Dissertation on

"A STUDY OF CEREBROSPINAL FLUID CHLORIDE LEVELS IN MENINGITIS "

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CERTIFICATE

This is to certify that the dissertation titled **"A STUDY OF CEREBROSPINAL FLUID CHLORIDE LEVELS IN MENINGITIS"** is the bonafide Original work done by **Dr. C.GOBINATH**, post graduate student, Institute of Internal medicine, Madras medical college, Chennai-3, in partial Fulfillment of the University Rules and Regulations for the award of MD Branch -1 General Medicine, under our guidance and supervision, during the academic year 2016 - 2019.

Prof. Dr.S.TITO M.D.,
Director (I/C)& Professor,
Institute of Internal Medicine,
Madras Medical College &RGGGH,
Chennai – 600 003 .

Prof. Dr.G.SUNDARAMURTHY M.D.,
Professor of Medicine,
Institute of Internal Medicine,
Madras Medical College &RGGGH ,
Chennai -600 003

Prof. Dr. JAYANTHI, M.D., FRCP(Glas)
DEAN,
Madras Medical College,
Chennai 600 003.

DECLARATION

I, **Dr. C.GOBINATH,** solemnly declare that dissertation titled **"A STUDY OF CEREBROSPINAL FLUID CHLORIDE LEVELS IN MENINGITIS"** is a bonafide work done by me at Madras Medical College and Rajiv Gandhi Government General Hospital, Chennai-3 during 2017-2018 under the guidance and supervision of my unit chief **Prof.Dr.G.SUNDARAMURTHY, M.D.,** Professor of Medicine, Madras Medical College and Rajiv Gandhi Government General Hospital, Chennai.

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Place : Chennai -03
Date :

Dr. C.GOBINATH
MD General Medicine,
Post Graduate,
Institute of Internal Medicine,
Madras Medical College,
Chennai – 03

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ABBREVATIONS

AFB	-	ACID FAST BACILLI
AIDS	-	ACQUIRED IMMUNODEFICIENCY SYNDROME
ATT	-	ANTI- TUBERCULAR TREATMENT
BCG	-	BACILLI CALMETTE GUERIN
CECT	-	CONTRAST ENHANCED COMPUTERISED TOMOGRAPHY
Cl	-	CHLORIDE
CMV	-	CYTOMEGALOVIRUS
CNS	-	CENTRAL NERVOUS SYSTEM
CSF	-	CEREBROSPINAL FLUID
C&S	-	CULTURE & SENSITIVITY
CT	-	COMPUTERISED TOMOGRAPHY
dL	-	DECILITRE
EEE	-	EASTERN EQUINE ENCEPHALITIS
EBV	-	EPSTEIN BARR VIRUS
HHV	-	HUMAN HERPES VIRUS
HIV	-	HUMAN IMMUNODEFICIENCY VIRUS
HSV	-	HERPES SIMPLEX VIRUS
IAP	-	INDIAN ASSOCIATION OF PAEDIATRICS
ICP	-	INTRA CRANIAL PRESSURE
IL	-	INTERLEUKIN
LA	-	LATEX AGGLUTINATION
LCMV	-	LYMPHOCYTIC CHORIOMENINGITIS VIRUS
LP	-	LUMBAR PUNCTURE

MDR	-	MULTI – DRUG RESISTANT
mg	-	MILLIGRAM
MIC	-	MINIMAL INHIBITORY CONCENTRATION
mm	-	MILLIMETRE
MRI	-	MAGNETIC RESONANCE IMAGING
MRS	-	MAGNETIC RESONANCE SPECTROSCOPY
OM	-	OTITIS MEDIA
PCR	-	POLYMERASE CHAIN REACTION
pH	-	POTENTIA HYDROGENII
L	-	LITRE
MTB	-	MYCOBACTERIUM TUBERCULOSIS
PAF	-	PLATELET ACTIVATING FACTOR
PGE	-	PROSTAGLANDLIN
NTM	-	NON TUBERCULOUS MYCOBACTERIA
TB	-	TUBERCULOSIS
TBM	-	TUBERCULOUS MENINGITIS
TLR	-	TOLL LIKE RECEPTOR
TNF	-	TUMOUR NECROSIS FACTOR
U	-	UNITS
VZV	-	VARICELLA ZOSTER VIRUS
WBC	-	WHITE BLOOD CELL
WHO	-	WORLD HEALTH ORGANISATION
WNV	-	WEST NILE VIRUS

CONTENTS

INTRODUCTION

INTRODUCTION

Meningitis is a one of the important cause of morbidity and mortality worldwide. Still it continues to one of lethal infections especially in a developing country like ours. Since the mortality is very high prompt, early definite initiation of treatment could save lot of lives. For presumptive initiation of treatment, simple and cost effective investigations giving a clear and definite diagnosis would of great help to the physician

The present work is a modest attempt at briefly looking at the profile of meningitis patients in a tertiary care setup. It also tries imply the significance of various parameters that aid us to diagnose a meningitis etiologically and whether a once considered vital investigation like CSF chloride levels hold good at aiding and abetting in clear diagnosis.

It is very well known fact that CSF chloride levels were decreased in bacterial meningitis including tuberculous meningitis. Infact in tuberculous meningitis it was low compared to pyogenic meningitis. In viral meningitis CSF chloride levels were unaltered.

AIMS AND OBJECTIVES

AIMS OF THE STUDY

To study the cerebrospinal fluid chloride levels in various types of meningitis compare along with other routine investigations done on meningitis patients.

