A STUDY ON EXUDATIVE ETIOLOGY OF PLEURAL EFFUSION IN CHRONIC KIDNEY DISEASE IN A TERTIARY CARE HOSPITAL

DISSERTATION SUBMITTED FOR

M.D GENERAL MEDICINE

BRANCH – I

APRIL 2017

THE TAMILNADU

DR.M.G.R. MEDICAL UNIVERSITY

CHENNAI, TAMILNADU, INDIA

CERTIFICATE

This is to certify that the dissertation entitled "**A STUDY ON EXUDATIVE ETIOLOGY OF PLEURAL EFFUSION IN CHRONIC KIDNEY DISEASE IN A TERTIARY CARE HOSPITAL"** is the bonafide work of **Dr. A. MURALITHARAN** in partial fulfilment of the university regulations of the Tamil Nadu Dr.M.G.R Medical University, Chennai, for **M.D General Medicine Branch I** examination to be held in **April 2017.**

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DECLARATION

I **Dr.A. MURALITHARAN,** solemnly declare that, this dissertation "**A STUDY ON EXUDATIVE ETIOLOGY OF PLEURAL EFFUSION IN CHRONIC KIDNEY DISEASE IN A TERTIARY CARE HOSPITAL**" is a bonafide record of work done by me at the Department of General Medicine, Govt. Rajaji Hospital, Madurai, under the guidance of **Dr.R. BALAJINATHAN,M.D**, Professor, Department of General Medicine, Madurai Medical College, Madurai.

This dissertation is submitted to The Tamil Nadu Dr. M.G.R Medical University, Chennai in partial fulfilment of the rules and regulations for the award of **M.D Degree General Medicine Branch-I;** examination to be held in **April 2017.**

Place: Madurai

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ACKNOWLEDGEMENT

I would like to thank **Dr.M.R.VAIRAMUTHU RAJU,MD** Dean, Madurai Medical College, for permitting me to utilize the facilities of Madurai Medical College and Government Rajaji Hospital for this dissertation.

I wish to express my respect and sincere gratitude to my beloved teacher and head of department, **Prof.Dr.V.T.PREMKUMAR,M.D.,** Professor of medicine for his valuable guidance and encouragement during the study and also throughout my course period.

I would like to express my deep sense of gratitude, respect and thanks to my beloved Unit Chief and Professor of Medicine **Prof.Dr.R.BALAJINATHAN, M.D.,** for his valuable suggestions, guidance and support throughout the study and also throughout my course period.

I am greatly indebted to my beloved Professors, **M.D., Dr.M.NATARAJAN, M.D., Dr.G.BAGHYALAKSHMI, M.D., Dr.J.SANGUMANI, M.D., Dr.C.DHARMARAJ, M.D., and Dr.R.PRABHAKARAN, M.D.,Dr.S. RAVINDRAN,MD** for their valuable suggestions throughout the course of study.

I express my special thanks to **Dr.BALASUBRAMANIAN M.D**, **D.M**., Professor and HOD Department of Cardiology for permitting me to utilize the facilities in the Department, for the purpose of this study and guiding me with enthusiasm throughout the study period.

I express my special thanks to **Dr. SUMATHI MDRD,** Professor and HOD Department of Radiology for permitting me to utilize the facilities in the Department, for the purpose of this study and guiding me with enthusiasm throughout the study period.

I express my special thanks to **Dr. CHANDRAMOHAN, MD,DM** Professor and HOD Department of Nephrology for permitting me to utilize the facilities in the Department, for the purpose of this study and guiding me with enthusiasm throughout the study period.

I express my special thanks to **Dr. PRABAKARAN,MD** Professor and HOD Department of Thoracic Medicine for permitting me to utilize the facilities in the Department, for the purpose of this study and guiding me with enthusiasm throughout the study period.

I express my special thanks to **Dr.MEENAKUMARI,MD** Professor and HOD Department of Pathology for permitting me to utilize the facilities in the Department, for the purpose of this study and guiding me with enthusiasm throughout the study period.

I express my special thanks to **Dr.JAGATHESWARI,MD** Professor and HOD Department of Microbiology for permitting me to utilize the facilities in the Department, for the purpose of this study and guiding me with enthusiasm throughout the study period.

I express my special thanks to **Dr.MOHAN KUMARESAN,MD** Professor and HOD Department of Biochemistry for permitting me to utilize the facilities in the Department, for the purpose of this study and guiding me with enthusiasm throughout the study period.

I am extremely thankful to Assistant Professors of Medicine of my Unit,**Dr.V.N.ALAGAVENKATESAN,M.D**., and **Dr.P.V.BALAMURUGAN,**M**D**, for their valid comments and suggestions.

I extend my love and express my gratitude to my family and friends for their constant support during my study period in times of need.

Finally, I thank all the patients, who form the most vital part of my work, for their extreme patience and co-operation without whom this project would have been a distant dream and I pray God, for their speedy recovery.

CONTENTS

INTRODUCTION

Chronic kidney disease (CKD) encompasses a spectrum of different pathophysiologic processes associated with abnormal renal function, and a progressive decline in glomerular filtration rate (GFR). Pleural effusion in such patients is a common diagnostic dilemma as it may arise from CKD itself (fluid overload, nephrotic syndrome, uremic pleurisy), concomitant infections (especially, tuberculosis (TB) in our country), pulmonary embolisms or diseases causing pleuro-renal syndromes, like systemic lupus erythematosus.

In tuberculosis (TB)-endemic countries, patients with exudative pleural effusion and prolonged low grade fever in the absence of any other localization are “presumed” to be of tubercular origin in “clinical perception” and empirically administered antituberculosistherapy.Management of TB raises issues of drug dosing and interactions, especially in renal transplant recipients.

Uremic pleurisy results from an unknown putative agent, and therefore uremic pleuritis is a diagnosis of exclusion, that persists or recurs despite aggressive haemodialysis.

The presence of unilateral effusion suggests a diagnosis other than heart failure, like tuberculosis or parapneumonic or atelectasis. The reduced humoral and cellular immunity, in addition to delay in diagnosis because of an attenuated clinical response, may explain the high rate of empyema.

AIM OF THE STUDY

To study the etiology of pleural effusion in chronic kidney disease patients in a tertiary care hospital

REVIEW OF LITERATURE

NORMAL ANATOMY AND PHYSIOLOGY OF KIDNEY

The main function of the kidney is to maintain internal homeostasis and giving suitable environment for cellular metabolism and cellular function. Kidneys achieve these by excreting metabolic waste products, balancing solute and water transport, conserving nutrients and also by maintaining acid-base balance. Kidneys also functioning as a endocrine

organ by secreting renin, erythropoietin and 1,25-dihydroxy cholecalciferol (vitamin D) which regulates blood pressure and electrolyte balance, RBC production and calcium metabolism and bone mineral density respectively[2].

ANATOMY

Kidneys are two paired organs situated in the retroperitoneal space along the sides of the vertebral column. They are extending between T12 vertebra to L3 vertebra. Because of liver right kidney situated slightly lower than the left kidney. Each kidney is weighing approximately 125 to 175 grams in male and 115 to 155 grams in female. Length of the kidney is 11 to 12 centimeters, width is 5 to 7 centimeters and thickness is approximately 3 centimeters[2]. Renal artery, renal vein, ureters lymphatics and nerve plexus enters kidneys via the renal hilum which is situated along the medial surface of the kidney. There is a renal capsule which surrounds the kidney.

After entering into hilum renal artery divides into anterior and posterior branches. Anterior branch divides into three lobar or segmental arteries and supplies the anterior surface of the kidney. The posterior branch of the renal artery supplies the posterior

surface of the kidney and very rarely it gives an apical branch. These are end arteries; there are no anastomoses between these arteries.

Kidney consists of outer cortex and inner medulla. There are 8 to 18 renal pyramids in each kidney which are located in the medulla. The apices of the renal pyramid are towards the renal pelvis and forms papilla; bases of the pyramids are towards the cortex. Collecting duct opens into papilla.

Cortex contains all the glomeruli and portions of the tubules. The renal cortex is 1 cm thick and extends between the pyramids to form the renal columns of Bertini. From the base of the renal pyramid, at the corticomedullary junction, longitudinal elements termed the "medullary rays" extend into the cortex. These medullary rays are formed by collecting ducts, proximal and distal tubules[2].

Renal pelvis represents upper dilated end of ureter which is lined by transitional epithelium. Two or three major calyces extend from the renal pelvis, from which several minor calyces extends towards the renal papilla and drain the urine. Lower part of renal pelvis continued as

Renal pelvis represents upper dilated end of ureter which is lined by transitional epithelium. Two or three major calyces extend from the renal pelvis, from which several minor calyces extends towards the renal papilla and drain the urine. Lower part of renal pelvis continued as ureter and opens into the bladder. The renal pelvis represents the upper urinary tract and is lined by transitional epithelium. The major calyces which is two or three in number, extends from renal pelvis. From major calyces, several minor calyces extend toward the papillae and drain the urine. The ureters are 28 to 34 cm in length, arise from lower part of the renal pelvis and open into the bladder. The smooth

muscle is present in the walls of ureters produces peristaltic movement. With this movement, urine from the kidney drains into the bladder.

THE NEPHRON

The nephron is the functional unit of the kidney, each kidney consist approximately 1.2 million nephrons. The parts of the nephron are the glomerulus, proximal tubule, loop of Henle, distal tubule, and the collecting duct. The nephron develops from metanephricblastema. Embryologically collecting ducts develops from the ureteric bud. Nephrons are divided into two groups based on length of loop of henle. The loop of Henle consists of thin descending limb and thick ascending limb. Cortical nephrons have short loop of henle and juxta medullary nephrons have long loops.

GLOMERULUS

Glomerulus consists of tuft of capillaries lined by endothelial cells, mesangial cells with mesangial matrix, the visceral and parietal layer of Bowman's capsule with basement membrane. Bowman's space is situated between the visceral and parietal epithelial layers. The diameter of the glomerulus is around 200 μm^3. The glomerulus produces the ultra-filtrate of plasma. The filtering unit consists of endothelium, basement membrane, and the foot processes of the visceral epithelial cells.

Capillaries in the glomerulus is lined by fenestrated endothelial cells, these fenestrations are surrounded by intermediate filaments and microtubules. This glomerulus endothelium has negative charge; this is provided by Podocalyxin. Nitric oxide (vasodilator) and endothelin-1 are synthesized by glomerular endothelial cells. VEGF receptors are seen in the endothelial cells[3]. VEGF is produced by visceral epithelial cells and it increases permeability of endothelial cells by increasing the formation of endothelial fenestrations

and also VEGF is essential for survival and repair of endothelial cell in glomerular diseases. Each epithelial layer in the glomerulus has unique structural properties that allow components of the blood to pass through with the exception of blood cells and plasma proteins of molecular weight greater than 70,000. The endothelial cells are the 8 barrier to prevent the passage of blood components from reaching Bowman's space.

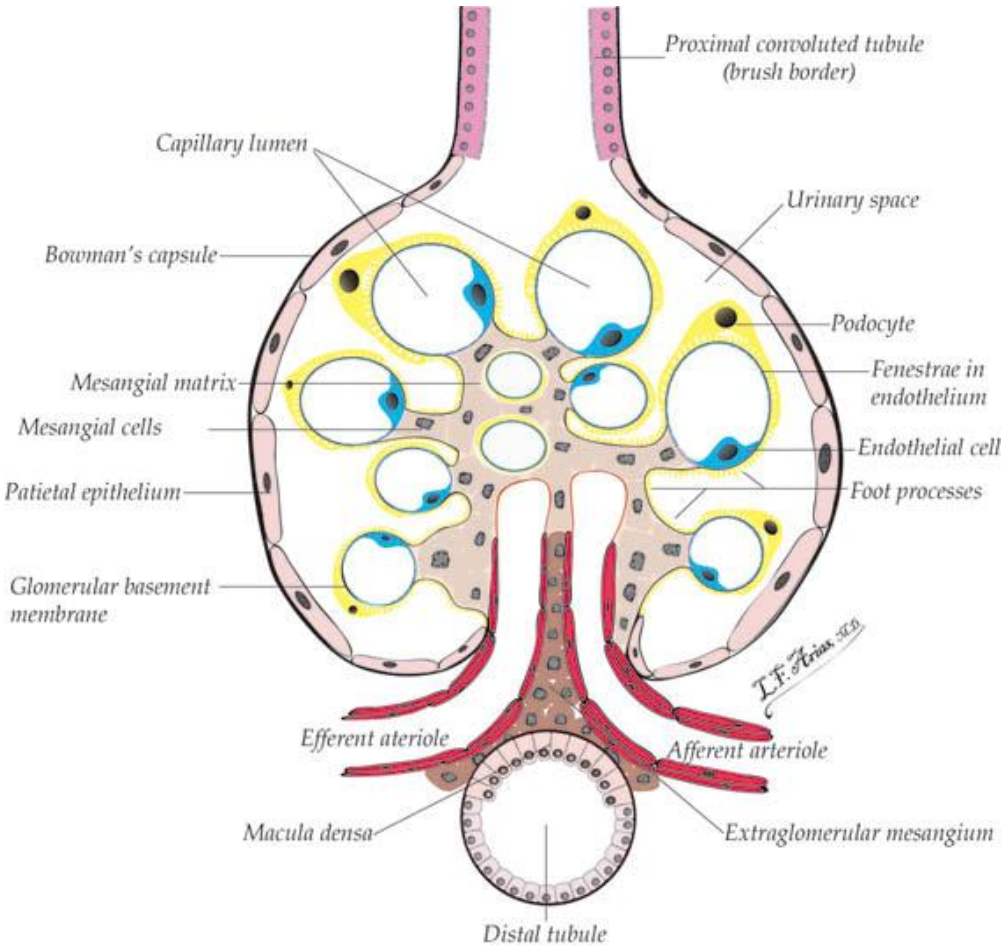


Fig-1 Normal glomerulus

VISCERAL EPITHELIAL CELLS

The distance between two visceral epithelial cell foot processes is 25 to 60 nm. This is filtration slit and is covered by a thin membrane called filtration slit membrane. A central

filament is seen in the filtration slit diaphragm. Nephrin is the main constituent of the filtration barrier. NPHS1 gene located in the chromosome 19 codes this nephrin; Mutation of NPHS1 is noticed in congenital nephrotic syndrome of the Finnish type[5]. Nephrin is seen in the visceral epithelial cells particularly in the slit diaphragm.

Deletion of CD2AP, which binds the nephrin to the cytoskeleton, is responsible for congenital nephrotic syndrome. Mutation of the Podocin; a membrane protein that is seen in filtration barrier is responsible for familial steroid-resistant nephrotic syndrome[5]. The foot processes are replaced by cytoplasmic band which is termed as effacement of foot process. Podoplanin maintains shape of foot process. The visceral epithelial cells are responsible for the production and maintenance of the filtration membrane.

PARIETAL EPITHELIAL CELLS

Parietal epithelial cells are squamous epithelial cells. Recent evidences suggest that they are progenitors of podocytes. After injury to podocytes these parietal epithelial cells regenerates and forms podocytes. They also implicated in some form of proliferative form of glomerulonephritis.

