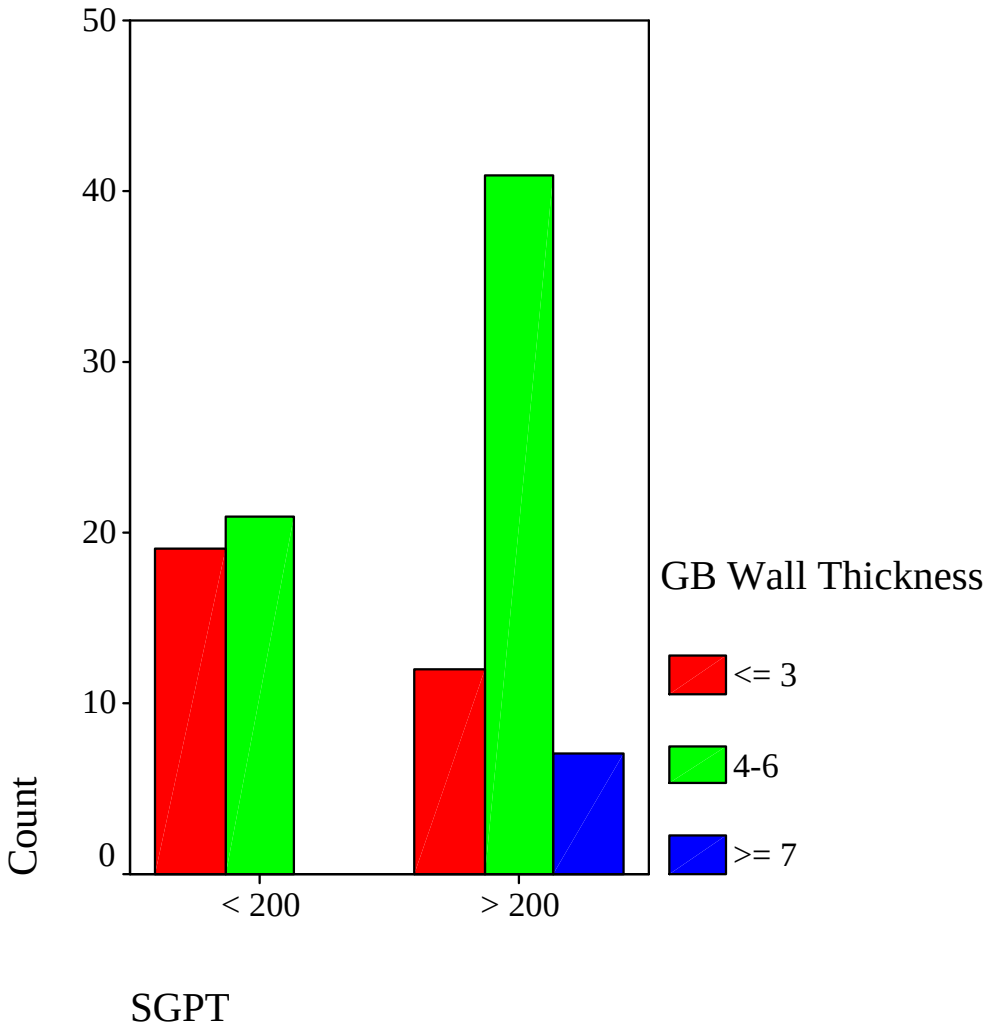
	Thickness					
Total	Count	31	62	7	100	
	% within SGOT	31.0%	62.0%	7.0%	100.0%	
	% within GB Wall Thickness	100.0%	100.0%	100.0%	100.0%	


50
40
30
20
10
0
Count
< 200
> 200
SGOT
GB Wall Thickness
<= 3
4-6
>= 7

COMPARISON BETWEEN SGPT AND GBWT

			GB Wall Thickness			Total	P value
			<= 3	4-6	>= 7		
SGPT	< 200	Count	19	21	0	40	
		% within SGPT	47.5%	52.5%	.0%	100.0%	
		% within GB Wall Thickness	61.3%	33.9%	.0%	40.0%	0.003
	> 200	Count	12	41	7	60	
		% within SGPT	20.0%	68.3%	11.7%	100.0%	
		% within GB Wall	38.7%	66.1%	100.0%	60.0%	

	Thickness					
Total	Count	31	62	7	100	
	% within SGPT	31.0%	62.0%	7.0%	100.0%	
	% within GB Wall Thickness	100.0%	100.0%	100.0%	100.0%	



Comparison between both SGPT and SGOT with GBWT showed statistical significance suggesting that more plasma leakage is associated with liver injury.