REVIEW OF LITERATURE

REVIEW OF LITERATURE

Meningitis is a syndrome characterized by inflammation of meninges of the brain and spinal cord

PROBLEM STATEMENT

The incidence differs from country to country depending upon its population demography, environmental and social factors along with the medical resources. On the whole its incidence is increasing in the developing countries and it is presumed incidence to be higher than reported.

In the western world the trend is such that the incidence is decreasing but still is a significant source of morbidity and mortality.

HISTORY

Meningitis is known since the period of Hippocrates. His works have a mention of meningitis. Sir Robert whytt was the first to describe tuberculousmeningitis[1] by the year 1768 posthumously In 1805,first outbreak of meningitis was documented in Geneva.Gaspard vieusseux, Andre matthey and Elisa north described epidemic meningococcal meningitis. Subsequently many epidemics were reported. In 1840,there were further outbreaks in Africa. One of the major outbreaks was that in Nigeria and Ghana.

In 1887, Austrian bacteriologist Anton Vaykselbaum was the first to report meningococci as a causative organism in bacterial meningitis. Subsequently other organisms. *Streptococcus pneumoniae* and *Haemophilus influenza*[1] . The technique of lumbar puncture was demonstrated and an early analysis of cerebrospinal fluid was done by Henrich Quincke in 1891.

The clinical features of meningitis were described by Russian physician Vladimir kernig (1884) and polish physician Josef brudzinski (1899). Kernig's sign and Brudzinski's sign were named after them.

Influenza A, Influenza B ,Adenoviral infection causing meningitis were later described after world war 2. AA Smorodinstev recorded 200 different viral meningitis with subtyping them.

VACCINES

In 1906 horses were used to create antibodies against meningococcal bacteria.[8]

American scientist Simon Flexner developed this to decrease death and disability rates. The advent of haemophilus vaccines caused a great reduction in the prevalence of meningitis due to haemophilus**.**[8]

ANTIBIOTICS

Initial successful treatment of meningitis was with serum therapy for meningococcal meningitis by Georg joachmann and Simon Flexner.[1]

In 1944 penicillin was used for treatment of meningitis and marked by good response. Francois schwentker used sulfonamides and Chester keefer used penicillin appropriately to give results.

STEROIDS

Evidence emerged that use of steroids in tuberculous meningitis could improve the disability rates. It revolutionized therapeutics in meningitis patients.In 2007, Advisory committee on Immunization Practices recommends routine meningococcal vaccine to children of 11 and 12 years.

In India, National immunization schedule has routine haemophilus vaccine. The government medical services ensures that each and every children are vaccinated. Apart from this the Indian Association of Paediatrics (IAP) vaccination schedule recommends pneumococcal vaccine. Also IAP recommends vaccination against Japanese encephalitis and Meningococci.[2][8]

DESCRIPTION

Meningitis could be the inflammation involving the 3 layers of membranes that encase the CNS structures. They involved structures are:

1.Dura the outer membrane tough in nature

2. Arachnoid middle membrane lacy and weblike

3.The subarachnoid space containing feeding blood vessels to brain and spinal cord may be involved.

Anatomical classification of meningitis:

Pachymeningitis – inflammation of the dura.less common.

Leptomeningitis – inflammation of arachnoid and sub arachnoid space. More common

Meningitis can be divided into the following categories:

Bacterial meningitis

Granulomatous meningitis

Aseptic meningitis

Meningitis can also be classified as

Acute less than 24 hours – considered almost to be bacterial

Subacute 1 – 7 days

Chronic > 7 days

RISK FACTORS

Extremes of ages both less than 5 or greater than 60

Diabetes mellitus

Immunosuppression

HIV infection especially encapsulated organisms

Crowding

Bacterial endocarditis

Chronic kidney disease

Adrenal insufficiency

Post splenectomy status

Alcoholism

Chronic liver disease

Sickle cell disease

Contiguous infection

Head injury patients

Patients who underwent neurosurgical procedures like vp shunts

Iv drug abusers

Thalassemia major

Hypoparathyroidism

Cystic fibrosis

Congenital cranial deformities

Malignancy

ETIOLOGY

Bacterial meningitis

Streptococcus pneumoniae gram positive coccus the most common cause of bacterial meningitis worldwide.[2] It is the commonest organism associated in skull base fractures and CSF leak. It may be associated with pneumonia, endocarditis (as in Austrian syndrome) and /or sinusitis. It may be present in healthy individuals in pharynx and nasal cavity. Choroid plexus seeding from bacteremia / contiguous spread seems the mode of causation of meningitis.[3][4][5]

Niesseria meningitides , gram negative diplococcus in nasopharynx of normal individuals .It is the leading cause of meningitis in young adults as of now.It invades the airway epithelium by way of penetration. Sporadic cases by B , C , Y strains . Epidemics caused by A , C strains.[6][7]

Haemophilus influenzae a small gram negative coccobacillus. It's normal habitat is the upper airways**.** Encapsulated type b strain was commonly

isolated strain. Since the advent of Hib vaccine the overall incidence has drastically fallen**.** [12][13]

Listeria monocytogenes, small gram positive bacillus characterized by high rates of mortalities. Most common mode of infection is food borne. It is associated with outbreaks in people consuming contaminated milk cheese and alfalfa tablets.It has a predilection to infect children and elderly.