MESANGIAL CELLS

Irregularly shaped mesangial cells and its matrix constitute the mesangium. Mesangial cells have dense nucleus and elongated cytoplasmic processes. These processes consist of microfilaments such as actin, actinin and myosin. These cells bridge the gap between glomerulus and basement membrane and prevent distension of capillaries. Mesangial matrix composed of glycosaminoglycans and collagen[4]. Mesangial cells are specialized form of pericyte; having many characteristics of smooth muscle

cells. They are providing support to glomerular capillaries, regulates glomerular filtration rate and synthesizes Mesangial matrix[4].

GLOMERULAR BASEMENT MEMBRANE

The glomerular basement membrane consists of two thin layers the lamina raraexterna and the lamina rarainterna and a dense layer the lamina densa. Basement membrane composed of type IV collagen. Mutation of the α3, α4, and α5 chains causes Alport's syndrome. Podocalyxin present in the glomerular basement membrane gives its negative charge. Presence of anionic site in the basement membrane is demonstrated by Caulfield and Farquhar with the use of lysozyme. These anionic sites in the basement membrane are made up of glycosaminoglycans such as heparan sulfate4.

JUXTAGLOMERULAR APPARATUS

Juxtaglomerular apparatus is situated where the afferent and efferent arterioles meet the distal convoluted tubule. It is named because of its proximity to the glomerulus. JG apparatus controls function of each kidney. Components of the juxtaglomerular apparatus are macula densa, juxtaglomerular cells and extra glomerular mesangium. Macula densa is formed by cells of the distal convoluted tubule. Macula densa senses the sodium chloride concentration in the tubular fluid and secretes the locally acting vasoactive substance, there by controls the GFR by changing efferent arteriole diameter as a part of tubuloglomerular feedback[4].

JUXTAGLOMERULAR GRANULAR CELLS

Juxtaglomerular granular cells are present in the walls of the arteriole and extra glomerular mesangial region. They are having characteristics of both smooth muscle cells and epithelial cells. These cells contain renin and its precursor granules.

EXTRA GLOMERULAR MESANGIAL CELLS

Also known as lacis cells or the cells of goormaghtigh situated between the afferent arteriole and macula densa. Functions of the cells are not clearly known. It may be associated with secretion of erythropoietin.

PROXIMAL TUBULE

Proximal tubule is a portion of the nephron which extends from the Bowman's capsule and extends up to loop of henle. It consists of proximal convoluted portion knows as pars convoluta and distal straight portion known as pars recta. Pars convoluta entirely situated in the cortex. It maintains the PH of the filtrate absorbs the most of the filtered components and secretes the creatinine and organic acids[6]. Approximately two-third of the filtered water, 100% of the glucose and amino acids are absorbed from the proximal convoluted tubule.

LOOP OF HENLE

It is a U shaped portion of nephron situated in between the proximal and distal convoluted tubule. Most important function of the loop of henle is to provide high osmotic gradient inside the medulla by counter current system. With the

help of ion channels it creates high concentration in the medulla, so water is absorbed from the filtrate according to osmotic gradient.

DISTAL CONVOLUTED TUBULE

It is situated between the ascending limb of loop of Henle and collecting duct of the renal tubule. It maintains the PH, regulates electrolyte balance. Vasopressin acts through the receptors situated in the collecting duct and facilitates water reabsorption. Na+/cl- channels present in the distal convoluted tubules are thiazide sensitive. By inhibiting these channels, thiazide causes luminal Na+ gradient and also diuresis[6].

FUNCTIONS OF THE KIDNEY

A. Maintain water homeostasis.

B. By producing erythropoietin, active form of vitamin D and renin acts as a endocrine organ

C. Regulation of acid base balance.

D. Elimination of metabolic waste products.

E. Excretion of toxic substances from the body.

F. Blood pressure maintenance

G. Catabolism of small peptide hormones

CHRONIC KIDNEY DISEASE

Chronic kidney disease is emerging as a major health related issue worldwide. Developing countries like India are not able to manage these patients because of increasing cost. Incidence and prevalence of CKD is increasing because of the increased survival and improved quality of treatment. The term chronic renal failure corresponds to CKD stages 3-5, applies to the processes of irreversible reduction in nephron number. End stage renal disease represents the stage in which survival is not possible, unless the uremic toxins are removed by appropriate renal replacement therapy. This syndrome is caused by accumulation of toxins, fluids and electrolytes that are normally excreted by kidneys.

Most common causes of ESRD are diabetes, hypertension, polycystic kidney disease and glomerulonephritis. These together contribute to more than 90% of the cases of ESRD. Other causes for CKD include interstitial nephritis and HIV1[19]. Nephropathy due to systemic hypertension is the most common cause for end stage renal disease in elderly patients. Nephrosclerosis from vascular disease process correlates with coronary and cerebrovascular disease. Because of decreased mortality related to atherosclerotic coronary complications, greater segment of the population manifests the renal counter part of generalized vascular disease. In early stages of CKD, 34 patients usually will die of cardiovascular and cerebrovascular complications before they progress to ESRD. Renal disease progression varies from person to person, so this leads to genetic research to identify the inheritable component. A number of genetic loci that are contributing to the development of kidney disease have been identified.

Chronic kidney disease is divided into five stages based on the estimated glomerular filtration rate (GFR). In stage 1and stage 2 the GFR is normal or near normal, so based on the structural or functional defect these two are differentiated.

DEFINITION OF CHRONIC KIDNEY DISEASE

The National Kidney Foundation [Kidney Disease Outcomes Quality Initiative (KDOQI)] has proposed a definition and classification scheme of CKD. The National kidney foundation guidelines define CKD on the basis of kidney damage and/or reduced renal function. Kidney damage may be confirmed through a variety of methods including renal imaging, abnormalities in the serum or urine biochemistry and histological evidence. Albuminuria is the most frequent early indicator of kidney damage.

CRITERIA:

1. Structural or functional abnormality of the kidney for more than 3 months, with or without decreased urine output, manifested by

- Pathological abnormalities
- Markers of kidney damage
- Urinary abnormalities (proteinuria).
- Blood biochemical abnormalities.
- Imaging abnormalities.

2. GFR<60 ml/min/1.73m2 BSA for >3 months with or without

kidney damage.

RISK FACTORS FOR CKD

Established risk factors:

- Age
- Gender
- Race
- Diabetes mellitus
- High blood pressure
- Proteinuria
- Atherosclerosis
- Family history of kidney disease
- Reduced nephron number at birth
- Obesity
- Metabolic syndrome
- Family history of kidney disease
- Smoking
- Exposure to nephrotoxins
- Dyslipidaemia
- Recurrent urinary tract infection

Emerging risk factors:

- Elevated plasma homocysteine level
- Oxidative stress
- Prothrombotic factors (e.g. Plasminogen activator protein)
- Anaemia

STAGES OF CHRONIC KIDNEY DISEASE

Kidney disease outcome quality initiative (NKF-KDOQI) staging system: Importances of this staging are

1. It shifts the focus from GFR as the sole criteria for defining chronic

kidney disease to the identification of markers of early kidney

damage including proteinuria and abnormal urinary sediment.

2. The concept of CKD with normal glomerular filtration rate, but with markers of kidney damage like persistent proteinuria is providing guidelines for optimal treatment at early stage.

This system of staging helps us to plan for further treatment and also helps in predicting the outcomes. Thus there is a need for early detection

and treatment.

CAUSES OF CHRONIC KIDNEY DISEASE

1. Diabetic glomerulosclerosis 2. Hypertensive Nephrosclerosis.

3. Glomerular diseases:

- Glomerulonephritis
- Amyloidosis, light chain disease.
- Systemic lupus erythematosus.
- Wegener's granulomatosis.

4. Tubulointerstitial diseases:

- Reflux nephropathy (chronic pyelonephritis).
- Analgesic nephropathy.
- Obstructive nephropathy (stones, benign prostatic hypertrophy).
- Myeloma kidney.

5. Vascular diseases:

- Scleroderma.
- Vasculitis.
- Reno vascular renal failure
- Atheroembolic renal disease.

6. Cystic diseases:

- ADPKD.• Medullary cystic kidney disease.

There is a difference between the etiologies of CKD in India when compared to world-wide incidence. For example, in North America the

commonest cause for CKD is diabetic nephropathy and the next being hypertensive glomerulosclerosis. But in India although large scale data are unavailable, glomerulonephritis is the leading cause for CKD over diabetes and hypertension.

In most of the patients while diagnosing CKD, there is an associated systemic hypertension. If there is no identifiable cause for glomerular disease or tubular pathology, the etiology is often attributed to systemic hypertension. But such patients without identifiable etiological factors are considered in the following categories.

1) Patient with silent primary glomerulopathy, like focal segmental glomerulosclerosis without overt nephrotic or nephritic manifestations of glomerular disease.

2) Patients with chronic renal ischemia attributed to systemic vascular disease involving large and small vessels, cardiac and cerebral pathology. Here systemic hypertension is considered to be the renal correlate of systemic vascular disease.

PATHOPHYSIOLOGY OF CKD

It involves two broad sets of mechanisms

1. According to the mechanisms that are specific to the underlying etiology

that initiate the kidney damage. (e.g. Genetic abnormalities in the development of kidney, deposition of immune complexes and inflammatory mediators as in glomerulonephritis or exposure of toxins in diseases of renal tubules and interstitium).

2. Progressive mechanisms involving hyper filtration and hypertrophy of the remaining viable nephrons that are common consequence following reduction of renal mass, irrespective of the underlying etiology. These adaptive responses to reduction in nephron

number are mediated by a number of vasoactive hormones, cytokines and growth factors. Renin aldosterone system is responsible for hyperfiltration and subsequent

hypertrophy and sclerosis. The increased intra-renal renin activity contributes to both initial inciting event and also to the progressive mechanisms, finally leading on to

the glomerular sclerosis, renal failure and uremic syndrome.

PATHOPHYSIOLOGY OF UREMIC SYNDROME

The pathophysiology behind the uremic syndrome can be classified into 1) Due to the accumulation of toxins that are normally excreted via the kidneys.

2) Due to impairment of fluid and electrolyte homeostasis and hormone regulation.

3) Progressive systemic inflammation and its consequences Various excretory products accumulating in renal dysfunction are nitrogenous and non-nitrogenous products such as urates, products of nucleic acid metabolism, phenols, guanido compounds, hippurates, indoles, middle molecules, etc. Accumulation of these waste products leads to

anemia, metabolic abnormalities of carbohydrate, protein and fat and malnutrition resulting in a clinical syndrome which is characteristic feature of end stage renal disease. There is alteration of metabolism of many hormones like insulin, glucagon, PTH and vitamin-D due to increased renal excretion, decreased degradation and abnormal regulation.

FACTORS INFLUENCING RENAL PROGRESSION

There are some factors affecting the progression of renal disease.

The rate of disease progression can be modified by modifying these riskfactors. It includes:

1. Hypertension.

2. Diabetes.

3. Hyperlipidaemia.

4. Abnormal calcium-phosphorus homoeostasis.

5. Genetic factors.

6. Cigarette smoking.

7. Renin-angiotensin system activation.

8. Excessive dietary protein.

9. Obesity.

10. Prematurity/low birth weight.

CLINICAL PRESENATION

Most of the patients are asymptomatic in the early stages of chronic kidney disease; mostly they do not come to medical attention until most of the kidney function is compromised by the disease process. Any organ system can be affected by the kidney disease. Anemia, proteinuria and hypertension are the most common manifestations present in the most of the patients. Clinical presentation depends upon the systems involved.

These include:

1) Disorders of fluid, electrolyte and acid-base homeostasis

2) Disorders of calcium and phosphate metabolism

3) Disorders of cardiovascular system

4) Haematological abnormalities

5) Neuro-muscular abnormalities

6) Gastro-intestinal and nutritional abnormalities

7) Endocrine-metabolic disturbances

8) Dermatological abnormalities

ELECTROLYTE AND ACID-BASE DISORDERS

SODIUM AND WATER HOMEOSTASIS

In patients with stable CKD, there is a clinically insignificant increase in total body water and sodium content. In most of the CKD patients daily intake of sodium exceeds its urinary excretion leading to sodium retention and extracellular volume expansion. This is also one of the contributing factors for development of hypertension. Hyponatremiais very rarely seen in CKD patients; even if present it will respond to water restriction.

Definition

Pleural effusion is defined as the abnormal accumulation of pleural fluid within the pleural cavity. Crucial feature of the breathing apparatus is the pleural space. This is a potential space between the parietal pleura and the visceral pleura It is the coupling system between the lung and the chest wall .

ANATOMY OF PLEURA

The lung parenchyma, the diaphragm , the mediastinum and the rib cage are

covered by a serous membrane called the pleura. Pleura is divided into visceral pleura and parietal pleura. At the lung root , the visceral and parietal pleura meet.

Visceral pleura :

It covers the lung parenchyma in its points of contact with the diaphragm ,the mediastinum and the chest wall and also in the interlobar fissures.

Parietal pleura :

It lines inside of the thoracic cavities. It is subdivided on the basis of intrathoracic structures that it lines in to

1. Costal parietal pleura ,

2. Mediastinal parietal pleura,

3. Diaphragmatic parietal pleura.

Pulmonary ligament :

This is a thin double fold of pleura formed due to the downward extension of the pleura , posterior to the lung root.

Pleural space :

This is a potential space between the the visceral pleura and parietal pleura.

Pleural fluid :

This is a thin film of fluid normally present in between the visceral pleura and parietal pleura ie., pleural space

Functions of pleural fluid - acts as a lubricant . During the respiratory movements the pleural fluid allows the visceral pleura which is covering the lung to slide along the parietal pleura which is lining the thoracic cavity.

HISTOLOGY OF PLEURA :

Parietal pleura - composed of loose , irregular connective tissue which is covered by a single layer of mesothelial cells. Within the pleura there are blood vessels , mainly capillaries and lymphatic lacunas. Endothoracicfascia is situated deeper to parietal pleura. This is a continuous dense band of irregular connective tissue. This is mainly composed of elastin and collagen and it covers ribs and intercostal spaces.

Visceral pleura – composed of two layers namely the mesothelium and the connective tissue.

Connective tissue layer functions :

1. Contributes to elastic recoil of lung ,helps in expelling air from thelung

2. Restricts the volume of lung to which the lung can be inflated , and thereby protecting the lung

Mesothelialcells functions :

It forms a monolayer of pavement like cells lining the pleural surfaces.

1. Movement and transport of particulate matter and fluid across thepleuralsurfaces .

2. Migration of leucocytes in response to inflammation .

3. Synthesis of cytokines , growth factors , EC matrix proteins .

4. Antigen presentation and transformation to myofibroblasts .

Blood supply :

Parietal pleura receives blood supply from systemic capillaries such as intercostal artery ,pericardiophrenic artery , superior phrenic and musculophrenic artery and drained by intercostal veins , phrenic veins. Visceral pleura : Blood supply of thin pleura is derived from pulmonary circulation , and that of thick pleura is derived from bronchial arteries. Venous drainage is through the pulmonary veins.

Lymphatic drainage :

Lymphatic plexus in the parietal pleura drains in to intercostal ,mediastinal, tracheobronchial , parasternal and phrenic nodes. In the parietal pleura the lymphatic vessels are in communication with the stomas, the diameter of which ranges between 2 to 6 microns. The main pathways for the elimination of particulate matter is the stomas with lacuna and lymphaticsvessels . In the visceral pleura there are abundant lymph vessels which joins bronchial lymph vessels.