DISCUSSION

Dengue is a vector borne disease that has caused recurrent epidemics throughout the world. This study was conducted was conducted at the time of the epidemic in 2016. A similar epidemic occurred in 2015 which caused a great deal of mortality and morbidity throughout the country. The study was done in a tertiary government hospital where at the time most of the attention was given to the recent dengue breakout. And since it was higher referral centre most of the cases were already either diagnosed or were in poor condition that required urgent medical attention.

The most crucial part of treatment of dengue is the monitoring of the critical phase of dengue. This part is crucial that the patient may be asymptomatic to begin but will be having early features of plasma leakage. Only if the plasma leakage is early diagnosed can the disease be prevented from going for further complications. Once complications sets in dengue has a high mortality rate.

The critical phase of dengue fever is closely monitored by blood investigations mainly haematocrit and platelet count. This is a laborious task especially at the time of epidemic where the laboratories will be over-flooded. Research has been underway since many years for better, faster methods of assessing plasma leakage. One of the practical approach

is the assistance of radiological techniques namely ultrasound to detect serositis i.e. seepage of fluid in spaces lining internal organs. Many studies have revealed the importance of gall bladder wall thickening in dengue. Although acalculous cholecystitis is a part of dengue spectrum of diseases, the increase in gall bladder thickness has been found to correlate to the severity of plasma leakage. There has been proven study in many journals and research centres where they used serial ultrasound to assess the gall bladder wall thickness and found out that it is a reliable method to assess disease severity and plasma leakage. Also there have been reports of other signs of serositis such as pleural effusion, perinephric fluid collection and perihepatic fluid collection to have helped in assessing status of dengue fever.

In the current study onetime assessment of 100 patients of confirmed dengue fever was done with signs of bleeding, vitals, complete blood count, liver function test, renal function test and ultrasound for gall bladder wall thickness.

The date was compiled and using statistical tools were analysed. The current was almost in par with the observations of similar studies done outside.

Comparing the different variables of the study revealed the importance of gall bladder thickness.

Age groups and gender did not give much statistical significance when compared with gall bladder wall thickness. Only observation was that it was slightly more in younger population. Vitals like pulse and blood pressure were greatly deranged when it came to gall bladder wall thickness of 7 and above. This is backed up by statistical significance hence proves that plasma leakage is directly proportional to gall bladder wall thickness.

It was also noted that bleeding manifestations was also higher in cases of gall bladder wall thickness more than 7mm. This helps in monitoring for gall bladder wall thickness in stable patients to detect whether they are having increasing thickness which suggest that they high chance of bleeding. Early diagnosis of DHF can be done by following this test.

The increased gall bladder wall thickness also pointed to high incidence of multi organ damage as evidenced by the increase in blood urea, serum creatinine, total bilirubin, liver enzymes. All these variables have statistical significance in comparative data analysis. Also to be noted is the incidence of perinephric collection in select patients who had bleeding manifestations, multiorgan failure and shock all suggestive that this may be a finding associated with severe dengue.

The low platelet count and high haematocrit was directly proportional to gall bladder thickness, and showed statistical significance. This would mean gall bladder wall thickening can be used as a method of assessing plasma leakage along with haematocrit and platelet count. This will reduce the number of needle pricks, the lesser number of infection spread, and much lesser need of laboratory assistance.

The study also had various short comings. The study was done in a tertiary hospital so the study group included mostly severe dengue infected patients who were referred from primary or secondary care hospitals. This might caused a greater number of people who were in the extreme zone of to have been included in the study. Also many patients are on domiciliary treatment for dengue and could not be include in the study. The laboratory values can also can have its share of errors which can also affect a part of the study. A follow up study was not included which would have thrown more light as to aspects of how many the variables would have shifted further more in the course of time.

CONCLUSION

From the study, it has come into conclusion that gall bladder wall thickness is a significant contributor to assessment of plasma leakage and hence the severity of dengue. Many authorised studies have backed up this observation. The main advantage of this method is that it a fast and easily approachable method and can be easily practised in most centres. With this added tool the monitoring of dengue patients become more comprehensive and hopefully can used to curb the onset dengue associated complications like dengue shock syndrome. Many other tools for better assessment of dengue severity and monitoring are in research so are research for vaccines and drugs. Hopefully all these will ensure that the morbidity and mortality of dengue and controlled and someday the disease itself be brought into control.