Staphylococci, gram positive cocci present in normal skin flora . It causes Meningitis in patients who underwent neurosurgical procedures, head injury, CSF Shunts and infective endocarditis. *S.epidemidis* is frequent offender in shunt infections.

Sterptococccus agalactiae , gram positive coccus inhabitant of lower gastro intestinal tract/ female genitalia . It is common cause of neonatal meningitis but known to affect diabetics, alcoholics, hepatic, renal failure patients.

Many aerobic gram negative bacteria like *Escherichia coli,* Klebsiella pneumoniae,*Serratia marcescens*, *Pseudomonas aeruginosa* , Salmonella species. A peculiar risk factor involves disseminated strongylodiasis causing gram negative bacillary bacteremia. The movement of *Strongyloides stercoralis* larvae across the gut helps the gram negative bacilli to translocate the gut causing bacteremia subsequently meningitis.[9][10][11]

Tuberculous meningitis

In India this one of the most common form of meningitis as compared with the western world by the shear prevalence of pulmonary and other forms of tuberculosis which favours the CNS dissemination. CNS tuberculosis accounts about 15% of tuberculosis of this Tb meningitis is by far the commonest CNS presentation of tuberculosis. The mortality rate is as high as 27%. With the epidemic of HIV infections there are more newly acquired and reactivated tuberculous infections.[14][15] More than 50% of HIV infected patients are found to have had tuberculosis infection during the course of their illness. Thus these patients serve as an active reservoir to the spread of TB in the community.

Virtually all tuberculous infections of the CNS are caused by the human tubercle bacillus, *Mycobacterium tuberculosis.* Infections caused by *M. bovis* acquired from the ingestion of contaminated milk are now quite rare, as are infections caused by other nontuberculous mycobacteria (NTM) pathogenic for human, except in immunocompromised patients, where infection of *M. avium* and *M. intercellulare* are common.[19]

Viral meninigitis

Acute viral meningitis of the central nervous system (CNS) have a sudden onset and run a short course over days to weeks. Certain features of viral infections are noteworthy. This includes tropism—viruses may infect specific cells and anatomical areas of the nervous system, e.g. anterior horn

cells are affected in poliomyelitis, the dorsal root ganglion cells in varicella zoster infection and the neurons in rabies.

Certain viruses (e.g. herpes simplex and varicella zoster) have the ability to remain latent in the nervous system and get reactivated months to years later. Most viruses replicate in extraneural tissues before invading the CNS and involvement of the nervous system is usually only an occasional complication of the systemic viral infection. The majority of viruses enter the nervous system via the haematogenous route, except herpes simplex and rabies viruses.[20] Often the viral agent cannot be identified during the acute illness and the diagnosis can only be made retrospectively. Viruses may affect the CNS by means other than direct invasion; peri-venous encephalomyelitis usually follows a systemic viral infection or vaccinations and is an allergic reaction to viral antigen.The following table shows some common viral agents.

Acute Meningitis	
Common	**Less Common**
Enteroviruses (coxsackieviruses, echoviruses, and human enteroviruses 68–71)	Herpes simplex virus 1
Varicella-zoster virus	Human herpesvirus 6
Herpes simplex virus 2	Cytomegalovirus
Epstein-Barr virus	Lymphocytic choriomeningitis virus
Arthropod-borne viruses	Mumps
HIV	

Fungal meningitis

Cryptococcus neoformans, an encapsulated yeast-like fungus is the most common CNS mycosis. It is found in mammal and bird faeces, particularly in pigeon droppings. CNS infection can be meningeal or less commonly parenchymal. Disseminated disease occurs commonly in immunocompromised while cryptococcomas (granulomas) occur in imm unocompetent hosts. Cryptococcal meningitis is thought to be a reactivation of the dormant lesion in the lung similar to Ghon's focus of pulmonary tuberculosis. Basal meningitis may cause obstructive hydrocephalus. Focal lesions like cryptococcomas or infarction present with focal neurological deficits or seizures. The commonest parenchymal sites are the mid-brain and the basal ganglia. Infarctions in basal ganglia,internal capsule and thalamus may rarely occur.

Aspergillus is a ubiquitous fungus in soil, water, decaying vegetation and organic debris. *Aspergillus fumigatus, A. terreus,* and *A. flavus* cause CNS infection. Spread to CNS occurs haematogenously or by direct inoculation into the CNS during surgical procedures or from contiguous structures. CNS aspergillosis can present as solitary or multiple lesions, meningitis.

PATHOGENESIS

In many cases of meningitis are caused by an infectious organism that has colonized or established a localized infection elsewhere in the body. Possible sites of colonization or infection include the skin, the nasal cavity, pharynx, the respiratory tract, the gastrointestinal (GI) tract, and the genitourinary tract. The organism enters the submucosa at the above sites by escaping host defenses (eg, physical barriers, local immunity, and phagocytes or macrophages). An infectious organism (ie, a bacterium, virus, fungus, or parasite) can gain access to the central nervous system and cause meningeal disease via any of the 3 following pathways:

- Blood stream invasion followed hematogenous seeding of the CNS
- A neuronal (eg, olfactory and peripheral nerves) pathway by in retrograde fashion (eg, Naegleria fowleri or Gnathostoma spinigerum)
- Contiguous spread (eg, sinusitis, congenital malformations, trauma, OM or direct inoculation during intracranial manipulation)

Bloodstream invasion and subsequent seeding is the most common mode of spread for most agents. This pathway is very peculiar of meningococcal,

cryptococcal, syphilitic, and pneumococcal meningitis. Infrequently, meningitis arises secondary to invasion via septic thrombi or osteomyelitic erosion from infected adjacent structures. Meningeal seeding may occur with a direct bacterial inoculate during injury, neurosurgery. Meningitis in the newborn is usually transmitted vertically, involving pathogenic organisms that have colonized the maternal intestinal or genital tract, or horizontally, from nursing staff or caretakers at home.