Nerve supply :

Intercostal nerves supply the costal and peripheral part of diaphragmatic pleura. So the pain sensation due to inflammation of this pleura is perceived in the chest wall. Phrenic nerve supplies the central part of diaphragmatic pleura . So when this part of pleura is irritated or inflamed the pain is felt in the ipsilateralshoulder.

PHYSIOLOGY OF PLEURA

Formation of the Pleural Fluid :

Pleural fluid can originate in the

- pleural capillaries,
- the intra-thoracic lymphatics,
- theintrathoracic blood vessels,
- the peritoneal cavity , or
- the interstitial spaces of the lung,

Pleural Capillaries

Starling's law of transcapillary exchange governs the movement of fluid between the pleural capillaries and the pleural space .

Hydrostatic pressure :

In the parietal pleura , the hydrostatic pressure is approximately 30 cm H2O,but the pleural pressure is approximately -5 cm H2O. The net hydrostatic pressure is therefore 30 - (-5) = 35 cm H2O .This pressure favorsthe movement of fluid from the capillaries in the parietal pleura to the pleural space.

Oncotic pressure :

This hydrostatic pressure gradient is opposed by oncotic pressure gradient. Plasma oncotic pressure is approximately 34 cm H2O. Normally, the pleural fluid has an oncotic pressure of approximately 5 cm H2O, as it contains a small amount of protein .The net oncotic pressure gradient is 34 - 5 = 29 cm H2O. Thus, the net gradient is 35 - 29 = 6 cm

H_2O. It favours the movement of fluid to the pleural space from the capillaries in the parietal pleura. The net gradient for fluid movement across the visceral pleura in humans is probably close to zero, which has not been demonstrated. The

pressure in the parietal pleural capillaries is approximately 6 cm H_2O more than that in the visceral pleural capillaries.

This is because the visceral pleural capillaries is drained by the pulmonary veins. Also this is the only pressure that differs from those pressure affecting fluid movement across the parietal pleura. The net gradient for the parietal pleura is 6 cm H_2O. So the net gradient is approximately zero for the fluid movement across the visceral pleura. The capillaries in the visceral pleura when compared to those in the parietal pleura , are much farther from the pleural space .So the filtration coefficient (Lp) for the visceral pleura is substantially less than that for the parietal pleura . When compared with the intercostal spaces ,the fluid formation is more across the parietal pleura over the ribs. Also fluid formation was more over the caudal ribs than over the cranial ribs. But in contrast, pleural liquid absorption was more primarily in the parietal pleura adjacent to the intercostal space rather than in the parietal pleura overlying the ribs. The formation of pleural fluid was more, if the breathing frequency was ncreased.

Interstitial Origin

It has been demonstrated that the interstitial spaces of the lungs, is the origin of much of the fluid that enters the pleural space. Pleural fluid accumulates if there is either high-pressure or high-permeability pulmonary edema.Theelevation in the wedge pressure is directly related to the amount of pleural fluid formed. But only after the development of pulmonary edema, increases in pleural fluid accumulation occur.

In patients with congestive heart failure , the origin of the pleural effusion is probably the pulmonary interstitial space. It is likely that many conditions associated with lung injury, such as lung transplantation and pulmonary embolization , the origin of the pleural fluid is also the interstitial spaces of the lung. It has been shown that the subpleural interstitial pressure increases, with increasing levels of interstitial fluid. Even though the visceral pleura is thin, the barrier to the movement of fluid across the visceral pleura appears to be weak. Therefore, once there is increase in subpleural interstitial pressure, the

fluid will enter to the pleural space through the visceral pleura. Peritoneal Cavity

If there is free fluid in the peritoneal cavity, pleural fluid accumulation can occur. Peritoneal fluid enters the pleural space through the openings in the diaphragm. Since the pressure in the pleural cavity is less than the pressure in the peritoneal cavity the fluid will flow from the peritoneal space to the pleural space. In the following conditions like hepatic hydrothorax, Meigs' syndrome, and peritoneal dialysis, the peritoneal cavity is the origin of the pleuralfluid.

Thoracic Duct or Blood Vessel Disruption

If there is disruption of thoracic duct, there is accumulation of lymph in the pleuralspace.Thiswill produce a chylothorax. With chylothorax the rate of fluid accumulation can be more than 1,000 mL/day.

Origin of Normal Pleural Fluid

It is believed that the fluid that normally enters the pleural space originates in the capillaries in the parietal pleura. The amount of pleural fluid formed daily is approximately 15 mL in a 50-kg individual. Since in the interstitial spaces the protein level is normally approximately 4.5 g/dL, and the protein level in normal pleural fluid is

only approximately 1 to 1.5 g/dL, the origin of the fluid does not appear to be the interstitial spaces of the lung . Pleural fluid with lower protein levels are produced by higher vascular pressures . Evans blue dyed albumin studieswith rabbits have demonstrated that most fluid originates in the parietal pleura over the ribs .

Pleural Fluid Absorption

Lymphatic Clearance

The lack of fluid accumulation in normal individuals is due to the clearance of fluid through the pleural lymphatics. By means of stomas in the parietal pleura , the pleural space is in communication with the lymphatic vessels in the parietal pleura. Visceral pleura lacks such stomas. The lymphatics in the parietal pleura, removes proteins, cells, and all other particulate matter from the pleural space. The carbon particles exit the pleural space through the stomas ,where the mesothelial cells are small and not flattened . These stoma increases in diameter in response to increased levels of nitric oxide in the

pleural space. In a 60-kg individual the lymphatic drainage from each pleural space is on

the order of 20 mL/hr or 500 mL/day. Once the volume of the pleural liquid exceeds a certainthreshold, thelymphatics operate at maximum capacity. The capacity for lymphatic clearance is 28 times as high as the normal rate of pleural fluid formation.

Clearance through Capillaries in Visceral Pleura

Until the mid-1980s, it was thought that the capillaries in the visceral pleura in humans is the primary route for the exit of fluid from the pleural space. Through the lymphatics in the parietal pleura almost all the pleural fluid is removed. Several hundred milliliters of water probably traverse the pleural membranes each day. Since the osmolarity is nearly

identical on each side of the membrane , the net movement is of only a few milliliters.

Alternative Mechanisms for Pleural Fluid Removal

In the removal of protein from the pleural space , transcytosis plays a role and there is some evidence for that. Only 29% of the overall removal of albumin occurred through the stoma with small hydrothoraces, while 64% of the albumin from large hydrothoracesas removed through the stoma

Pathogenesis of Pleural Effusions

Whenever the rate of pleural fluid formation exceeds the rate of pleural fluid absorption, there is accumulation of pleural fluid. Normally, from the capillaries in the parietal pleura, a small amount (0.01 mL/kg/hour) of fluid constantly enters the pleural space. The lymphaticsin the parietal pleura removes almost all of this fluid . Lymphatics have a capacity to remove at least 0.20 mL/kg/hour. The lymphatics remove the fluid exceeding the normal rate of fluid formation by a factor of 20.

DIFFERENTIAL DIAGNOSIS OF PLEURAL EFFUSION :

I. Transudative pleural effusions

- Congestive heart failure
- Cirrhosis
- Nephrotic syndrome
- Cerebrospinal fluid leaks to pleura
- Hypoalbuminemia
- Sarcoidosis
- Peritoneal dialysis
- Glomerulonephritis

- Myxedema
- Superior vena caval obstruction
- Fontan procedure
- Urinothorax

II. Exudative pleural effusions

A. Neoplastic diseases

1. Metastatic disease
2. Mesothelioma
3. Pyothorax-associated lymphoma
4. Body cavity lymphoma

B. Infectious diseases

1. Bacterial infections
2. Tuberculosis
3. Viral infections
4. Parasitic infections
5. Fungal infections

C. Pulmonary embolization

D. Gastrointestinal disease

1. Pancreatic disease

2. Subphrenic abscess

3. Intrahepatic abscess

4. Heart diseases Postcoronary artery bypass graft surgery

5. Postcardiac injury (Dressler's) syndrome

6. Pericardial disease

7. Diaphragmatic hernia

8. Endoscopic variceal sclerosis

9. Postliver transplant

10. Pulmonary vein stenosis postcatheter ablation of atrial fibrillation

11. Intrasplenic abscess

12. Esophageal perforation

13. Postabdominal surgery

E.Obstetric and gynecologic disease

1. Ovarian hyperstimulation syndrome

2. Fetal pleural effusion

3. Endometriosis

4. Postpartum pleural effusion

5. Meigs' syndrome

F.Collagen vascular diseases

1. Rheumatoid pleuritis

2. Systemic lupus erythematosus

3. Familial Mediterranean fever

4. Churg-Strauss syndrome

5. Wegener's granulomatosis

6. Drug-induced lupus

7. Immunoblastic lymphadenopathy

8. Sjogren's syndrome

G.Drug-induced pleural disease

1. Ergot drugs

2. Amiodarone

3. Interleukin 2

4. Nitrofurantoin

5. Dantrolene

6. Methysergide

7. Procarbazine

8. Clozapine

9. Methotrexate

H.Miscellaneous diseases and conditions

1. Sarcoidosis

2. Uremia

3. Trapped lung

4. Acute respiratory distress syndrome

5. Whipple's disease

6. Iatrogenic pleural effusions

7. Asbestos exposure

8. Postlung transplant

9. Postbone marrow transplant

10. Yellow nail syndrome

11. Electrical burns

12. Extramedullaryhematopoiesis

13. Rupture of mediastinal cyst

14. Therapeutic radiation exposure

15. Drowning

16. Amyloidosis

17. Milk of calcium pleural effusion

I.Hemothorax

J. Chylothorax

GENERAL TESTS TO DIFFERENTIATE THE CAUSES OF

EXUDATIVE PLEURAL EFFUSION :

1.Appearance of the fluid :

Mostly transudative and many exudative pleural effusions are clear , straw colored , nonviscid and odourless. The red colour of the fluid indicates the presence of blood. To confirm hemothorax we have to do a hematocrit. If the hematocrit of the pleural fluid was more than 50 % of the peripheral blood hematocrit , then it is a hemothorax. When the pleural fluid is blood tinged the RBC count is 5000 to 10000 / mm3 . If the pleural fluid macrophages contain haemoglobin inclusions , then it indicates that the blood was present before thoracentesis and the blood is not due to traumatic tap. Increased lipid content or increased cellular content both can make pleural fluid to appear turbid . If after centrifuge the supernatant fluid remains turbid then it is due to lipid content. But if the supernatant fluid is clear , then the turbidity is due to cellular debris .

Amebiasis with a hepatopleural fistula – chocolate sauce or anchovy paste.

The mixture of blood ,cytolysed and normal liver tissue make this appearance.

Malignant mesothelioma – high viscocity due to elevated hyaluronic acid .

Anaerobic bacterial infection – feculent odour

Urinothorax – smell of urine

2.WBC count :

Most transudates have WBC count below 1,000/mm3 and exudates have more than 1,000/mm3.

WBC count > 10,000/mm3 – parapneumonic effusions

WBC count > 50,000/mm3 – pancreatic disease and pulmonary embolism

Neutrophils predominate – suggests acute inflammation . It is seen in pneumonia , pancreatitis , pulmonary embolisation ,subphrenic abscess , early tuberculosis .

Eosinophils predominate – indicates air or fluid in the pleural space. It is seen in patients with spontaneous pneumothorax who undergone thoracotomy , introduction of air during thoracentesis into pleural space , traumatic hemothorax , pulmonary embolization , CABG , asbestos related effusion , drugs like dantrolene , bromocriptine , parasitic disease like amebiasis , ascariasis .

Basophils predominate – pneumothorax , pneumonia , leukemic pleural involvement .

Pleural fluid lymphocytosis - malignancy , TB , CABG , leukemia or lymphomas .

Mesothelial cells – Tuberculosis in HIV patients . Whereas it is absent in complicated parapneumoniceffusions , malignancy after pleurodesis.

3.Glucose levels :

Glucose level < 60 mg / dL – malignancy ,parapneumoniceffusions,rheumatoid disease , tuberculosis . Other causes include hemothorax , lupus pleuritis ,paragonimiasis , churg – strauss syndrome .

4.Amylase level :

It is elevated in pancreatic disease , malignancy , esophageal rupture . In later two cases the amylase is of salivary type.

5.Lactate dehydrogenase level :

LDH in the pleural fluid is a reliable indicator of degree of inflammation of the pleura. More the inflamed surfaces , higher the LDH levels . The most common causes of elevated LDH levels are parapneumonic effusions and malignancy . These two conditions mostly meet the light's criteria on the basis of levels of LDH than the protein levels .The isoenzymes elevated in these conditions are LDH – 4 and LDH – 5. They are thought to arise from the inflammatory WBC .

Usually LDH isoenzyme is not used routinely . This is done in conditions where there is a bloody pleural fluid tap in a patient who is having transudative pleural effusion clinically .The pleural fluid protein meets the criteria for transudative pleural effusion but LDH levels meets the criteria for exudative pleural effusion. In these conditions isoenzyme LDH – 1 , confirms that the rise in LDH was due to blood .

6.Pleural fluid pH :

If the pleural fluid pH is less than 7.2 then we have to consider the following causes : complicated parapneumonic effusions , esophageal rupture , rheumatoid pleuritis , tuberculouspleuritis malignant pleural disease , hemothorax , systemic acidosis , lupus pleuritis , paragonimiasis , urinothorax .

7.AdenosineDeaminase :

ADA has two isoenzymes – ADA 1 and ADA 2

ADA 1 is produced by lymphocytes , neutrophils , monocytes , macrophages

ADA 2 is produced by macrophages and monocytes .

The cut off level for ADA level to diagnose tuberculous pleural effusion is 40 to 45 U/L . The diagnosis of TB pleural effusion is more likely if the level is higher ie., more than 70 U/L .

Other conditions with elevated ADA levels are empyema , rheumatoid pleuritis, neoplasms , Q fever , brucellosis . If the ADA 1 to ADA ratio is less than 0.42 the diagnosis of TB pleuritis is increased .

8.Interferon gamma :

In patients with tuberculouspleuritis CD 4 lymphocytes produce interferon gamma . It enhances the elimination of intracellular parasites by increasing the production of polymyristate acetate induced hydrogen peroxide in macrophages. In monocytes this inhibits the mycobacterial growth . If the interferon gamma level is more than 200 pg / ml then the diagnosis of tuberculouspleuritis is made.

9.Polymerase chain reaction :

It is used in patients with low numbers of tubercle bacilli in pleural fluid . It is also used on pleural biopsy specimens .

10. C – Reactive proteins more than 50 mg /L , high levels of lysozyme are also used to diagnose tuberculouspleuritis .

10.Lipids :

Chylothorax – Accumulation of chyle in the pleural space due to distruption of the thoracic duct. In these situations the triglyceride levels are increased .Chyliform pleural effusions – This is characterised by high levels of lecithin globulin levels .

Pseudo chylous effusions – There is increased levels of cholesterols crystals .

Triglyceride levels more than 110 mg / dL – Chylothorax is confirmed . But if the levels are less than 50 mg / dL then the patient is not having chylothorax .

If triglyceride level is between 50 to 110 mg / dL then we need to perform a lipoprotein analysis. Chylothorax is diagnosed if there is presence of chylomicrons in the lipoprotein analysis of pleural fluid.