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"GALL BLADDER THICKNESS IN DENGUE AND ITS ASSOCIATION WITH DISEASE SEVERITY"

PROFORMA

Name: Age/Sex:

Address: Occupation:

SYMPTOMS:

Fever

Myalgia and arthralgia

Bleeding manifestations

PAST HISTORY:

Any co morbid illness

Previous history of dengue

PERSONAL HISTORY:

Any significant past history

GENERAL EXAMINATION:

Level of consciousness

VITAL SIGNS:

PR-

BP-

RR-

TEMP-

SYSTEMIC EXAMINATION:

CVS:

RS:

ABDOMEN:

CNS

INVESTIGATIONS

COMPLETE HEMOGRAM

RFT

LFT

Dengue IgM

USG Abdomen

INSTITUTIONAL ETHICS COMMITTEE
MADRAS MEDICAL COLLEGE, CHENNAI 600 003

EC Reg.No.ECR/270/Inst./TN/2013
Telephone No.044 25305301
Fax: 011 25363970

CERTIFICATE OF APPROVAL

To
Dr. Ramu Krishnan.U.
Post Graduate in M.D. General Medicine
Madras Medical College
Chennai 600 003

Dear Dr. Ramu Krishnan.U,

The Institutional Ethics Committee has considered your request and approved your study titled **"GALL BLADDER WALL THICKNESS IN DENGUE AND ITS ASSOCIATION WITH THE DISEASE SEVERITY " - NO.08032016.**

The following members of Ethics Committee were present in the meeting hold on **01.03.2016** conducted at Madras Medical College, Chennai 3

1.Dr.C.Rajendran, MD.,	:Chairperson
2.Dr.R.Vimala,MD.,Dean,MMC,Ch-3	:Deputy Chairperson
3.Prof.Sudha Seshayyan,MD., Vice Principal,MMC,Ch-3	: Member Secretary
4.Prof.B.Vasanthi,MD.,Inst.of Pharmacology,MMC,Ch-3	: Member
5.Prof.P.Raghumani,MS, Dept.of Surgery,RGGGH,Ch-3	: Member
6.Dr.Baby Vasumathi, Director, Inst. of O&G,Ch-8	: Member
7.Prof.M.Saraswathi,MD.,Director, Inst.of Path,MMC,Ch-3:	Member
8.Prof.Srinivasagalu,Director,Inst.of Int.Med.,MMC,Ch-3	: Member
9.Tmt.J.Rajalakshmi, JAO,MMC, Ch-3	: Lay Person
10.Thiru S.Govindasamy, BA.,BL,High Court,Chennai	: Lawyer
11.Tmt.Arnold Saulina, MA.,MSW.,	:Social Scientist