Local extension from extracranial infection (eg, OM, mastoiditis, or sinusitis) is a common cause. Possible access for the migration of pathogens from the middle ear to the meninges are:

- The bloodstream
- Preformed tissue planes (eg, posterior fossa)
- Temporal bone fractures
- The oval/ round window membranes of the labyrinths

The brain is naturally protected from immune mechanism of host by the barrier that the meningeal coverings form between the bloodstream and the brain. Normally, this protection is a beneficial as the barrier prevents the immune system from attacking the CNS. In meningitis, the blood-brain barrier can becomes broken. Once infectious agents have found their way to the brain, they are not easily accessible to the immune system and can spread. When the host tries to fight the infection, the problem aggravates, blood vessels become leaky and allow plasma, WBCs, and host immune related cytokines to enter the CNS. This process, in turn, causes brain edema and can finally result in

hypoperfusion to parts of the brain, leading to deterioration of infection. Based on the severity of pyogenic meningitis, the inflammatory process may remain localised to the subarachnoid space. In less severe forms, the pia matar is not penetrated, and the underlying brain parenchyma remains intact. However, in more extreme forms of pyogenic meningitis, the pial barrier is breached, and the underlying CNS is invaded by the inflammatory process. Thus, pyogenic meningitis may lead to widespread parenchymal destruction, particularly when not treated.

Multiplying bacteria, increasing numbers of WBC'S, cytokine-induced alterations in membrane transport, and increased vascular and membrane permeability accentuate the infectious process in pyogenic meningitis. These are reasons for the peculiar changes in CSF cell count, pH, lactate, protein, and glucose in patients with this disease. Exudates extend throughout the cerebrospinal fluid, particularly to the basal cisterns, resulting in:

- Cranial nerves getting affected (eg, cranial nerve VIII, with resultant deafness)
- Disruption of CSF pathways (causing obstructive hydrocephalus)
- Vasculitis and thrombophlebitis (causing cerebral ischemia)

Intracranial pressure and cerebral fluid

A major complication of meningitis is the development of raised intracranial pressure (ICP). The mechanism of this complication is complex and may involve a lot of proinflammatory substances as well as mechanical . Interstitial edema (leading to obstruction of CSF pathway, as in

hydrocephalus), cytotoxic edema (swelling of cellular elements of the CNS through the release of toxic substances from the organisms and neutrophils), and vasogenic edema (increased blood brain barrier leakiness) are all hand in hand. Without medical management, the cycle of decreasing cerebrospinal fluid, worsening cerebral edema, and increasing ICP proceeds unhampered. Ongoing endothelial injury may result in vasospasm and thrombosis may lead to stenosis of major and minor vessels. Systemic hypotension (septic shock) also may decrease cerebrospinal fluid , and the patient soon dies as a result of systemic complications or diffuse cerebral ischemic injury.[28][29]

Cerebral edema

Increased cerebrospinal fluid viscosity results from the inflow of plasma components into the subarachnoid space and decreased venous outflow resulting to interstitial edema. The accumulation of the products of inflammation other cellular activation leads to cytotoxic edema. The resulting brain edema (ie, vasogenic, cytotoxic, and interstitial) contributes to intracranial pressure and a subsequent hypoperfusion. Anaerobic metabolism happens, resulting in raised lactate levels and hypoglycorrhachia. Also, hypoglycorrhachia results from decreased glucose transport into the CSF compartment. If this process is not interrupted by appropriate treatment, reversible neuronal dysfunction or permanent neuronal damage results.[29]

Cytokines and secondary mediators in bacterial meningitis

Important knowledge of mechanism of meningitis include insight into the major roles of cytokines (eg, tumor necrosis factor alpha [TNF-α] and interleukin [IL]-1), chemokines (IL-8), and other proinflammatory molecules in causing pleocytosis and neuronal damage during of pyogenic meningitis. Raised cerebrospinal fluid levels of TNF-α, IL-1, IL-6, and IL-8 are characteristic findings in pyogenic meningitis. Cytokine levels, including those of IL-6, TNF-α, and IFN- gamma, have been found to be increased in patients with viral meningitis. The hypothesised events involving the inflammation mediators in pyogenic meningitis start with the exposure of endothelial cells, leukocytes, microglia, astrocytes, and meningeal macrophages to bacterial products released during multiplication and death; this exposure results in the production of cytokines and proinflammatory mediators. The cycle is initiated by the adhesion of the bacterial components like peptidoglycan and lipopolysaccharide to pattern-recognition receptors, such as the Toll-like receptors (TLRs).TNF-α and IL-1 are most prominent among the cytokines that mediate this inflammatory cascade. TNF-α is a glycoprotein derived from activated monocyte-macrophages, lymphocytes, astrocytes, and microglial cells.IL-1 is also produced by activated mononuclear phagocytes and results in the induction of fever during bacterial infections. Both IL-1 and TNF-α have been detected in cerebrospinal fluid of individuals with pyogenic meningitis. In trial models of meningitis, they appear early during the disease process and

have been detected within 30-45 minutes of intracisternal endotoxin inoculation.