11.Bilirubin

Bilirubin has a high molecular weight (584) .With respect to its concentration between serum and protein it behaves in a manner identical to that of the high molecular weight proteins . Any serous membrane inflammation often leads to increased capillary permeability and this enables the diffusion of high molecular weight bilirubin .

A pleural fluid bilirubin of more than 0.48 mg / dL and a pleural fluid bilirubin to serum bilirubin ratio of more than 0.62 is considered as exudates.

12.Cholesterol

The mechanism of increased concentration of cholesterol in Exudative pleural effusion is not known clearly. The permeability of pleura is increased due to “serum leakage” and this leads to the accumulation of cholesterol in exudative pleural effusion .A pleural fluid cholesterol of more than 60 mg / dL is used in diagnosing exudates.

RADIOGRAPHIC EXAMINATIONS OF PLEURAL EFFUSIONS

Typical Arrangement of Free Pleural Fluid

In the pleural space the distribution of free fluid is influenced by two main factors.

First, since the lung is less dense than pleural fluid, accumulation of the pleural fluid occurs in the most dependent part of the thoracic cavity. The distribution of fluid within the free pleural space obeys the law of gravity. The lung also maintains its shape when compressed. Bearing, these 2 factors in mind it is easy to predict the distribution of excess pleural fluid. The fluid first gravitates to the base of the hemithorax and comes to rest between the inferior surface of the lung and the diaphragm, where the pleural sinus is the most inferior, particularly posteriorly. The fluid spills out into the costophrenic sinuses posteriorly, laterally, and anteriorly, when the fluid accumulation is higher. Additional fluid assumes a higher position in the thorax as it spreads upward in a mantle-like manner around the convexity of the lung and gradually tapers .

The lateral costophrenic angle is obliterated, in the posteroanteriorprojection.The density of the fluid is high laterally and curves gently medially and downward , to terminate at the mediastinum with a smooth, meniscus-shaped upper border. At the mediastinal border the layer of fluid is narrower than at the costal border.

The upper surface of the pleural fluid density is semicircular in the lateral projection. It is high in the anterior and posterior regions. It curves smoothly downward to its lowest point approximately midway between the posterior chest walland the sternum .

Frequently, in the lateral chest radiograph a middle lobe step is observed . The explanation for the middle lobe step is that the most dependent and the the first affected lobe is the lower lobe , the pleural fluid starts to accumulates here. Therefore, it starts to

float and shrink but maintains its shape. So the middle lobe is unaffected and its full volume is maintained . Accordingly, the result is a a middle lobe that retains its usual size and shrunken lower lobe . The fluid accumulation is mostly in the posterior part of the chest ,radiographically. The height of the pleural fluid is greater laterally , based on the radiologic appearance. When viewed en face ,this layer of fluid is of insufficient depth to cast a discernible shadow, so it assumes a meniscus shape.

Radiologic Signs

The fluid first accumulates between the inferior surface of the lower lobe and the diaphragm, when the patient is in the upright position. The pleural fluid occupies this position , if the amount of fluid is small (approximately 75 mL) and without spilling into the costophrenic sinuses. The normal configuration of the diaphragm is maintained, with this small amount of fluid.

The chest radiograph does not demonstrate that pleural fluid is present. When viewed in the lateral projection , accumulation of more fluid obliterates the costophrenic angle as it spills over into the posterior costophrenic angle . The posterior costophrenic angle is normally sharp . It is obliterated by a homogeneous , shallow shadow with a meniscus-shaped upper surface . There is also widening of the pleura that lines the posterior thoracic wall .

If the posterior part of one or both diaphragms is obscured or the posterior costophrenic angle is obliterated, this indicates the presence of pleural fluid. Then we should be do further diagnostic tests . Moreover, the presence of clinically significant amounts of free pleural fluid can be nearly excluded , if both posterior costophrenic angles are clear and sharp. In the postero - anterior chest radiograph , lateral costophrenic angle is blunted with increasing amounts of fluid . The entire outline of the diaphragm is lost on the

affected side, as more fluid accumulates . The fluid then extends upwards around the posterior , anterior and lateral thoracic walls. At the lung base, this fluid produces opacification which is the typical meniscus shape.

Supine Position

There are three characteristics that serve to differentiate the increased density due to parenchymal infiltrate from that due to a pleural fluid.

First, in a properly exposed film , the vascular structures of the lung will be readily visible through the density, if the density is caused by pleural fluid.

However, vascular structures are obliterated by the silhouette effect, if a similar density is produced by any intrapulmonary process.• Secondly , the density is usually completely homogenous, if it is due to pleural fluid. Whereas, the infiltrates are usually less homogenous, if it is caused by an intrapulmonary processes.

Third, the presence of air bronchograms . They are are present only if the increased density is due to a parenchymal infiltrate and not due to a pleural fluid.

Ultrasound

In a patient with pleural effusion , the ultrasound can be used for the following purposes. They are

(a) to determine the presence of pleural fluid;
(b) to identify an appropriate location for the attempted thoracentesis, chest tube placement, or pleural biopsy;
(c) to identify loculated pleural effusion;
(d) to distinguish pleural thickening from pleural fluid;
(e) tosemiquantify the amount of pleural fluid;

(f) to differentiate a lung abscess from a pyopneumothorax;

(g) to assess a whether a pleurodesis is present; and

(h) to evaluate the trauma patient for the presence of a pneumothorax or a hemothorax.

FIGURE 1

ULTRASOUND OF LEFT LUNG AND SURROUNDING STRUCTURES

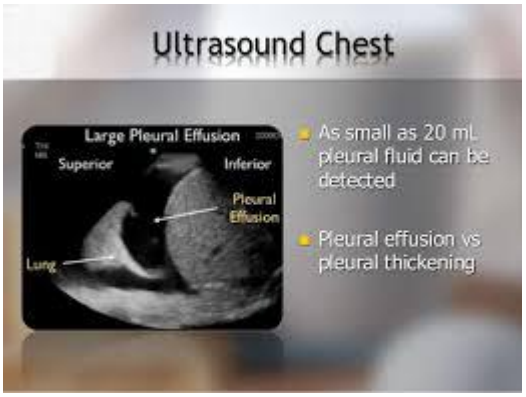


FIGURE 2.

ULTRASOUND OF RIGHT LUNG AND SURROUNDING STRUCTURES

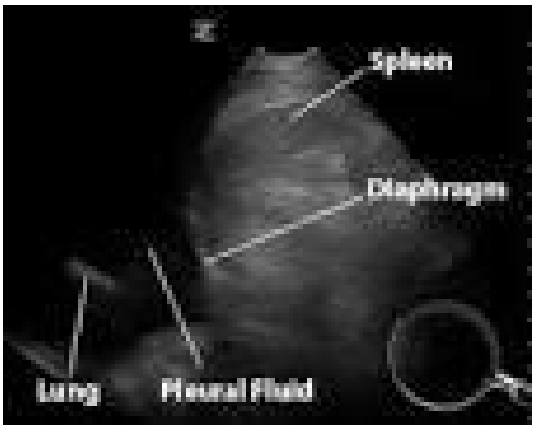


FIGURE 3

CHEST X RAY – POSTERIOR ANTERIOR VIEW SHOWING RIGHT SIDED PLEURAL EFFUSION .

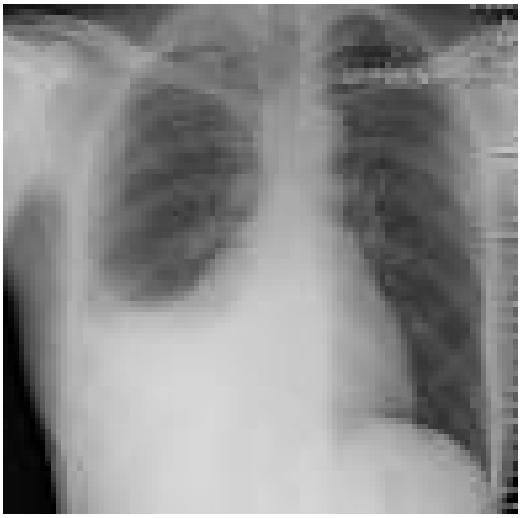


FIGURE 4

DIAGNOSTIC OR THERAPEUTIC THORACENTESIS

- RECOMMENDED POSITION OF THE PATIENT

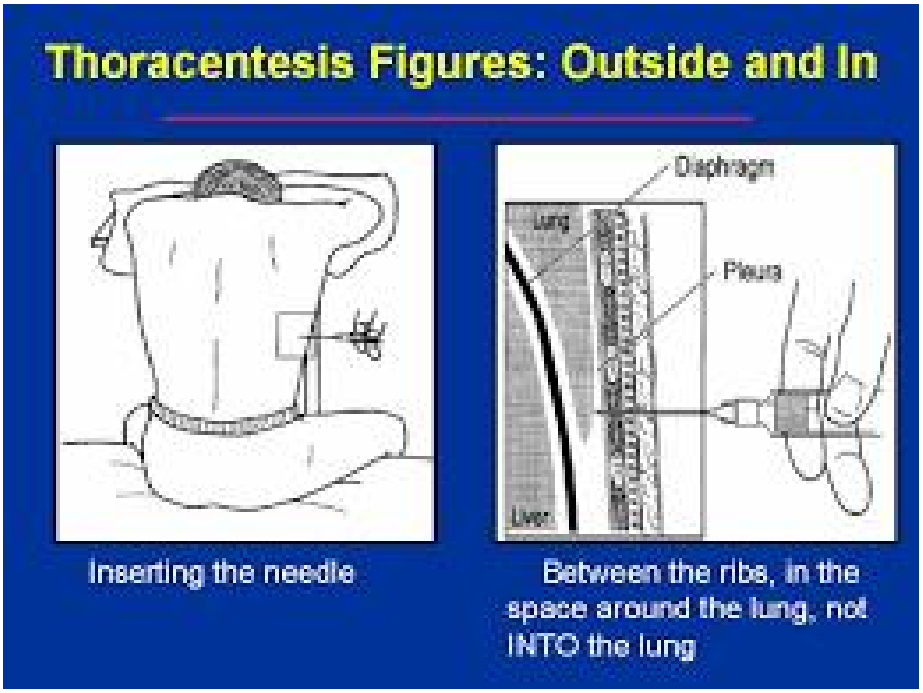
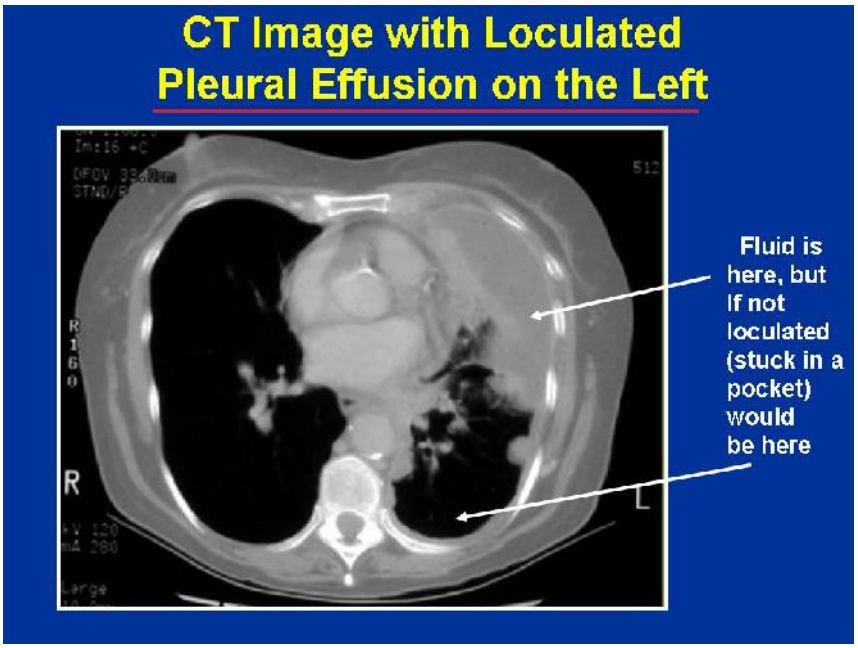


FIGURE 5

CT CHEST PLAIN SHOWING PLEURAL EFFUSION



TRANSUDATIVE PLEURAL EFFUSIONS

"Alternation in the systemic factors influencing the formation and absorption of the pleural fluids leads to accumulation of the pleural fluid and formation of transudative pleural effusions" .

The major causes are :

1.Congestive Heart Failure :

“The most common cause of pleural effusion is probably the congestive heart failure (CHF).The researchers interested in pleural effusions usually do not see most patients with pleural effusions of this cardiac origin and this is the reason for the low incidence of pleural effusions secondary to heart failure in most of the studies . The incidence of pleural effusions in patients with CHF is high”.

Pathophysiology :

“In the concepts of pleural fluid formation and reabsorption in patients with heart failure , there are significant modifications in the recent years. It was believed in the past that the accumulation of the pleural fluid in patients with CHF was due to increased pressure in the parietal or the visceral pleural capillaries. According to Starling's equation, these increased pressures results in a decreased removal of fluid through the visceral pleura and an increased entry of fluid into the pleural space from the parietal pleura” .

“In patients with CHF , according to current theories on pleural fluid formation and reabsorption, there is a different entry pathway and a different exit pathway for pleural fluid. It is believed that almost all fluid exits the pleural space through the lymphatics in the parietal pleura rather than by passively diffusing across the visceral pleura. In patients with CHF, accumulation of pleural fluid occurs when the rate of entry of fluid into the pleural space exceeds the capability of the lymphatics in the parietal pleura to remove the fluid” .

Clinical Manifestations :

“In patients with pleural effusions due to CHF they are usually associated with other manifestations of that disease. The patient has a history of increasing dyspnea on

exertion, orthopnea or paroxysmal nocturnal dyspnea , increasing peripheral edema. The dyspnea is frequently out of proportion to the size of the effusion".

Physical examination :

"Physical examination usually reveals signs of the pleural effusions as well as signs of both left-sided heart failure with an S3 ventricular gallop and rales and right-sided heart failure with peripheral edema and distended neck veins".

Investigations :

"The chest radiograph almost always reveals usually bilateral pleural effusions and cardiomegaly. The most common cause of bilateral pleural effusions is congestive heart failure . But only 88% of the patients studied had bilateral pleural effusions ,ifcardiomegaly is not present. The mean volume of pleural fluid in the right pleural space (1,084 mL) when compared to the mean volume of pleural fluid in the left pleural space (913 mL),was only slightly greater. Also mediastinal lymphadenopathy is common in patients with pleural effusions that are secondary to CHF".

Diagnosis :

If the patient has bilateral pleural effusions and cardiomegaly, not febrile, and no history of pleuritic chest pain, we have to first initiate treatment of the CHF. Then we have to observe the patient and determine whether the pleural fluid is reabsorbed. We then perform a diagnostic thoracentesis , if the effusions do not disappear within a few day.

"One problem with this approach is that the characteristics of the pleural fluid may change from those of a transudate to those of an exudates , since the patients are with dieresis".

Serum pleural fluid albumin or protein gradient :

The serum to pleural fluid protein gradient should be examined , if the pleural fluid meets exudative criteria but the effusion is thought to be due to CHF. If this gradient is greater than 3.1 g/dL, additional diagnostic studies are not indicated because the pleural effusion is probably due to the CHF .

Currently, as the protein gradient is already available when Light's criteria are measured , the protein gradient of 3.1 g/dL is preferred to the albumin gradient.