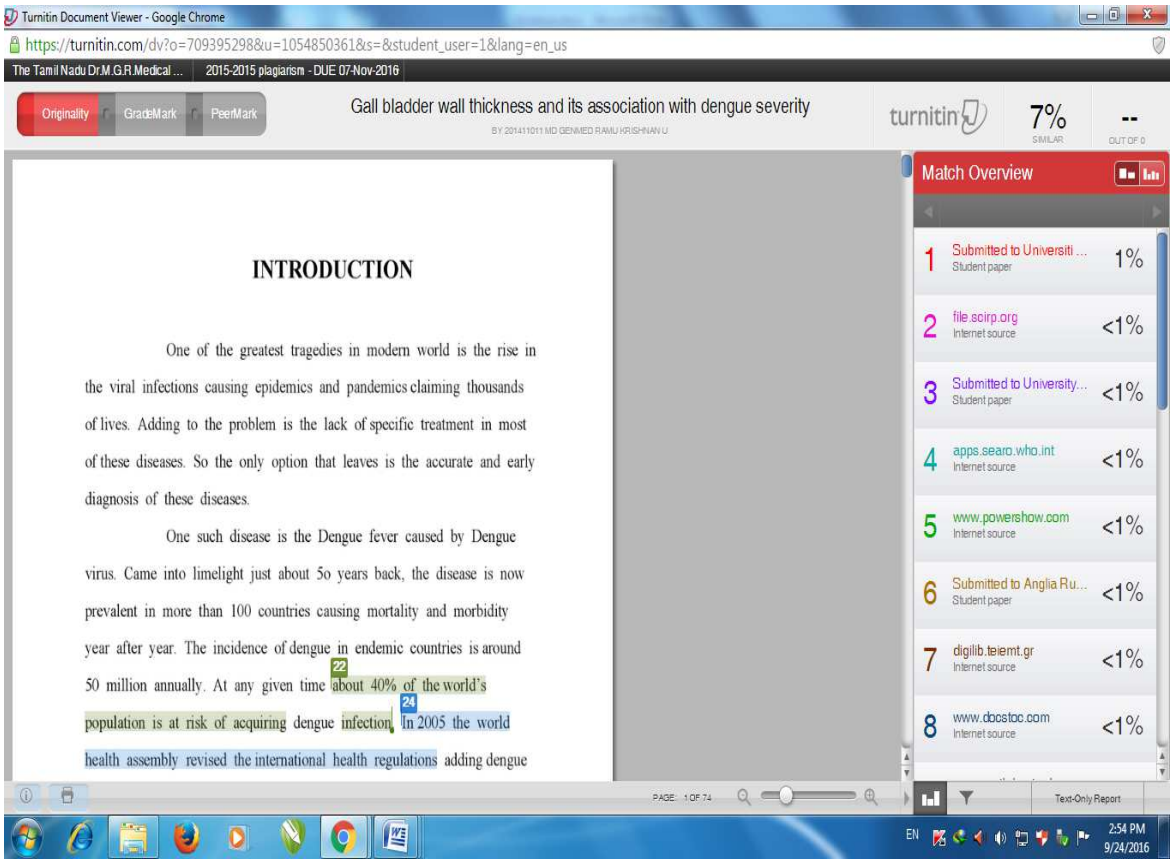
We approve the proposal to be conducted in its presented form.

The Institutional Ethics Committee expects to be informed about the progress of the study and SAE occurring in the course of the study, any changes in the protocol and patients information/informed consent and asks to be provided a copy of the final report.

Member Secretary – Ethics Committee

MEMBER SECRETARY
INSTITUTIONAL ETHICS COMMITTEE
MADRAS MEDICAL COLLEGE
CHENNAI-600 003

TURNITIN PLAGIARISM SCREENSHOT



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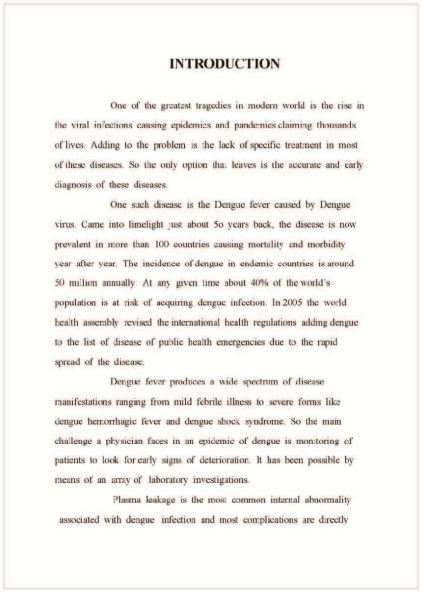

INTRODUCTION

One of the greatest tragedies in modern world is the rise in the viral infections causing epidemics and pandemics claiming thousands of lives. Adding to the problem is the lack of specific treatment in most of these diseases. So the only option that leaves is the accurate and early diagnosis of these diseases.

One such disease is the Dengue fever caused by Dengue virus. Came into limelight just about 50 years back, the disease is now prevalent in more than 100 countries causing mortality and morbidity year after year. The incidence of dengue in endemic countries is around 50 million annually. At any given time about 40% of the world's population is at risk of acquiring dengue infection. In 2005 the world health assembly revised the international health regulations adding dengue to the list of disease of public health emergencies due to the rapid spread of the disease.

Dengue fever produces a wide spectrum of disease manifestations ranging from mild febrile illness to severe forms like dengue hemorrhagic fever and dengue shock syndrome. So the main challenge a physician faces in an epidemic of dengue is monitoring of patients to look for early signs of deterioration. It has been possible by means of an array of laboratory investigations.