Many secondary mediators, such as IL-6, IL-8, nitric oxide, prostaglandin E_2 (PGE_2), and platelet activation factor (PAF), are presumed to augment this inflammatory process, either synergistically or independently. IL-6 induces acute-phase reactants in response to bacterial infection. The chemokine IL-8 propagates neutrophil chemoattractant responses initiated by TNF-α and IL-1[28].Nitric oxide a free radical substance that can be cytotoxic when produced in excess amounts. PGE_2, a product of cyclooxygenase (COX), is thought to participate in the induction of increased blood-brain barrier permeability. PAF, with its elaborate biologic activities, is believed to catalyze the formation of thrombi and the activation of clotting factors within the blood vessels. However, the exact roles of all these secondary mediators in meningitis remain unclear.This finally results in vascular endothelial injury and raised blood-brain barrier permeability, leading to the entry of many blood components into the subarachnoid space. This results to vasogenic edema and raised cerebrospinal fluid protein levels. In response to the cytokines and chemotactic substances, neutrophils migrate from the blood and invade the damaged blood-brain barrier, resulting the profound neutrophilic pleocytosis peculiar to pyogenic meningitis[29].

Genetic predisposition to inflammatory response

The inflammatory response and the release of proinflammatory mediators are important to the migration of excess neutrophils to the subarachnoid space. The activated neutrophils release cytotoxic agents, including oxidative agents and metalloproteins that cause collateral damage to brain parenchyma.

Pattern recognition receptors, of which TLR A4 (TLRA4) , result increasing the myeloid differentiation 88 (MyD88)-dependent pathway and increased production of proinflammatory mediators[29].

Bacterial seeding

Bacterial seeding of the meninges usually occurs through blood. In patients without an documented foci of infection, local tissue and hematogenic spread by bacteria that have occupied the nasopharynx may be a common source. Most of the meningitis-causing bacteria are carried in the nasopharynx, often asymptomatically. Most meningeal pathogens are transmitted through the respiratory pathways, including Neisseria meningitidis(meningococcus) and S pneumoniae(pneumococcus).

Few respiratory viruses are thought to facilitate the entry of bacterial agents into the vascular compartment, by damaging mucosal defenses. Once the organism are in the blood, they must escape immune mechanisms like antibodies, complement-mediated bacterial killing, and neutrophil phagocytosis. Hematogenous seeding into far off sites, including the brain, occurs.[29] The specific mechanisms by which the infectious agents reaches the

subarachnoid space remain not known. Once inside the brain, the infectious organisms survive because host immune mechanisms (eg, immunoglobulins, neutrophils, and complement components) appear to be limited in this body compartment. The presence and multiplication of infectious agents remain unabated and incite the cascade of meningeal inflammation already.

Tuberculous meningitis

Like all other forms of tuberculosis, CNS infection begins with inhalation of infectious particles. On reaching the alveoli, airborne droplet nuclei, each containing small number of organisms, multiply either within the alveolar space or within the alveolar macrophages. For first 2 to 4 weeks, when there is virtually no inflammatory response, haematogenous dissemination of the organism is believed to occur in every case. Two to four weeks following infection, cell-mediated immunity to bacteria develops. A tubercle is formed, consisting of macrophages, lymphocytes and other cells surrounding a necrotic caseous centre. Fate of these tubercles and subsequent course of infection are a function of both the immunologic capacity of the host and other incompletely understood genetic factors. When there is robust immunity, minute caseous foci are formed only to be eliminated completely by the surrounding macrophages leaving no residua. Less efficient but still effective immune response results in larger caseous foci which, despite fibrous encapsulation,continue to shelter viable mycobacteria, which may cause reactivated disease if host's immune vigilance lessens. In the presence of profound immunodeficiency, primary

tubercle continues to grow, the caseous centre may liquefy, organisms proliferate and tubercle ultimately ruptures, discharging organisms into the surrounding tissue.

When these events occur within the brain and meninges and the so-called Rich's foci ruptures discharging the organism in the subarachnoid space, tuberculous meningitis results. The vascular choroid plexus are common sites for tubercle formation and also common site for rupture of a tubercle as also foci located on the surface of the brain. Those tubercles located deep in the brain or spinal cord parenchyma will enlarge to form tuberculoma or tuberculous abscesses.[14][15]

Meningeal Exudate and Meningitis

The primary pathological event is the formation of thick tuberculous exudates within the subarachnoid space. These exudates diffuse with particular prominence at the base of the brain irrespective of the location of the discharging focus. The exudates accumulate around the interpeduncular fossa,enveloping the optic nerves at the chiasma and extending over the pons and cerebellum, often into the sylvian fissures and rarely up along the cerebral hemispheres. Thus, other cranial nerves such as III, IV, VI, VII, and VIII may be involved in the subarachnoid space in varying degrees.In appearance, the exudate is gelatinous and frequently nodular.