Pro-brain natriuretic peptide :

The measurement of the serum or pleural fluid pro-brain natriuretic peptide (pro-BNP) , is an another test that should be considered for establishing the diagnosis of CHF. The level NT pro-brain natriuretic peptide (NT pro-BNP) considereddiagnostic of CHF is 1500pg/mL

Treatment

In a patient with pleural effusion secondary to heart failure the preferred treatment is to treat the heart failure with the following drugs.,

- digitalis,

- diuretics – to reduce preload , and

- dilators - to reduce afterload .

The pleural effusion disappears , if we manage heart failure successfully. In most patients with heart failure , the pleural effusion is effectively managed only with above

management . Occasionally, the patients tends to be very dyspneic, if they are associated with large pleural effusions. Such persons may get rapid relief from the dyspnea , if about 0.5L to 1.0L of pleural fluid are removed . Sometimes therapeutic thoracentesis is indicated in patients with heart failure and large pleural effusions that are refractory to treatment, to get symptomatic relief . So consider interventions to control the pleural effusions , in such patients.

2. Hepatic Hydrothorax

One of the complication of hepatic cirrhosis is pleural effusion. But only when ascitic fluid is present, pleural effusions usually occur. They are usually called as hepatic hydrothorax.

Pathophysiology

It is evident from the foregoing studies, that the orgin of pleural fluid in these patients is from the ascitic fluid.

“The fluid in the peritoneal cavity passes directly through the defects in the diaphragm to the pleural space . The diaphragm may be stretched in patients with tense ascites, causing microscopic defects. This is because of the increased intraabdominal pressure. There is always a one-way transfer of fluid from the peritoneal to the pleural cavity ,in patients with ascites. The is because of increased hydrostatic pressure in the asciticfluid” .

In some patients, the lymphatic vessels play an important role in the production of the pleural effusion. The mechanism behind this is the transfer of ascitic fluid across the diaphragm by the lymphatic vessels .

To conclude , the dominant mechanism of hepatic hydrothorax is the direct movement of fluid across the diaphragm. Because the placement of the chest tube results in diminution in the amount of ascites, within minutes.

Clinical Manifestations

"The clinical pictures of cirrhosis and ascites dominate in patients with pleural effusions secondary to cirrhosis. At times, in association with large pleural effusions , these patients develop acute dyspnea. Although the pleural effusions may be small to moderate in size, they are frequently large and occupy the entire hemithorax. The diaphragmatic defect permits fluid to flow into the pleural cavity from the peritoneal cavity , until the pleural pressure approaches the peritoneal pressure and this results in development of large pleural effusion".

Diagnosis

"It is usually easy to diagnose the pleural effusion that is secondary to cirrhosis with ascites. We should perform both a paracentesis and a thoracentesis. This is to confirm that the ascites and pleural fluid are compatible with the diagnosis. Also to ascertain that they are not have high polymorphonuclear cell counts".

The pleural fluid is occasionally blood tinged or is frankly bloody. But due to the poor coagulation status of the patient , such findings have no significance. The differential cell count is dominated by polymorphonuclear leukocytes, small lymphocytes, or other mononuclear cells.

To rule out pancreatic ascites amylase levels should be determined. Also a cytologic examination should be performed to rule out malignant disease. This should be done in both pleural fluid and ascitic fluid.

Treatment

"Since the hydrothorax is an extension of the peritoneal fluid in patients with cirrhosis and ascites , the management of pleural effusions always should be directed toward treatment of the ascites" .

"The patient should be put on a low-salt diet, and moderate fluid restriction. Then diuretics should be administered. The combination of furosemide and spironolactone , is the best diuretic therapy. The initial starting dose is 40 mg of furosemide and 100 mg of spironolactone and they can be titrated upto a maximum dose of 160 mg of furosemide and 400 mg of spironolactone. This combination appears to have the optimal ratio for the two diuretics"

3. Nephrotic Syndrome

The nephrotic syndrome is common in patients with the pleural effusion.

Mechanism of pleural fluid accumulation :

"The combination of increased hydrostatic pressure and decreased plasma oncotic pressure , is the mechanism responsible for the transudative pleural effusion in patients associated with the nephrotic syndrome".

Diagnosis :

"In the typical clinical situation to diagnose pleural effusion secondary to the nephrotic syndrome it is not difficult. But to confirm that the pleural fluid is indeed a transudate ,a diagnostic thoracentesis should be performed"

“In patients with the pleural effusion and nephrotic syndrome, the possibility of pulmonary embolism should always be considered. In all patients with the pleural effusion and nephroticsyndrome , one should always obtain a lung scan or a CT angiogram. It is important that evidence of deep venous thrombosis should be sought with venograms, pulmonary arteriogram or a impedance plethysmograms, if the lung scan or spiral CT scan is equivocal.”

Treatment :

The main aim of treatment is to decrease the protein loss in the urine of patients with pleural effusion and associated with the nephrotic syndrome. This is done to decrease the increased extracellular volume and to increase the plasma protein.

This is best accomplished by administering

- diuretics in conjunction with a low-sodium diet,

- angiotensin-converting enzyme inhibitors.

As serial therapeutic thoracentesesonly deplete the protein stores, theyshould not be performed ..

EXUDATIVE PLEURAL EFFUSION

MOST COMMON CAUSES ARE :

1. Parapneumonic pleural effusion

2. Pleural effusion related to metastatic malignancies

3. Tuberculous pleural effusion

1.METASTAIC MALIGNANCIES AND PLEURAL EFFUSION :

"The exudative pleural effusion secondary to malignant disease involving the pleura is the second leading cause of exudative pleural effusion. Parapneumonic effusion ranks first in this category".

"Common carcinomas associated with malignant pleural effusions are :

1. Lung carcinoma ,

2. Breast carcinoma ,

3. Lymphoma ,

4. Ovarian carcinoma ,

5. Sarcoma"

Rarely carcinoma of uterus , cervix , stomach , colon , pancreas , bladder

2.TUBERCULOUS PLEURAL EFFUSION

The development of pleural effusion in a patient with absence of radiologically apparent TB indicates that it would be a sequelae to the primary infection that occurred 6 to 12 weeks before or it may be due to reactivation of TB .

Pathogenesis of tuberculous pleural effusion :

In tuberculous patients there are subpleuralcaseous focus. Tuberculous pleural effusion occurs due to rupture of the sub pleuralcaseous focus in the lung to the pleural space.

In the development of tuberculous pleural effusion the delayed hypersensitivity plays a major role .There is clonal expansion of lymphocytes sensitised to the tuberculousprotein . Initially the macrophages predominate in the pleural fluid from day 2 to day 6 and then the lymphocytes predominate in the pleural fluid.

It is clear that the delayed hypersensitivity increases the pleural capillaries permeability to protein. There is higher rate of pleural fluid formation due to the increased levels of pleural fluid protein. Also there is increased levels of VEGF, which also increases the permeability. This leads to the accumulation of pleural fluid and development of pleural effusion .

Also there is decrease in the clearance of proteins in the pleural space. This is because of the impedence to the clearance of proteins by the lymphatics as a result of delayed hypersensitivity reactions .

Clinical manifestation :

“Patients with pleural TB have symptoms such as fever, dry cough ,pleuritic chest pain, and dyspnea. Physical findings are those of pleural effusion such as dullness to percussion and absence of breath sounds”.

In HIV individuals there will be longer duration of illness. The incidence of chest pain is low, but night sweats , fatigue , diarrhoea , hepatomegaly , lymphadenopathy , splenomegaly are more common.

They have associated parenchymal lesions , smear for acid fast bacilli positive and also culture positive for AFB.

DIAGNOSIS :

“Tuberculin skin testing : Tuberculin skin testing is almost always positive if performed after 8 weeks of development of symptoms . So a negative skin testing after 8 weeks of development of symptoms can be used to rule out TB. However in malnourished individuals or HIV patients the test remains negative” .

Pleural fluid analysis :

1. Pleural fluid protein elevated and usually above 5 g/dL

2. WBC count has more than 50% small lymphocytes . If there is eosinophils it suggests previous thoracentesis or associated pneumothorax .

3. Mesothelial cells not more than 5 % .

4. Adenosine deaminase levels more than 70 U/L

5. Interferon gamma levels more than 3.7IU/ml

6. Low pleural fluid pH and CRP levels more than 30 mg/dl

7. Pleual biopsy – demonstration of parietal pleura granuloma , AFB , caseous necrosis.

8. Pleual fluid AFB staining and culture for mycobacteria

3.Parapneumonic effusion :

“When any pleural effusion is associated with bacterial pneumonia , lung abscess or bronchiectasis , it is called as parapneumonic effusion” .

An empyema is defined as pus in the pleural space. Many complicated parapneumonic effusions are empyema.

According to Weese et al. empyema is charecterised by specific gravity greater than 1.018 , protein more than 2.5 g/dL , WBC count more than 500 cells/ mm3 But according to Vianna empyema is defined as pleural fluid protein more than 3.0 g/dL , WBC greater than 15000 / mm3 or positive bacterial cultures.

Pathogenesis :

1.Exudative stage :

"This stage is characterised by rapid accumulation of sterile pleural fluid in pleural space. The fluid orginates from the interstitial spaces of lung and also from the visceral pleural capillaries due to increased capillary permeability. There is low WBC count , low LDH level and a normal glucose level in the pleural fluid at this stage. This stage resolves if appropriate antibiotics is instituted".

2.Fibropurulent stage

The pleural space is invaded by the bacteria , if antibiotics are not intiated. In this stage there is accumulation of large amounts of pleural fluids which is rich in bacteria,polymorphonuclearleucocytes and cellular debris . The visceral and parietal pleura are covered by a continuos sheet of fibrin. This leads to the formation of loculation and prevents the spread of pus . But this makes the insertion of chest tube difficult. In this stage there is higher pleural fluid LDH and lower pleural fluid glucose and pH

3.Organisation stage

This stage is characterised by pleural peel. The fibroblasts grow in to the exudates and an inelastic membrane is produced . The lung is encased by this inelastic pleural peel and makes it functionless. The exudates is thick at this stage and it may spontaneously drain through the chest wall called as empyema necessitatis or into the lung producing a bronchopleuralfistula .

The most common organisms are Staphylococcal aureus , Escherichia coli and anaerobe Bacteroids .

Clinical features :

Fever , cough with expectoration , chest pain are the major symptoms . In immunocomprimised person fever may be absent . If the fever is present for more than 48 hours after the institution of antibiotics then it is called as parapneumonic effusion. The history of alcoholism , seizures or an episode of unconsciousness should be sought as it leads to aspiration.

DETAILED STUDY PROPOSAL

TITLE:

A study on exudative etiology of pleural effusion in chronickidney disease in a tertiary care hospital

AIMS AND OBJECTIVES:

"The present study is conducted**:**

1. To determine the demographic characteristics of patients with chronic kidney disease developing pleural effusion.

2. To determine the incidence of exudative and transudativeetiologies of pleural effusion in CKD patients.

2. To find the incidence of various exudative etiologies of pleural effusion in CKD patients".

MATERIALS AND METHODS:

STUDY POPULATION:

"This study is a hospital based Prospective study conducted between February2016 to July 2016, among Patients with Chronic Kidney disease and pleural effusion admitted in medical ward in OfGovernment RajajiHospital, Madurai".

INCLUSION CRITERIA:

1. Patients with pleural effusion and an estimated Glomerular filtration rate (GFR) <60ml/min/1.73m2 for 3 or more months, with or without kidney damage. GFR was calculated using MDRD formula
2. Age >13 yrs.

Exclusion criteria:

1. Age <13 yrs.
2. Patients with HIV.
3. Patients with bleeding disorders.
4. Severe co morbidities like recent MI.
5. Patients not willing for thoracocentesis.

Study Procedure: A clinically suspected case of pleural effusion in a chronic kidney disease patient is diagnosed by Chest X-ray and ultrasound chest. Detailed demographic and clinical parameters including age, sex, smoking history, clinical symptoms with duration (Cough, fever, sputum production, haemoptysis, chest pain, breathlessness) and clinical signs (Pallor, clubbing, enlarged neck nodes, pulse rate, blood pressure) and systemic examination will be evaluated in all patients. In addition to chronic kidney disease, history for other co-morbid illness and habits like smoking and alcoholism will betaken.Co-morbid illnesses were defined as the presence of coexisting cardiac failure, ischemic heart disease, chronic lung disease (COPD), chronic liver disease, malignancies, neurological diseases and diabetes mellitus.

All patients will be subjected to blood investigations including Complete blood count, ESR, Blood sugar, renal function tests and Liver function tests and urine routine

examination. Sputum if present, for ZN stain, Gram's stain, culture and sensitivity.

Chest radiograph is classified according to the size of effusion. The size of the effusion will be assessed on the posterior-anterior radiograph by visually estimating the area of the hemi-thorax occupied by pleural fluid. Pleural effusions were deemed to be minimal if it occupied less than one third of hemi-thorax, moderate if it occupied between one third to two third, and massive if it occupied more than two thirds of the hemi-thorax. Thoracocentesis will be performed using a 20 gauze needle syringe and the fluid is studied forthe gross appearance, total WBC count, differential count, RBC count, protein, glucose, ADA, LDH, cytology and culture. Pleural fluid is classified as exudative effusion or transudative effusion by applying LIGHTŚ Criteria.

"Exudative Pleural Effusions meet at Least one of the following Criteria, whereas Transudative

Pleural Effusions meet none (Light's Criteria):

- Pleural fluid protein divided by serum protein greater than 0.5
- Pleural fluid LDH divided by serum LDH greater than 0.6
- Pleural fluid LDH greater than two thirds of the upper normal limit of serum LDH".

According to the above criteria patients with exudative pleural effusion are identified. The common exudative causes of pleural effusion are tuberculosis, bacterial infections, bronchogenic carcinoma, lymphomas, pulmonary infarction, collagen vascular diseases and Meig's syndrome. To identify each of these conditions clinical examination followed by appropriate investigations will be made.