Plasma leakage is the most common internal abnormality associated with dengue infection and most complications are directly

INFORMATION SHEET

We are conducting a study on **"GALL BLADDER THICKNESS IN DENGUE PATIENTS AND ITS CORRELATION WITH THE DISEASE SEVERITY"** among patients attending Rajiv Gandhi Government General Hospital, Chennai and for that your cooperation is valuable to us.

The purpose of this study is to assess the sensitivity of ultrasound abdomen in detecting subclinical plasma leakage as detected by an increased gall bladder thickness and its comparing with the disease severity.

We are selecting certain cases and if you are found eligible, we may be using your blood samples to do necessary tests only and an ultrasound of the abdomen which in any way do not affect your final report or management.

The privacy of the patients in the research will be maintained throughout the study. In the event of any publication or presentation resulting from the research, no personally identifiable information will be shared.

Taking part in this study is voluntary. You are free to decide whether to participate in this study or to withdraw at any time; your decision will not result in any loss of benefits to which you are otherwise entitled.

The results of the special study may be intimated to you at the end of the study period or during the study if anything is found abnormal which may aid in the management or treatment.

Signature of Investigator | Signature of Participant

Date :

Place :

ஆராய்ச்சி தகவல் தாள்

சென்னை ராஜீவ் காந்தி அரசு பொது மருத்துவமனைக்கு வரும் நோயாளிகளில் **டெங்கு நோயாளிகளின் பித்தப்பை தடிமன் மற்றும் நோயின் தீவிரபத்துடன் அதன் தொடர்பு பற்றிய ஆய்வு** நடைபெறுகிறது.

நீங்களும் இந்த ஆராய்ச்சியில் பங்கேற்க நாங்கள் விரும்புகிறோம். அதனால் தங்களது நோயின் ஆய்வறிக்கையோ அல்லது சிகிச்சையோ பாதிப்பு ஏற்படாது என்பதையும் தெரிவித்துக்கொள்கிறோம்.

முடிவுகளை அல்லது கருத்துக்களை வெளியிடும்போதோ அல்லது ஆராய்ச்சியின்போதோ தங்களது பெயரையோ அல்லது அடையாளங்களையோ வெளியிட மாட்டோம் என்பதை தெரிவித்துக்கொள்கிறோம்.

இந்த ஆராய்ச்சியில் பங்கேற்பது தங்களுடைய விருப்பத்தின்பேரில்தான் இருக்கிறது. மேலும் நீங்கள் எந்த நேரமும் இந்த ஆராய்ச்சியிலிருந்து பின்வாங்கலாம் என்பதையும் தெரிவித்துக்கொள்கிறோம்.

இந்த சிறப்பு பரிசோதனைகளின் முடிவுகளையும் நோயின் தன்மை பற்றியும் ஆராய்ச்சியின்போது அல்லது ஆராய்ச்சியின் முடிவின்போது தங்களுக்கு அறிவிப்போம் என்பதையும் தெரிவித்துக்கொள்கிறோம்.

ஆராய்ச்சியாளர் கையொப்பம் **பங்கேற்பாளர் கையொப்பம்**

நோயாளியின் உறவினர்/ காப்பாளர் கையொப்பம்

PATIENT CONSENT FORM

Study Detail : "**GALL BLADDER THICKNESS IN DENGUE AND ITS CORRELATION WITH DISEASE SEVERITY**"

Study Centre : Rajiv Gandhi Government General Hospital, Chennai.

Patient's Name :

Patient's Age :

Identification Number :

Patient may check (√) these boxes

a) I confirm that I have understood the purpose of procedure for the above study. I have the opportunity to ask question and all my questions and doubts have been answered to my complete satisfaction. ❑

b) I understand that my participation in the study is voluntary and that I am free to withdraw at any time without giving reason, without my legal rights being affected. ❑

c) I understand that sponsor of the clinical study, others working on the sponsor's behalf, the ethical committee and the regulatory authorities will not need my permission to look at my health records, both in respect of current study and any further research that may be conducted in relation to it, even if I withdraw from the study I agree to this access. However, I understand that my identity will not be revealed in any information released to third parties or published, unless as required under the law. I agree not to restrict the use of any data or results that arise from this study. ❑

d) I agree to take part in the above study and to comply with the instructions given during the study and faithfully cooperate with the study team and to immediately inform the study staff if I suffer from any deterioration in my health or well being or any unexpected or unusual symptoms. ❑

e) I hereby consent to participate in this study. ❑

f) I hereby give permission to undergo detailed clinical examination and blood investigations as required. ❑