Microscopically, it consists of polymorphonuclear leucocytes, red blood cells, macrophages and lymphocytes within a fibrin network. Typical tubercles,occasionally with large zones ofcaseation necrosis develop within the

exudate. In untreated cases, a large number of tubercle bacilli can be detected at the margins of caseous necrosis. With treatment fibroblasts and elements of connective tissues replace the exudates.[14]

Spinal TB meningitis

Spinal meningitis is a common asymptomatic accompaniment of cranial meningitis. In most cases, there is extension of basal exudates downwards. However, tuberculous spinal arachnoiditis can present first time as spinal cord disorder and may move upwards often asymptomatically into the cranial cavity.[17]

Vertebral involvement accounts for more than 50% of all skeletal tuberculosis. Thoracic and lumbar spines are most commonly involved due to paucity of movement. Multiplicity of vertebral body involvement (up to 50%) and posterior element lesions are frequently seen, which may lead to sudden paraplegia due to ‘concertina’ collapse of the involved vertebrae or vascular thrombosis. In about 70% of cases, paraplegia recovers completely if treated promptly[16]

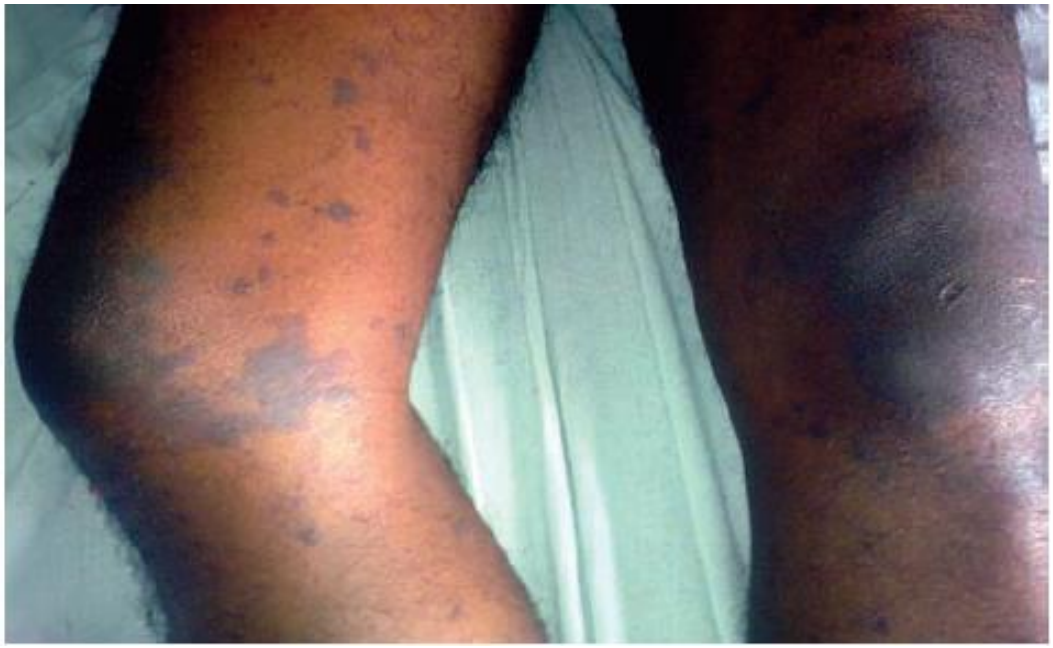
CLINICAL FEATURES

Meningitis can present as either an acute fulminant illness that progresses rapidly in a few hours or as a subacute infection that progressively worsens over several days. The classic clinical triad of meningitis is fever, headache, and nuchal rigidity, but the classic triad may not be present. A decreased level of consciousness occurs in >75% of patients and can vary from

lethargy to coma. Fever and either headache, stiff neck,or an altered level of consciousness will be present in nearly every patient with bacterial meningitis. Nausea, vomiting, and photophobia are also common complaints. Seizures occur as part of the initial presentation of bacterial meningitis or during the course of the illness in 20–40% of patients. Focal seizures are usually due to focal arterial ischemia or infarction, cortical venous thrombosis with hemorrhage, or focal edema. Generalized seizure activity and status epilepticus may be due to hyponatremia, cerebral anoxia, or, less commonly, the toxic effects of antimicrobial agents.[3][5][6]

Raised ICP is an expected complication of bacterial meningitis and the major cause of obtundation and coma in this disease. More than 90% of patients will have a CSF opening pressure >180 mmH2O, and 20% have opening pressures >400 mmH2O. Signs of increased ICP include a deteriorating or reduced level of consciousness, papilledema,dilated poorly reactive pupils, sixth nerve palsies, decerebrate posturing, and the Cushing reflex (bradycardia, hypertension, and irregular respirations).

One of the most important clues is the rash of meningococcemia, which begins as a diffuse erythematous maculopapular rash resembling a viral exanthem; however, the skin lesions of meningococcemia rapidly become petechial. Petechiae are found on the trunk and lower extremities, in the mucous membranes and conjunctiva, and occasionally on the palms and soles.[6]



Characteristic skin rash in a patient with meningococcaemia[6][7]

The clinical picture of TBM is quite variable, with substantial differences among patients of different ages. The clinical manifestations depend upon a variety of factors related both to the organism and the host like pre-existing malnutrition,coexistence of HIV infection, BCG vaccination, etc. Among children, majority of cases (75% to 85%) are below the age of 5 years. The onset of the disease may be acute, i.e. within 6 days, sub-acute or gradual, taking more than 3 weeks to develop. Among adults, the disease typically presents in a somewhat indolent fashion. The classical form of the disease evolves through a prodromal stage, a stage of meningeal irritation, leading to a stage of diffuse or focal cerebral involvement. Nausea, vomiting, anorexia, abdominal pain, constipation and behavioural changes are among most commonly reported symptoms. Headache is reported in less than 25% of children than in adults (50% to 75%) . Some degree of fever is usual, but it may be of low grade and absent in 10% to 15% of children and 25% to 30% of

adults. As the disease progresses, signs of meningeal irritation will develop, though it is less commonly seen in infants, instead fullness of fontanelle is seen. Seizures may present at any stage of the disease. Ten to twenty per cent of subjects may have seizures during the initial period, later it may be seen in up to 50% of cases. Psychobehavioural changes are frequently observed at onset in adults.[5] Signs and symptoms of raised intracranial pressure like enlargement of head in children and papilloedema may be seen early in the disease.