Serial no.	Causes	Investigations
1	Tuberculosis	CXR, sputum examination, pleural fluid analysis, LDH, ADA levels in pleural fluid, gene expert
2.	Bacterial infections –Staph aureus, Streptococuus, E-coli, enterococcus, klebsiella, H.Inflenza, pseudomonas	Pleural fluid gram stain, pleural fluid analysis, pleural fluid culture.
3	Bronchogenic carcinoma	CXR, Pleural fluid analysis
4	Lymphomas	CXR, USG, complete blood count with peripheral smear.
5.	Pulmonary infarction	CXR, ECG, ECHO
6.	Collagen vascular diseases	CBC with peripheral smear, ANA
7.	Meig's syndrome	CXR, USG

LABORATORY INVESTIGATIONS

Complete hemogram

Renal function test

Liver function test

Electrocardiogram

Echocardiogram

Sputum AFB, gram stain & culture

Chest x-ray PA view

Pleural fluid analysis

ADA, LDH, ANA, NAAT

DESIGN OF STUDY:

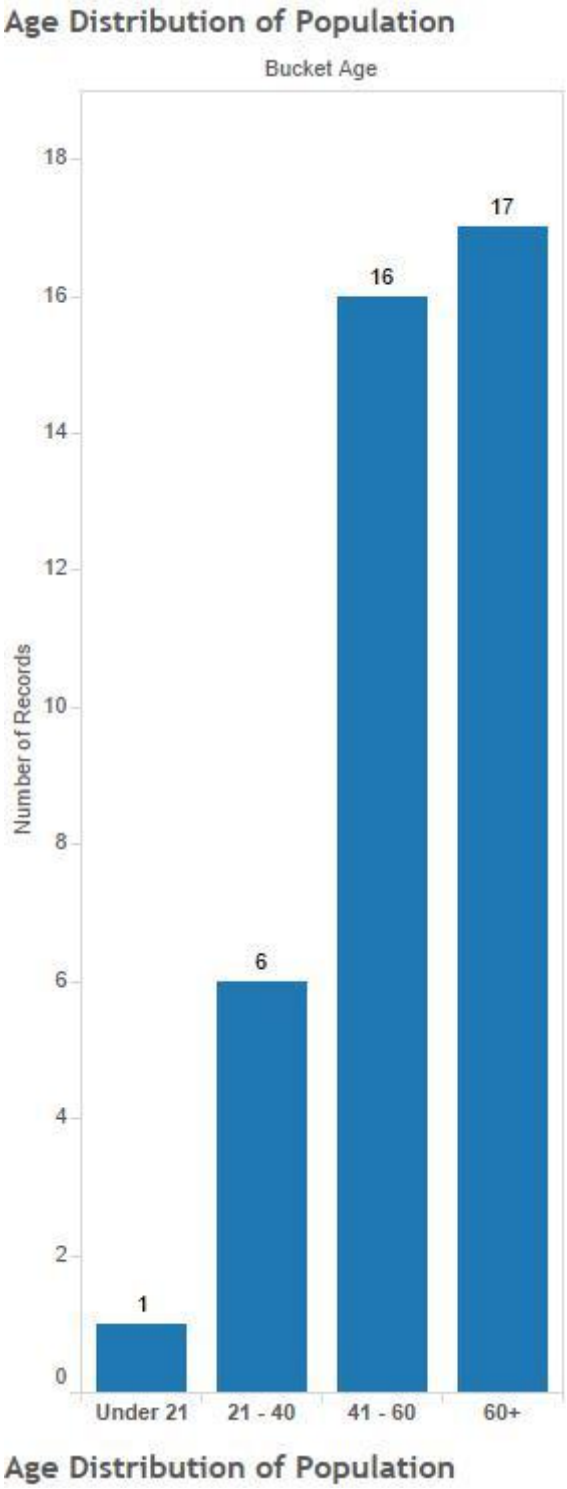
Hospital based prospective observational study.

PERIOD OF STUDY:

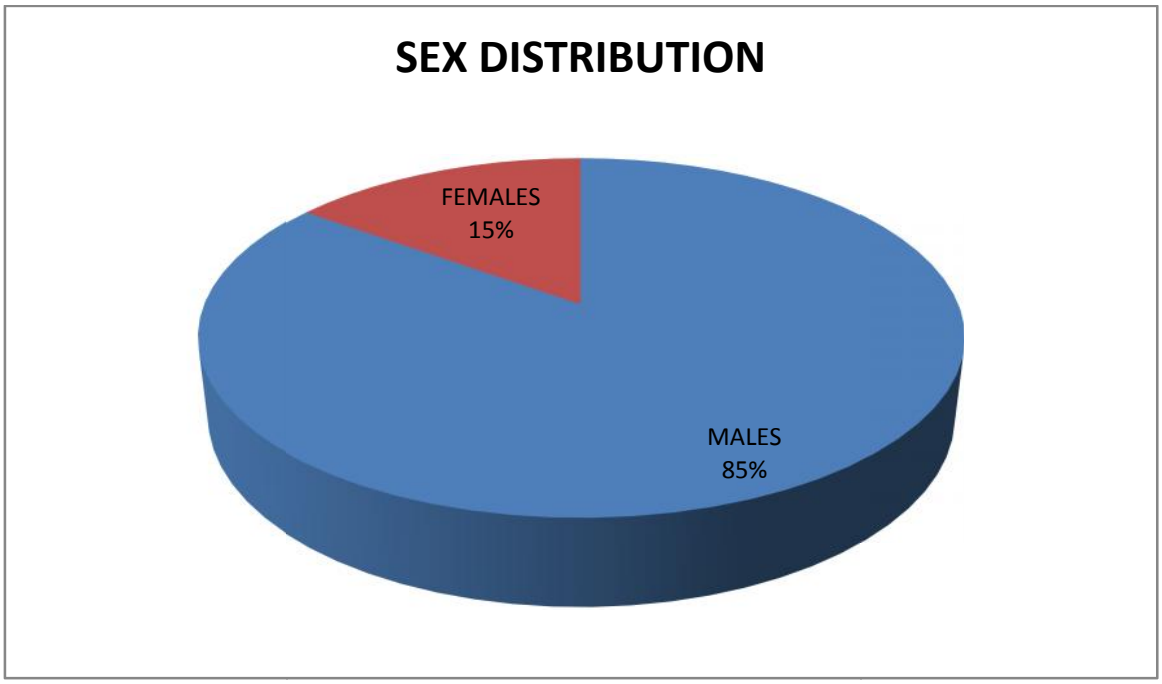
February to July 2016 (6 months)

RESULTS AND INTERPRETATION

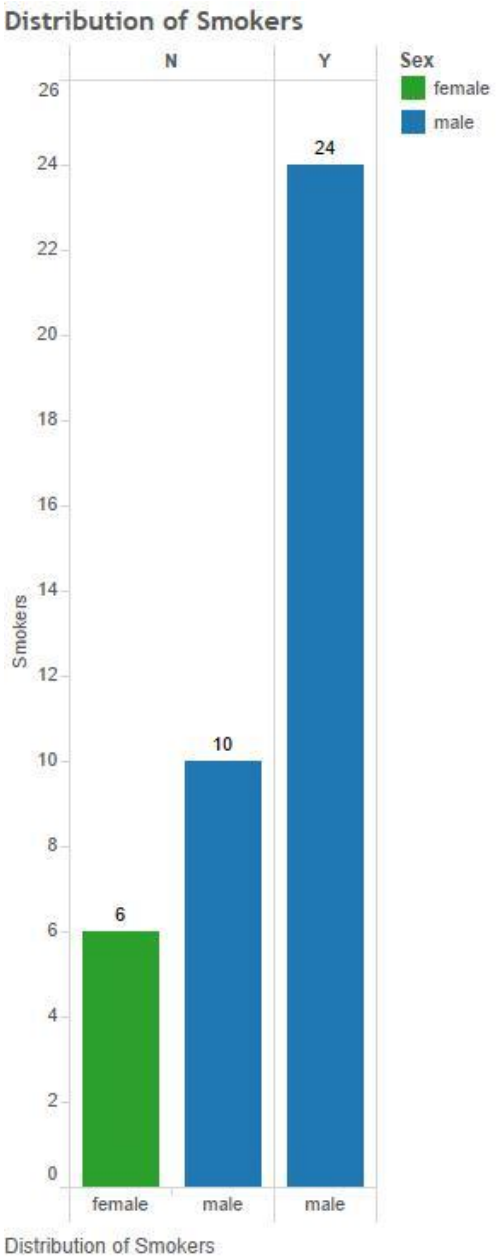
Age Distribution: Out of the 40 patients included in the study, patients less than 20 years of age were 1(2.85%), between 21 to 40 years of age were 6(14.28%) and 41 to 60 years of age were 16(40%) and above 60 years were 17(42.85%).



Sex Distribution: The study consisted of 40 patients, out of which 34(85%) were males and 6(15%) were females. Sex ratio (Male: Female) is 5.6:1



Smoking Status: Of the 40 patients,23(58%) were smokers, 17(42%) were non smokers,among the non smokers 6 were females and 10 males …..



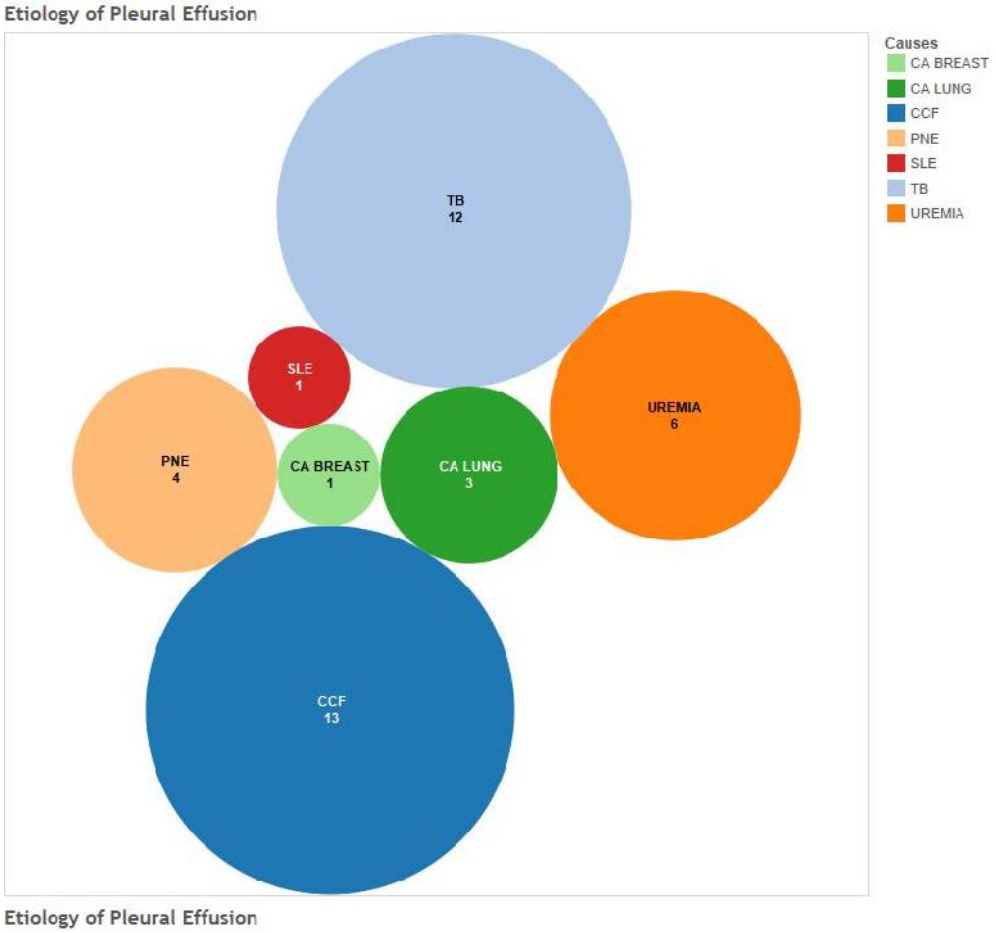
Distribution of Smokers

Comorbidities and Associated Diseases: In the present study 16(40%) had diabetes and 26(65%) were hypertensive, 12(29%) had both diabetes and hypertension, 12(30%) had history of coronary artery disease and 12(31%) had history of tuberculosis and 12(31%) had other comorbidities like sle,malignancy etc.

Etiology of Pleural Effusion: Etiology

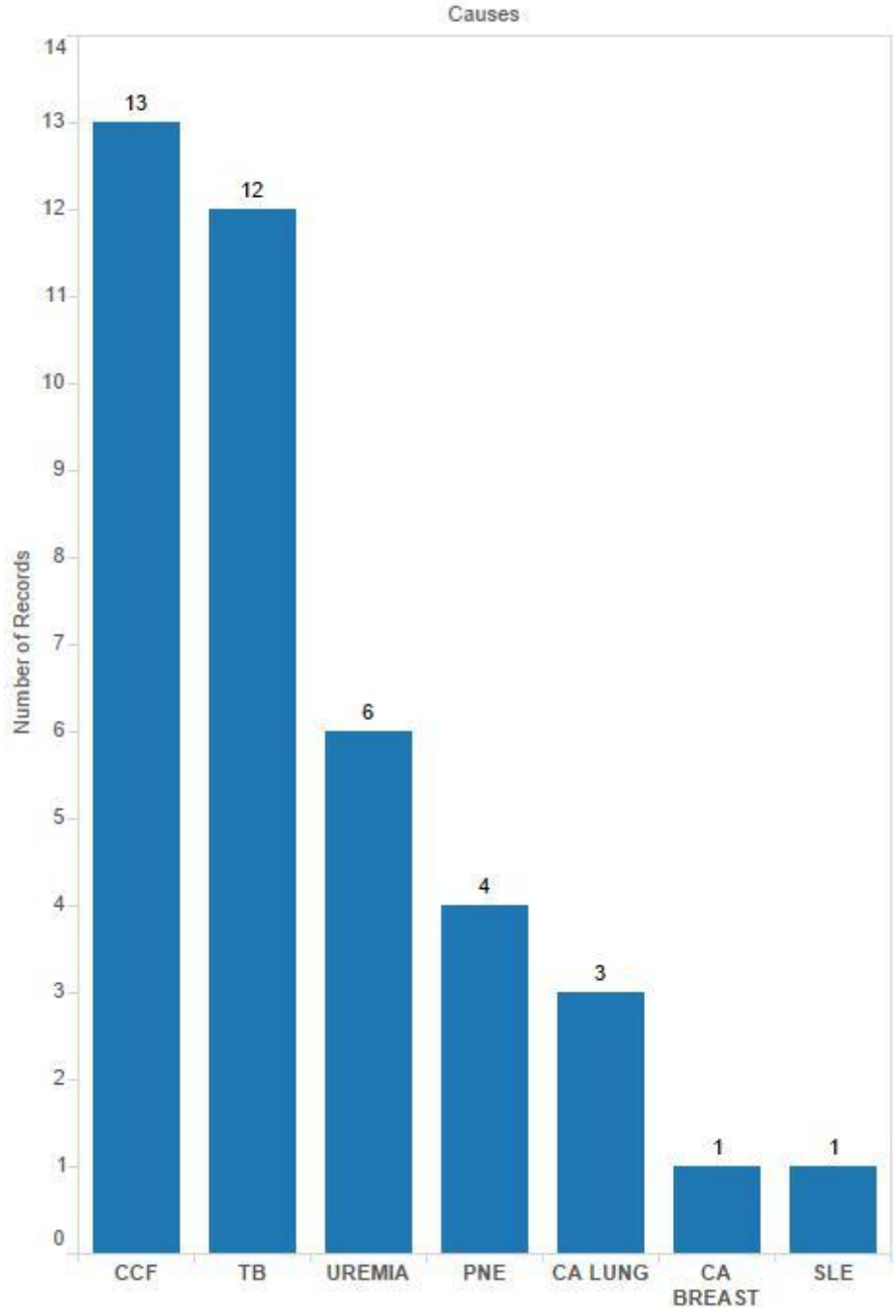
No. of Cases (n=35)

Cardiac failure	13(31 %)
Tuberculosis	12(28 %)
Malignancy	4(9 %)
Connective tissue disorders	1(2 %)
Parapneumonic effusion	4(11.4 %)
Uremic effusion	6(14.2 %)