Signature/thumb impression	Signature of Investigator
Patient's Name and Address:	Study Investigator's Name: **Dr. RAMU KRISHNAN. U**

ஆய்வு பற்றிய சுய ஒப்புதல் படிவம்

ஆய்வின் தலைப்பு

டெங்கு நோயாளிகளின் பித்தப்பை தடிமன் மற்றும் நோயின் தீவிரபத்துடன் அதன் தொடர்பு

ஆய்வு நிலையம் : சென்னை மருத்துவக் கல்லூரி மற்றும்
ராஜீவ் காந்தி அரசு பொது மருத்துவமனை,
சென்னை - 3.

பங்கு பெறுவரின் பெயர் : உறவுமுறை:

பங்குபெறுபவரின் எண் :

பங்குபெறுபவர் இதனை (✓) குறிக்கவும்

மேலே குறிப்பிட்டுள்ள மருத்துவ ஆய்வின் விவரங்கள் எனக்கு விளக்கப்பட்டது. என்னுடைய சந்தேகங்களை கேட்கவும், அதற்கான தகுந்த விளக்கங்களை பெறவும் வாய்ப்பளிக்கப்பட்டது. ☐

நான் இவ்வாய்வில் தன்னிச்சையாகதான் பங்கேற்கிறேன். எந்த காரணத்தினாலோ எந்த கட்டத்திலும் எந்த சட்ட சிக்கலுக்கும் உட்படாமல் நான் இவ்வாய்வில் இருந்து விலகி கொள்ளலாம் என்றும் அறிந்து கொண்டேன். ☐

இந்த ஆய்வு சம்பந்தமாகவோ, இதை சார்ந்த மேலும் ஆய்வு மேற்கொள்ளும் போதும் இந்த ஆய்வில் பங்குபெறும் மருத்துவர் என்னுடைய மருத்துவ அறிக்கைகளை பார்ப்பதற்கு என் அனுமதி தேவையில்லை என அறிந்து கொள்கிறேன். நான் ஆய்வில் இருந்து விலகிக் கொண்டாலும் இது பொருந்தும் என அறிகிறேன். ☐

இந்த ஆய்வின் மூலம் கிடைக்கும் தகவல்களையும், பரிசோதனை முடிவுகளையும் மற்றும் சிகிச்சை தொடர்பான தகவல்களையும் மருத்துவர் மேற்கொள்ளும் ஆய்வில் பயன்படுத்திக்கொள்ளவும் அதை பிரசுரிக்கவும் என் முழு மனதுடன் சம்மதிக்கின்றேன். ☐

இந்த ஆய்வில் பங்கு கொள்ள ஒப்புக்கொள்கிறேன். எனக்கு கொடுக்கப்பட்ட அறிவுரைகளின்படி நடந்து கொள்வதுடன், இந்த ஆய்வை மேற்கொள்ளும் மருத்துவ அணிக்கு உண்மையுடன் இருப்பேன் என்று உறுதியளிக்கிறேன். ☐

இந்த ஆய்வில் எனக்கு மருத்துவபரிசோதனை, இரத்தப் பரிசோதனை, சிறுநீர் பரிசோதனை, ஊடுகதிர்படம், இதய மின்துடிப்பு வரைவி மற்றும் நுண்கதிர் வயிறு பரிசோதனை செய்து கொள்ள முழு மனதுடன் நான் சம்மதிக்கிறேன். ☐

பங்கேற்பவரின் கையொப்பம் ..... இடம்..... தேதி.....

கட்டைவிரல் ரேகை:

நோயாளியின் உறவினர்/ காப்பாளர் கையொப்பம் ..... இடம்..... தேதி.....

பங்கேற்பவரின் பெயர் மற்றும் விலாசம் .....

ஆய்வாளரின் கையொப்பம் ..... இடம்..... தேதி.....

ஆய்வாளரின் பெயர் .....