Focal neurological signs, which are common in the later part ofthe disease, most frequently consists of unilateral or, less commonly, bilateral cranial nerve palsies. Most frequently affected is the sixth cranial nerve followed by III, IV, VII and less commonly II, VIII, X, XI and XIIth.[17][18] Visual impairment may be there due to optochiasmatic arachnoiditis, tuberculoma compressing the optic nerve, secondary optic atrophy from papilloedema or ethambutol toxicity[18]. Fundoscopic examination may reveal papilloedema, disc pallor or choroid tubercles, which are seen in 10% of cases with TBM and it is a very useful clue to diagnosis. There may be isolated pupillary involvement without other features of III nerve palsy. Rarely, there may be internuclear ophthalmoplegia and horizontal gaze paresis due to intrinsic brainstem lesion. Other common findings include hemiparesis, monoparesis and aphasia due to ischaemic infarction in 10% to 45% of cases. Less frequently neurological signs include a variety of abnormal movements like chorea, hemiballismus, athetosis, myoclonus and cerebellar ataxia[15][16].

Persistent movement disorder may persist even after recovery from meningitis, especially among children.

In untreated cases, there may be deterioration of the consciousness from drowsiness to deep coma and brainstem dysfunction. Rarely intra-cranial bleeding may complicate TBM. Intraventricular haemorrhage may result from rupture of tuberculous mycotic aneurysm and parenchymal haemorrhage from moyamoya phenomenon of tuberculous arteritis. In order to assess severity of the disease and guide to prognosis, it is useful to stage patients clinically at the time of diagnosis,based on the British Medical Research Council classification.

Stage 1 (early disease)

Patient has meningeal signs only, consciousness is undisturbed and no focal neurological signs are present.

Stage 2 (medium severity)

Consciousness is disturbed but the patient is not comatose or delirious. Focal neurological signs and cranial nerves palsies are present. Raised intra-cranial pressure may occur secondary to hydrocephalus. In infants, fontanelle bulges and head enlarges,and in adults there is papilloedema.

Stage 3 (advanced disease)

Patient is deeply comatose with evidence of brainstem dysfunction, decerebrate or decorticate posturing, fixed dilated pupils, irregular pulse and respiration. Untreated patients progress the three stages and usually die.

TB Spinal meningitis

This may be due to involvement of spinal meninges, of spinal cord secondary to vasculopathy or tuberculoma, or of the bony elements of the spine (caries) with secondary involvement of the cord (Pott's paraplegia). Tuberculous spinal meningitis may be due to secondary spread of cranial meningitis or from spinal caries, or may be primary spinal meningitis presenting with single or multiple level ascending or transverse radiculomyelopathy. Symptoms include fever, spinal pain, radicular pain, paraesthesia, combined upper and lower motor features in lower limbs and bladder disturbances. Chronic spinal arachnoiditis may be indistinguishable from spinal cord compression.[16][17]

Vertebral involvement accounts for more than 50% of all skeletal tuberculosis. Thoracic and lumbar spines are most commonly involved due to paucity of movement. Multiplicity of vertebral body involvement (up to 50%) and posterior element lesions are frequently seen, which may lead to sudden paraplegia due to 'concertina' collapse of the involved vertebrae or vascular thrombosis. In about 70% of cases, paraplegia recovers completely if treated promptly

Viral meningitis

In viral meningitis, immunocompetent adult patients usually present with headache, fever, and signs of meningeal irritation coupled with an inflammatory CSF profile . Headache is almost invariably present and often characterized as frontal or retroorbital and frequently associated with photophobia and pain on moving the eyes. Nuchal rigidity is present in most cases but may be mild and present only near the limit of neck anteflexion. Constitutional signs can include malaise, myalgia, anorexia, nausea and vomiting, abdominal pain, and/or diarrhea. Patients often have mild lethargy or drowsiness; however, profound alterations in consciousness, such as stupor, coma, or marked confusion, do not occur in viral meningitis and suggest the presence of encephalitis or other alternative diagnoses. Similarly, seizures or focal neurologic signs or symptoms or neuroimaging abnormalities indicative of brain parenchymal involvement are not typical of viral meningitis and suggest the presence of encephalitis or another CNS infectious or inflammatory process[20].

INVESTIGATIONS

When bacterial meningitis is suspected, blood cultures should be immediately obtained and empirical antimicrobial and adjunctive dexamethasone therapy initiated without delay . The diagnosis of bacterial meningitis is made by examination of the CSF. The need to obtain neuroimaging studies (CT or MRI) prior to LP requires clinical judgment. In an

immunocompetent patient with no known history of recent head trauma, a normal level of consciousness, and no evidence of papilledema or focal neurologic deficits, it is considered safe to perform LP without prior neuroimaging studies. If LP is delayed in order to obtain neuroimaging studies, empirical antibiotic therapy should be initiated after blood cultures are obtained. Antibiotic therapy initiated a few hours prior to LP will not significantly alter the CSF WBC count or glucose concentration, nor is it likely to prevent visualization of organisms by Gram's stain or detection of bacterial nucleic acid by polymerase chain reaction (PCR) assay.