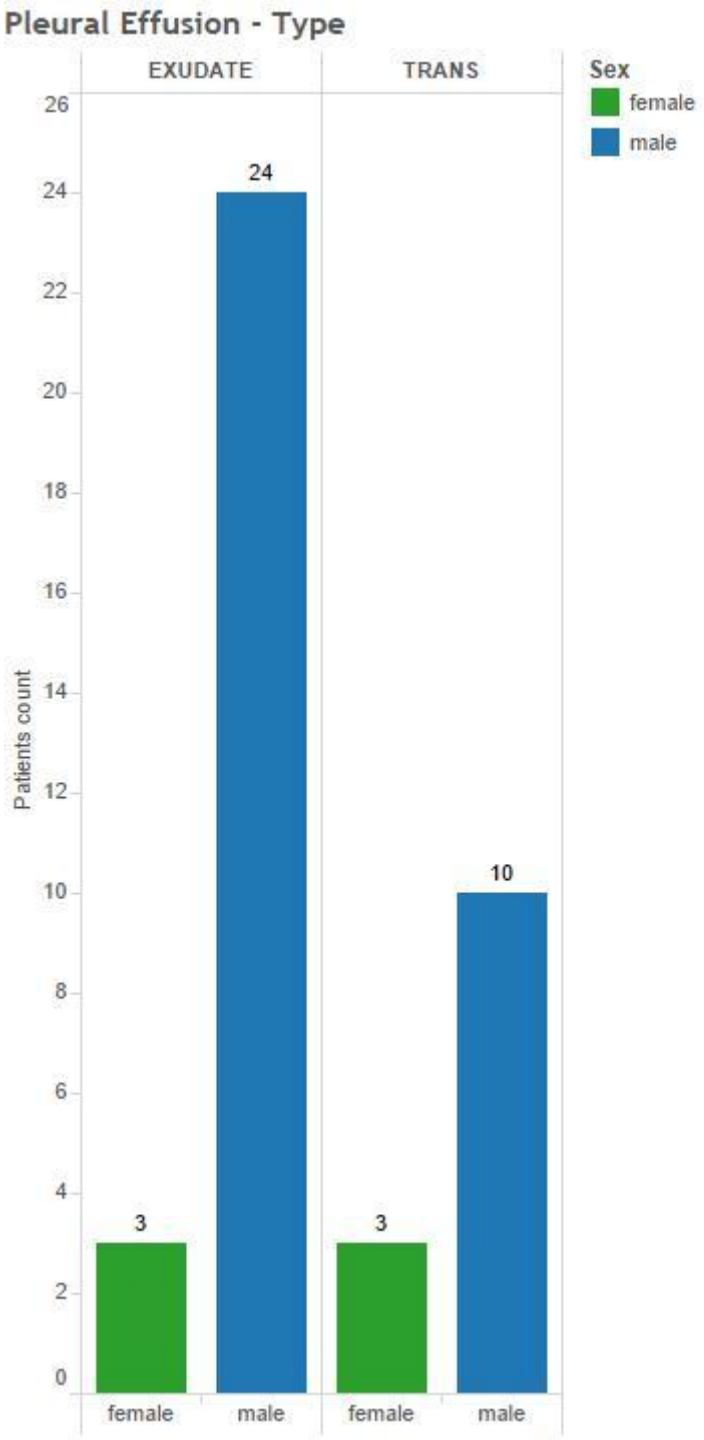
Etiology of Pleural Effusion

Etiology of Pleural Effusion



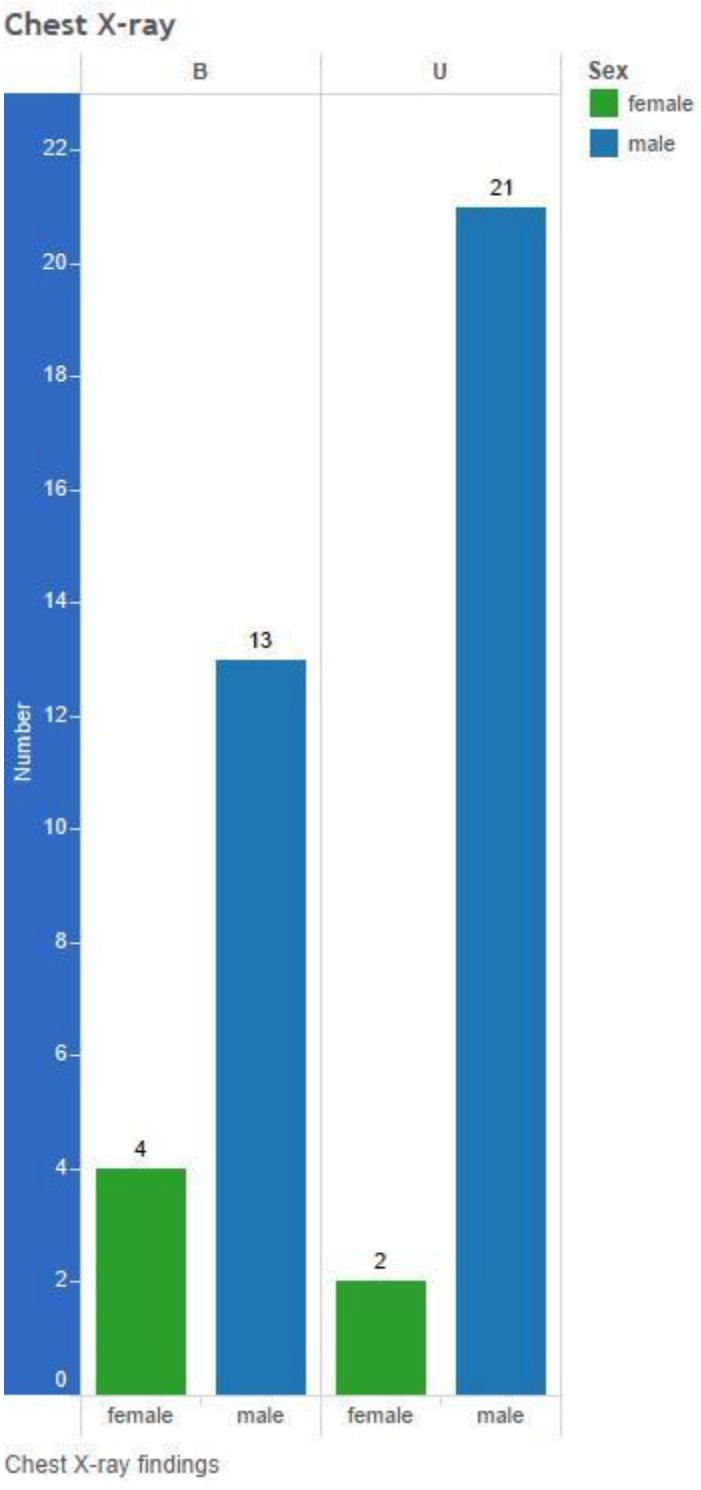
Etiology of Pleural Effusion

Type of Effusion: In 13 cases it was transudative effusions and in 27 cases it was exudative effusions..among the exudative effusion 24 were males and 3 females ,

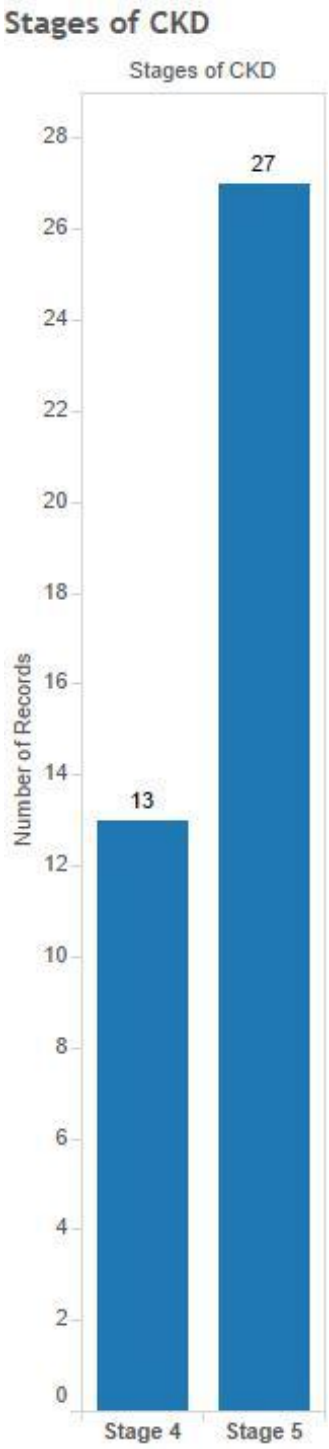


Pleural Effusion -Type

Chest X-Ray Findings: Bilateral effusion were observed in 17 cases, and unilateral effusion were observed 23,among that 21 males and 2 females.



No. of Pleural Effusion Cases in Relation to Severity of CKD: Of the 40 cases, no cases were seen in stage 1 and 2, 3,13 (32.5%) cases were seen in stage 4, 17(42.5%) cases were seen in stage 5 …..



Stages of CKD according to MDRD formula.

Lab Investigation Results: The mean haemoglobin (HB%) value was , 8.1±1.3, .The mean random blood sugar level was 153.8±85, and the mean blood urea level was 120± 55.The mean serum creatinine was 4.0±2.75.

Lab data	values
haemoglobin	8.1±1.3
The mean random blood sugar level	153.8±85
The mean blood urea	120± 55.
mean serum creatinine	4.0±2.75

DISCUSSION:

"Chronic kidney disease (CKD) is becoming a major global health problem. It is estimated that 1, 00, 000 new patients of end stage renal disease (ESRD) enter renal replacement programs annually in India.Given the prevalence of CKD, the frequency (>50%) of haemodialysis in these patients, and the propensity for these patients to have pleural disease, it is not surprising that the constellation of CKD, haemodialysis, and pleural effusion is common".

"So the aim of the present study was to look at the various etiologies of pleural effusion occurring in chronic kidney disease patients, and their characteristics. After getting informed consent 40 patients were included in the study of which 34 were males and 6 were females. Mean age of the group was 52.88yrs. Patients above 40 years constituted 82.5%".

Comorbidities:

In the present study of the 40 patients, all of them complained of dyspnoea (100%), 11(27.4%) had chest pain, 15(42.8%) had cough, and 12(30%) complained of fever, 10 (25%) had significant loss of appetite and loss of weight, 19 cases (47.28%) had pedal oedema. The dyspnoea in many patients may also be due to other co morbidities like anaemia and cardiac dysfunction. When the dyspnoea is accompanied by a pleuritic chest pain or fever or cough, it may imply an under lying pleuropulmonary pathology. Hypertension was the common comorbidity26 (65%) followed by diabetes mellitus 16(40%).

Radiology of Pleural Effusion:

In the present study bilateral pleural effusion was present in 17 cases (42.8%) and unilateral pleural effusion in 23 cases.

In pleural effusion due to heart failure 13 out of 13[33%] cases were bilateral, in tuberculous effusion mostly unilateral.

Type of Effusion:

In the present study transudative pleural effusions were 13(33%), all were bilateral, and exudative pleural effusions were 27(67%), out of which 4 were bilateral, 23 were unilateral.

Etiology of Pleural Effusion:

In the present study the aetiology of pleural effusion was attributed to cardiac effusion in 13(31%) cases out of 40 cases, tuberculous pleural effusion in 12(28 %) cases, uremic pleural effusion in 6(14.2 %) cases, and in 4(11.4 %) cases parapneumonic effusion was present. Malignant pleural effusion was present in 4(9 %) cases, pleural effusion due to connective disorder was present in 1(2 %) cases.

Pleural Effusion Characteristics in Individual Conditions:

Tuberculous Pleural Effusion:

Chronic kidney disease patients are at a growing risk for tuberculosis (TB) worldwide. A high incidence of TB has been reported among patients with CKD in India, 8.7% in patients on maintenance dialysis and 12.3% in renal allograft recipients.therapy predispose CKD patients to active TB Defective-cell-mediated immune response and uraemia, along with co morbid conditions such as diabetes and prolonged corticosteroid and immunosuppressive

In addition to this, impairment of CMI makes infection with mycobacterium tuberculosis more difficult to detect and more likely to progress to TB disease than in immune competent individuals. Smear negative and extra-pulmonary forms are more frequent than in an immunocompetent individual. A high incidence of post-transplant TB has been reported in India, especially miliary TB.

In the present study 28% of pleural effusions were due to tuberculosis. . Total number of male patients were 8, female patients were 2. Male to female ratio was 4:1. Fever was present in 70% of the patients, cough was present in 70% of the patients, dyspnoea was present in all patients.

Chest pain was complained by 50% of the patients,loss of appetite and loss of weight,pedaledema were observed. Radiologically all are unilateral effusions. 40% of patients had given past history of tuberculosis. some of patients were onhaemo dialysis. Thus from the above data it is suggested that all patients who are known to have advanced CKD, and those who are on dialysis, and those with a transplantation, should be screened actively for tuberculosis. In patients with exudative effusions, despite failure to establish tuberculosis aetiology, if therapy with common antibiotics fails, a trial of anti-tubercular therapy is justified especially in high tuberculosis endemic country like India.

Uremic Pleural Effusion:

Uremic patients undergoing haemodialysis may suffer from uremic pleural effusion. Uremic pleuritis is a fibrinous pleuritis that results from unknown putative agents.

The characteristic exudative effusion is typically serosanguineous or hemorrhagic with increased lymphocytes. Uremic pleuritis has been reported in 1 to 57%.7,8 of patients with end-stage renal disease. The typical patient with uremic pleural effusion has been undergoing dialysis for one or two years. Patients usually have symptoms at the onset of effusion, with fever, cough, or chest pain. pleural effusion generally resolves with continued dialysis over several weeks. Some may recur and some patients will progress to fibro thorax.

In the present study, 14% of the pleural effusions were due to uraemia. . Total number of male patients were 5, female patients were 1. Fever was present in 60% of the patients, cough was present in 60% of the patients, and dyspnoea was present in all patients. Chest pain was complained by 40% of the patients. Pedal oedema was present in 80% of the patients.

Parapneumonic Effusion:

CKD and ESRD patients, per se, have a greater risk of pulmonary infections. Among pulmonary infections, pleural empyema has a high mortality. It is usually a complication of pneumonia but may arise from haematogenous seeding from an extra pulmonary focus,Klebsillae pneumoniae was the most frequently isolated sole pathogen.

“However, in ESRD patients receiving maintenance dialysis, aerobic Gram-positive organisms were the predominant pathogens. S aureus and Enterococcus spp. were the most frequently isolated pathogens”.

Most stage 4 CKD patients with culture-positive empyema had underlying comorbidities, most patients were relatively Immunocompromised with either diabetes mellitus[40%] , malignancy (9%), or liver cirrhosis.

“It is well known that immunocompromised patients are prone to pleural involvement with fungal or aerobic GNB infections. The markedly high rate of Gram-negative bacterial infection in the empyema of the stage 4 CKD patients may be associated with the high incidence of underlying disease and poor renal function. However, ESRD

patients receiving long-term dialysis had a higher rate of bacteraemia and aerobic Gram-positive empyema despite a similar incidence of underlying disease and a similar frequency of central venous catheter implants.

However In the present study 11% of patients had parapneumonic effusions. Total number of male patients was 4, there were no female patients. Dyspnoea was present in all patients, fever and cough with expectoration present.

Radiologically all were unilateral effusions. Pleural fluid analysis showed a mean total leukocyte of polymorph predominance, ADA levels of 53±6.40, pleural fluid for culture and sensitivity showed growth of klebsiella in two cases, streptococcus pneumonia in one case and pseudomonas in third case.