AGE	GENDER	PULSE	BP	PLATELET	PCV	BLEEDING MANIFESTATIONS	B. UREA	S. CREAT	Br	SGOT	SGPT	GB WALL THICKNESS	PERINEPHRIC COLLECTION
24	M	100	100/60	14000	39		46	1	0.8	112	87	5	
31	F	104	90/60	21000	38	menorrhagia	38	0.8	0.7	164	121	5	
28	F	86	110/70	33000	31		40	0.9	0.5	202	205	3	
59	F	110	90/60	8000	42	malaena,subconj hge	54	1.1	1	341	320	7	present
41	F	80	120/80	23000	33		54	0.8	0.6	141	136	3	
18	M	120	80/60	14000	50	malaena,subconj hge	60	1.4	1.1	236	341	8	present
38	M	50	110/50	67000	38		28	0.8	0.5	128	106	2	
52	F	68	100/80	56000	37		28	0.8	0.8	212	206	3	
33	F	90	90/60	40000	32		36	0.8	0.4	282	312	4	
24	M	60	110/80	90000	30		22	0.4	0.2	56	52	3	
27	F	100	100/60	70000	40		36	0.7	0.4	186	192	4	
32	M	100	90/60	22000	32	subconj hge	41	0.8	0.9	300	302	4	
43	M	120	80/60	12000	46	malaena,subconj hge	56	1.3	0.7	280	281	8	present
37	F	84	100/70	50000	40		40	1.2	0.6	262	212	4	
54	M	100	100/60	30000	44	subconj hge	54	1.2	1.7	341	280	5	present
49	M	80	100/70	28000	38	subconj hge	40	1	0.9	212	206	4	
38	F	54	110/80	74000	29		23	0.4	0.3	202	205	3	
26	F	118	90/60	22000	40	menorrhagia	38	0.5	0.5	128	140	5	
36	F	130	70/50	4000	50	menorrhagia,malaena,subconj hge	56	1.2	1.7	400	402	8	present
27	M	90	90/60	8000	32	subconj hge	31	0.9	1.1	282	284	5	
19	M	56	100/80	44000	30		28	0.6	0.6	131	134	3	
54	F	68	90/60	53000	39		26	0.6	0.5	168	161	3	
18	F	120	80/60	8500	44	menorrhagia,sub conj hge	44	0.8	0.7	312	316	5	
20	F	106	90/60	7000	38	menorrhagia	36	0.7	0.5	262	205	6	present
38	M	98	100/80	14000	33	subconj hge	34	0.5	0.5	168	162	4	
35	F	100	100/70	27000	38		30	0.7	0.8	156	152	4	
29	F	100	100/60	23500	28	menorrhagia	30	0.5	0.6	161	168	4	
26	M	100	110/60	22000	40	malaena,subconj hge	60	1.2	1.1	312	306	6	present
31	M	78	120/80	68000	38		42	1	1.1	246	256	4	
40	M	100	100/60	24000	38	subconj hge	40	1.1	0.9	286	268	5	
28	M	110	90/60	17000	39	subconj hge,malaena	46	1.2	0.7	268	242	6	present
22	F	110	90/60	9000	42	menorrhagia,malaena	60	1.3	1.4	382	322	6	present
55	F	80	110/80	42000	22		30	0.5	0.4	121	106	3	
46	F	100	100/70	48000	26		21	0.4	0.3	282	206	3	
18	F	100	90/60	54000	40		30	0.5	0.4	202	240	3	
19	M	90	110/80	55000	32		28	0.6	0.4	201	207	3	

26	M	100	80/50	10000	50	malaena	50	0.9	0.8	262	342	6	present
40	F	100	120/80	90000	38		26	0.5	0.3	292	212	4	
45	M	80	120/80	104000	32		38	0.6	0.3	212	212	3	
31	M	80	110/70	120000	35		36	0.6	0.4	286	345	3	
36	M	80	110/80	98000	36		22	0.5	0.3	121	106	3	
32	F	100	100/70	30000	40		42	0.9	0.8	386	312	5	
39	F	100	90/60	26000	36	menorrhagia	40	0.8	0.8	346	342	6	
25	F	100	120/80	850000	33		32	0.8	0.4	302	303	4	
35	M	90	100/80	40000	33	malaena	40	0.9	0.6	282	286	5	present
22	F	120	80/60	3000	55	malaena,subconj hge,menorrhagia	68	1.4	0.8	441	368	8	present
46	M	80	120/80	88000	32		32	0.8	0.6	212	220	4	
51	F	60	110/70	64000	30		26	0.5	0.7	268	288	3	
18	F	50	110/70	94000	32		22	0.4	0.2	206	222	3	
22	M	80	110/70	80000	26		26	0.2	0.4	84	86	3	
40	F	100	100/80	37000	40		39	0.6	0.8	302	286	5	
36	M	100	90/60	44000	36		30	0.5	0.6	202	201	4	
38	F	100	100/80	56000	32		40	0.5	0.3	192	106	4	
35	F	90	100/80	36000	28	malaena	38	0.8	0.4	186	224	4	
45	F	60	110/70	102000	26		22	0.4	0.4	34	31	3	
52	M	90	100/80	20000	22	malaena	39	0.5	0.5	230	226	5	
50	M	100	100/80	25000	46	malaena	42	0.8	0.8	341	338	6	
18	F	110	80/60	8000	45	malaena	46	0.7	0.9	302	321	7	present
20	F	100	100/70	12000	38	malaena	40	0.8	0.8	208	222	5	
50	F	80	100/80	56000	31		20	0.2	0.4	231	206	3	
58	F	90	100/80	78000	34		26	0.3	0.3	201	236	4	
20	M	100	100/80	42000	36		28	0.4	0.4	234	226	4	
22	F	110	90/60	14000	44	menorrhagia,malaena	40	0.9	0.9	308	306	6	present
44	F	80	110/80	120000	34		32	0.5	0.5	38	32	2	
42	F	80	120/80	100000	36		30	0.5	0.6	68	64	2	
37	F	100	100/80	74000	39		32	0.5	0.6	56	54	3	
56	F	90	150/90	56000	40		40	0.8	0.6	280	234	4	
59	M	100	120/80	82000	22		23	0.5	0.5	40	40	4	
28	F	80	110/80	66000	29		22	0.6	0.4	66	78	3	
18	M	110	80/60	11000	42	malaena,subconj hge	39	0.9	0.8	256	278	6	
18	M	120	70/50	7000	41	malena ,subconj hge	48	1	1	298	376	6	present
50	F	100	100/80	36000	29		30	0.5	0.6	48	98	5	
48	F	100	100/80	42000	29		36	0.6	0.8	236	286	5	

45	M	102	100/80	36000	31	malaena	32	0.2	0.6	88	58	5	
42	F	80	100/80	57000	34		24	0.5	0.4	46	88	3	
36	F	90	110/80	66000	30		22	0.5	0.4	106	110	3	
32	M	80	120/80	78000	32		24	0.6	0.5	149	146	3	
28	F	100	90/60	32000	30		28	0.5	0.5	206	208	4	
52	F	100	80/60	15000	41	malaena	56	1.3	1.2	286	293	4	
42	M	100	100/80	52000	28		30	1.2	0.8	122	106	4	
37	M	80	110/80	67000	26		22	0.4	0.4	168	172	4	
40	M	96	130/80	90000	20		28	0.3	0.2	78	72	3	
52	M	80	130/80	82000	29		23	0.4	0.8	42	46	3	
60	F	100	100/80	28000	39		46	0.9	0.9	301	306	4	
20	M	80	100/80	56000	40		35	0.8	0.8	282	280	5	
18	M	98	90/60	32000	27		36	0.4	0.4	161	168	5	
24	F	92	110/80	36000	40		34	0.6	0.6	160	200	4	
27	M	102	100/80	20000	38		42	0.8	0.7	236	240	5	
24	F	80	130/80	38000	29		36	0.4	0.4	134	134	5	
31	F	80	110/80	42000	36		24	0.5	0.3	112	126	4	
18	F	110	80/60	5000	42	malaena ,subconj hge	48	1.1	1	312	328	6	present
20	F	100	100/70	16000	40	malaena	40	0.8	1	286	294	5	
40	M	100	120/80	36000	36		38	0.7	0.4	184	188	4	
32	M	70	110/80	32000	30		32	0.5	0.5	56	34	4	
36	M	90	130/80	54000	38		28	0.6	0.7	256	202	3	
44	F	80	120/80	68000	26		36	0.5	0.4	110	112	3	
40	F	78	110/80	44000	28		40	0.4	0.3	212	228	4	
48	F	84	100/80	30000	30		28	0.3	0.3	202	192	4	
28	F	90	120/80	22000	32	malaena	26	0.4	0.6	112	118	5	
18	M	120	80/50	1000	44	malaena,subconj hge	48	0.8	1.2	341	326	7	present

normal gall bladder thickness less than 3mm

pernephric collection sign of severe dengue or plasma leakage