Pleural Effusions due To Heart Failure:

Congestive heart failure (CHF) is probably the most common cause of pleural effusion in chronic kidney disease.In the past, it was believed that pleural fluid accumulation in CHF was due to increased pressure in the capillaries in visceral or parietal pleura which resulted in an increased entry of fluid into the pleural space from parietal pleura and a decreased removal of fluid through visceral pleura.

Current theories propose that pleural fluid accumulates in patients with CHF when they have left ventricular failure. The high pressures in pulmonary capillaries lead to increased amounts of fluid in the interstitial spaces. Which enters the pleural space through the highly permeable visceral pleura. Fluid accumulates when the entry of fluid into the pleural space overwhelms the capacity of the lymphatics in the parietal pleura to remove the fluid. Small amounts of fluid may enter the pleural space from the capillaries in either pleural surface. Elevation of systemic venous pressure may decrease the lymphatic clearance from the pleural space.

Pleural effusions due to CHF produce dyspnoea on exertion frequently out of proportion to the size of the effusion, peripheral oedema, orthopnoea or paroxysmal nocturnal dyspnoea. Signs of both right-sided heart failure, left-sided heart failure and pleural effusions may be seen. Chest radiograph almost always reveals cardiomegaly and usually bilateral pleural effusions. CHF is by far the most common cause of bilateral pleural effusion. If patient is febrile, has pleural effusions that are

greatly disparate in size, has unilateral pleural effusion, pleuritic chest pain, or does not have cardiomegaly, an alternative diagnosis must be sought.

A test useful for establishing diagnosis of CHF is measurement of serum or pleural fluid pro-brain natriuretic peptide (pro-BNP). When the ventricles are subjected to increased pressure or volume, BNP is released. Levels below 100pg/mL make CHF unlikely, whereas above 500pg/mL are considered diagnostic of CHF.

In the present study13[31%] of pleural effusions were present due to heart failure. None of the patients had fever,anddyspnea,cough,pedaledema are predominant symptoms.

Radiologically all were bilateral effusions. most of patients had cardiomegaly in chest x ray.

Malignant Pleural Effusion:

In the present study 4(9%) cases were due to malignancy; among that 3 were lung carcinoma and 1 breastcarcinoma,the pleural fluid shows hemorrhagic effusion and also recurrent effusion…so if patient have recurrent hemorrhagic effusion, search malignant causes.

Connective Tissue Dissorders:

In 1(2%) of the 40 cases the effusion was due to systemic lupus erythematosis. The above findings suggest that though heart failure is the single most common cause of pleural effusion in CKD patients other causes like tuberculosis, uraemic effusions, parapneumonic effusions must be considered and investigated in the appropriate setting.

CONCLUSION:

There is a high prevalence of exudative pleural effusions in our study. So, all patients with chronic kidney disease and pleural effusion, thorough search for exudative causes must be done.

SUMMARY

- Pleural involvement is common in patients with chronic renal insufficiency mainly stage 4 and 5.
- Heart failure and TB was the most common cause among these effusions.
- Other causes included Para pneumonic effusions, malignancy and uraemia.
- The presence of unilateral effusion and absence of Cardiomegaly on chest x-ray, suggests a diagnosis other than heart failure, such as tuberculosis, uraemia and parapneumonic effusions which deserve prompt thoracocentesis, as these cannot be differentiated clinically.
- Tuberculous effusion must be differentiated from uremic effusion, since management is different.
- Previously transudative effusions were thought to be more common in CKD, but our study result shows that the incidence of exudative effusion is more common than transudative effusions due to high incidence of tuberculosis,
- Thereby, all the CKD patients having unilateral pleural effusion , exudative etiologies should be ruled out.

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PROFORMA:

Name:

Age / Sex:

IP no:

Occupation:

Presenting complaints:

Past History:

H/o DM, HT, CVD,CAD,DRUG INTAKE, Thyroid disorders, malignancies pulmonary or extra pulmonary tuberculosis , CLD, COPD.

Personal history

smoker/ nonsmoker

alcoholic/ non alcoholic

Family H/o CKD

Clinical Examination:

General Examination

Consciousness, Pallor, jaundice, Clubbing, Lymphadenopathy, hydration status

Vitals:

PR

BP

RR

SpO2

Systemic examination:

CVS:

RS:

ABDOMEN:

CNS:

Laboratory investigations:

Complete hemogram

Renal function test

Liver function test

Sputum AFB, gram stain & culture

Chest x-ray PA view

Pleural fluid analysis

Urine routine

Diagnosis

MASTER CHART

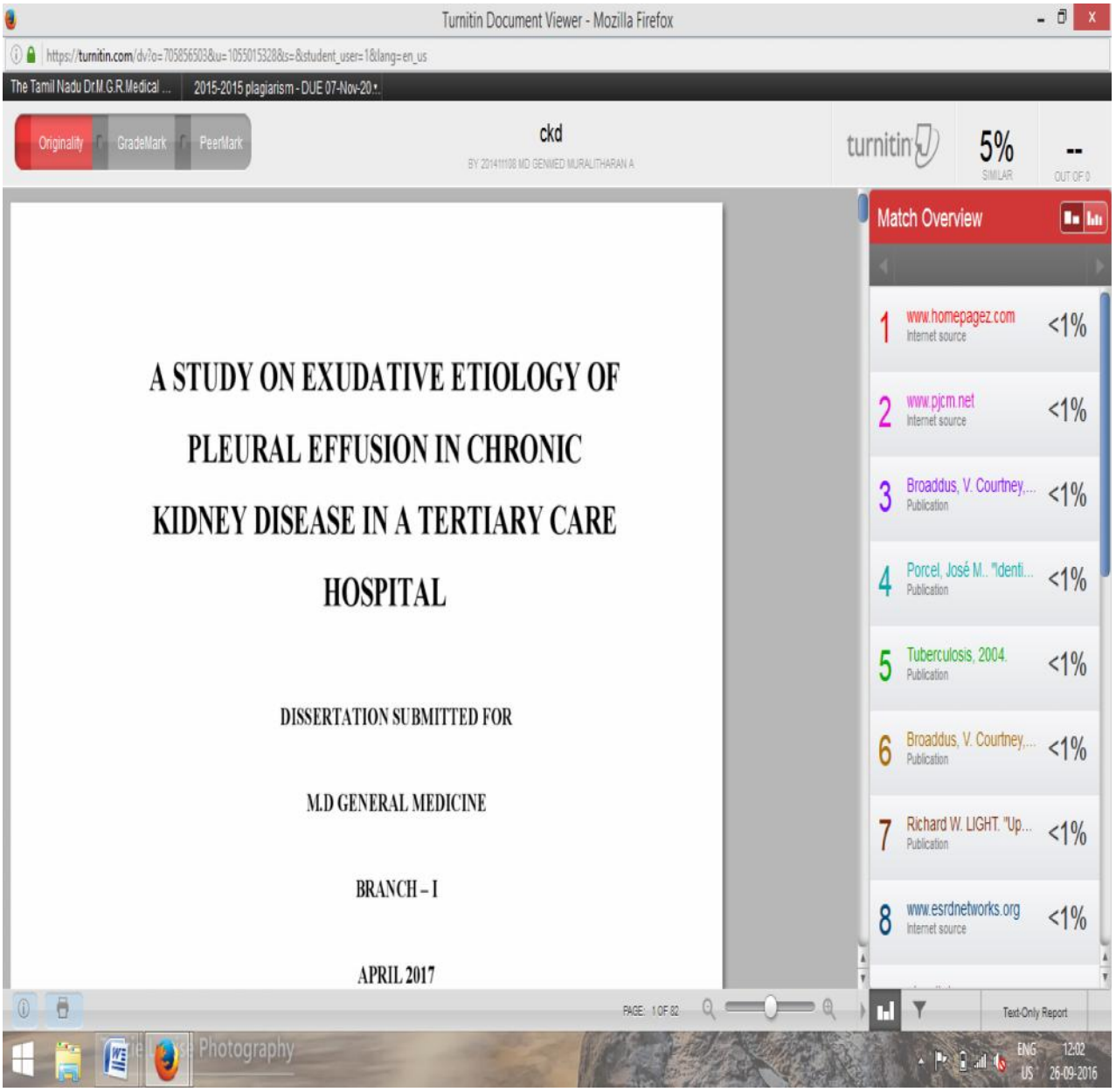
NAME	AGE/SEX	sex	SMOKER	SHT	DM	CAD	TB	OTHERS	CXR/PE	PLEURAL FLUID,T/E	HB	UREA	CR	STAGES	ADA	ECHO/EF	CAUSES
subramani	45/m	male	y	Y	+	+	+		U	EXUDATE	8.2	160	6.4	5	+	65	TB
perumal	69/m	male	y	Y	+	+	-		U	EXUDATE	8.1	173	6.67	5	-	65	PNE
saravanan	25/m	male	y	N	-	-	-		U	EXUDATE	6.7	160	6.5	5	-	65	UREMIA
karuppia	63/m	male	n	N	-	-	+		U	EXUDATE	7.9	95	3.7	4	+	65	TB
kaliyappan	69/m	male	y	N	-	-	+		U	EXUDATE	7.7	93	3.8	4	+	65	TB
ibrahim	33/m	male	n	Y	-	-	-		U	EXUDATE	6.9	175	5.4	5	-	65	UREMIA
muniyandi	51/m	male	y	Y	+	-	-		U	EXUDATE	7.8	170	6.7	5	-	65	UREMIA
duraimurugan	64/m	male	n	Y	-	-	+		U	EXUDATE	6.6	140	5.9	5	+	65	TB
allavudeen	67/m	male	y	Y	+	+	+		U	EXUDATE	8	160	5.8	5	+	65	TB
sasikmar	53/m	male	n	N	-	-	+		U	EXUDATE	6.9	168	6.6	5	+	65	TB
velusamy	44/m	male	y	Y	-	-	+		U	EXUDATE	8.5	102	4	4	+	65	TB
pandian	37	male	n	N	-	-	-		U	EXUDATE	8	137	4.3	4	-	65	PNE
kandhan	65	male	y	Y	+	+	-		U	EXUDATE	7	172	6.6	5	-	65	UREMIA
kesavan	49	male	n	N	-	-	+		U	EXUDATE	9	90	4	4	+	65	TB
lakshmi	19	female	n	N	-	-	-	SLE	U	EXUDATE	7.5	120	3.7	4	-	65	SLE
sangili	58	male	y	Y	+	+	-		U	EXUDATE	7.9	112	9.3	4	-	65	UREMIA
laksnmanan	39	male	n	N	-	-	-		U	EXUDATE	7.1	170	6.6	5	-	65	UREMIA
subbammal	67	male	n	N	+	+	-	CA BREAS	B	EXUDATE	6.6	169	6.5	5	-	65	CA BREAST
joythi	51	female	n	Y	-	-	+		U	EXUDATE	7	105	3.9	5	+	65	TB

MASTER CHART

manivanna	64	male	n	N	-	-	+		U	EXUDATE	7.6	127	6.2	5	+	65	TB
karuppasamy	63	male	y	Y	+	+	+		B	EXUDATE	8	133	6.1	5	+	65	TB
ravi	65	male	y	N	-	-	-	CALUNG	U	EXUDATE	8	146	6.5	5	-	65	CALUNG
selvaguru	43	male	y	Y	-	-	-		U	EXUDATE	8.5	151	6.1	5	-	65	PNE
vadivel	44	male	n	N	-	-	-		U	EXUDATE	9	125	5.4	5	-	65	PNE
valliammal	61	female	n	N	+	+	+		B	EXUDATE	7.9	153	6.4	5	+	65	TB
raman	50	male	y	Y	-	-	-	CA LUNG	U	EXUDATE	7.7	156	6.5	5	-	65	CA LUNG
muniappan	59	male	y	Y	+	-	-	CA LUNG	B	EXUDATE	8.1	160	7	5	+	65	CA LUNG
parthasarathy	35	male	y	N	-	-	-		B	TRANS	9.5	69	3	4		35	CCF
alex	39	male	y	Y	-	-	-		B	TRANS	9.4	75	3.6	4		45	CCF
revathy	47	female	n	Y	-	-	-		B	TRANS	9	94	4.2	5		39	CCF
rasu	49	male	y	Y	-	-	-		B	TRANS	8.1	85	4	4		41	CCF
sakthivel	45	male	y	Y	-	-	-		B	TRANS	9.5	89	4.8	5		43	CCF
manonmani	55	female	n	N	+	-	-		B	TRANS	8.7	90	5.1	5		36	CCF
jegannathan	65	male	y	Y	+	+	-		B	TRANS	8.2	94	5	5		38	CCF
mohammed ism	61	male	y	Y	-	-	-		B	TRANS	8.4	95	5.2	5		35	CCF
rathnam	62	male	y	Y	-	-	-		B	TRANS	8.5	102	4.7	5		42	CCF
kaleeswari	64	female	n	Y	-	+	-		B	TRANS	8	79	3.3	4		40	CCF
kaliaperumal	55	male	y	Y	-	-	-		B	TRANS	7.9	83	4	4		60	CKD
rajasekar	61	male	y	Y	+	-	-		B	TRANS	8.5	87	3.9	4		62	CKD
sahayaraj	63	male	y	N	+	+	-		B	TRANS	9.1	92	4.9	5		60	CKD

ABBREVIATION

CKD	Chronic Kidney Disease
PE	Pleural Effusion
U	Urea
Cr	Creatinine
CXR	Chest X Ray
Pl	Pleural Fluid Analysis
E	Exudative
T	Transudative Effusion
GE	Gene Expert
CAD	Coronary Artery Disease
Tb	Tuberculosis
DM	Diabetes Mellitus
HT	Hypertension
UL	Unilateral
BL	Bilateral
RFT	Renal Function Test
RBS	Random Blood Sugar
Hb	Haemoglobin
CCF	Congestive Cardiac Failure
PNE	Para Pneumonic Effusion
SLE	Systemic Lupus Erythematosis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DISSERTATION SUBMITTED FOR
M.D GENERAL MEDICINE
BRANCH – I
APRIL 2017
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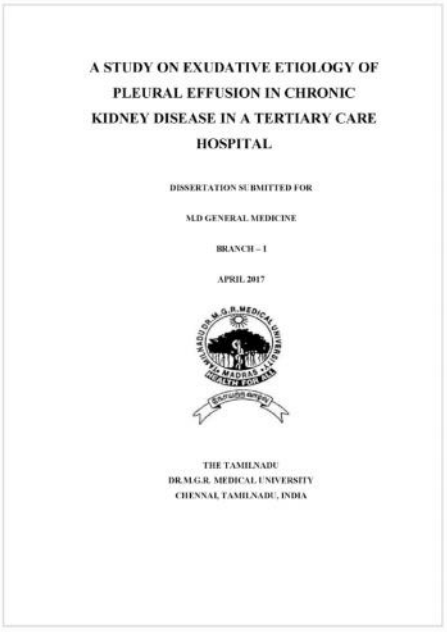

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DISSERTATION SUBMITTED FOR

MD GENERAL MEDICINE

BRANCH – I

APRIL 2017

THE TAMILNADU
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Period of Study	:	2014-2017
College	:	MADURAI MEDICAL COLLEGE
Research Topic	:	A STUDY ON ETIOLOGY OF PLEURAL FFUSION IN CHRONIC KIDNEY DISEASE IN A TERTIARY CARE HOSPITAL
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