The classic CSF abnormalities in bacterial meningitis are (1) polymorphonuclear (PMN) leukocytosis (>100 cells/μL in 90%), (2) decreased glucose concentration (<40 mg/dL) and/ or CSF/serum glucose ratio of <0.4 in ~60%), (3) increased protein concentration (>45 mg/dL in 90%), and (4) increased opening pressure (>180 mmH2O in 90%). CSF bacterial cultures are positive in >80% of patients, and CSF Gram's stain demonstrates organisms in >60%. CSF glucose concentrations <40 mg/dL are abnormal,and a CSF glucose concentration of zero can be seen in bacterial meningitis. Use of the CSF/serum glucose ratio corrects for hyperglycemia that may mask a relative decrease in the CSF glucose concentration. The CSF glucose concentration is low when the CSF/serum glucose ratio is <0.6. A CSF/serum glucose ratio <0.4 is highly suggestive of bacterial meningitis but may also be seen in other conditions, including fungal, tuberculous, and carcinomatous meningitis.[9]

A 16S rRNA conserved sequence broad-based bacterial PCR can detect small numbers of viable and nonviable organisms in CSF and is expected to be useful for making a diagnosis of bacterial meningitis in patients who have been pretreated with oral or parenteral antibiotics and in whom Gram's stain and CSF culture are negative. When the broad-range PCR is positive, a PCR that uses specific bacterial primers to detect the nucleic acid of *S. pneumoniae, N. meningitidis,Escherichia coli, L. monocytogenes, H. influenzae*, and *S. agalactiae* can be obtained based on the clinical suspicion of the meningeal pathogen[5][7]. The latex agglutination (LA) test for the detection of bacterial antigens of *S. pneumoniae, N. meningitidis, H. influenzae* type b, group B *Streptococcus*, and *E. coli* K1 strains in the CSF has been useful for making a diagnosis of bacterial meningitis but is being replaced by the CSF bacterial PCR assay. The Limulus amebocyte lysate assay is a rapid diagnostic test for the detection of gram-negative endotoxin in CSF and thus for making a diagnosis of gram-negative bacterial meningitis. The test has a specificity of 85–100% and a sensitivity approaching 100%.[6] Thus, a positive Limulus amebocyte lysate assay occurs in virtually all patients with gram-negative bacterial meningitis, but false positives may occur. Almost all patients with bacterial meningitis will have neuroimaging studies performed during the course of their illness. MRI is preferred over CT because of its superiority in demonstrating areas of cerebral edema and ischemia. In patients with bacterial meningitis, diffuse meningeal enhancement is often seen after the administration of gadolinium. Meningeal enhancement is not diagnostic of

meningitis but occurs in any CNS disease associated with increased blood-brain barrier permeability. Petechial skin lesions, if present, should be biopsied. The rash of meningococcemia results from the dermal seeding of organisms with vascular endothelial damage, and biopsy may reveal the organism on Gram's stain.

In Tuberculous meningitis typically the cerebrospinal fluid is clear or slightly opalescent with raised opening pressure. A cobweb may develop when the CSF is allowed to stand for short time, though it is not a specific finding. A moderate lymphocytic pleocytosis up to 500 cells/mm3 is characteristic of TBM. However, counts of more than 1000/mm3 and predominantly polymorphonuclear leucocytes may be found in the early part of the illness.[18] There is moderate elevation of CSF protein (100 to 500 mg/dL) and depression of glucose (<40mg/dL). Hypoglycorrhachia has been correlated with more advanced stage of clinical disease and a rise in CSF glucose after therapy indicates better prognosis. In tuberculoma, the CSF may be normal or may show a lymphocytic pleocytosis with increased protein levels. In spinal meningitis, there may be spinal block with CSF xanthochromia, very high protein levels (>1 gm/dL) and lymphocytic pleocytosis.[18]Identification of tuberculous bacilli in the CSF confirms diagnosis though it is difficult. A variety of techniques have been proposed.Detection rate is 15% to 20%. It may be increased by centrifuging large volume of CSF and preparing a thick smear of the deposit, and examination of cobweb.

Traditional culture in Lowenstein-Jensen media is a time consuming procedure. Newer radiometric (BACTEC 460 TB) and non-radiometric, semi-automated and fully automated liquid systems have decreased the time to a positive result to 1 to 3 weeks with good rates of positivity (80% to 95%).[18]

PCR technique held promise in the confirmation of diagnosis of TBM. It has a high specificity (98%) but low sensitivity (56%).Three regions of the *M. tuberculosis* genome are targeted: IS 6110 sequences, MBP 64 gene codes and 541 bp regions.

Real-time PCR combines rapid cycle DNA amplification with fluorimetry. In cultured samples it has 100% specificity and can detect as few as 10 organisms. Nested real-time PCR may further improve the sensitivity. Indirect tests that are helpful in the diagnosis of TBM include adenosine deaminase level in CSF, radiolabelled bromide partition test, CSF tuberculostearic acid level, and mycobacterial antigen and antibody detection by ELISA .[18]

Contrast-enhanced CT scan and MRI are invaluable in the diagnosis of neurotuberculosis but none of the radiological changes are pathognomonic. MRI is better than CT scan in detecting diffuse and focal meningeal granulomatous lesions, small tuberculoma and focal infarcts.[19]

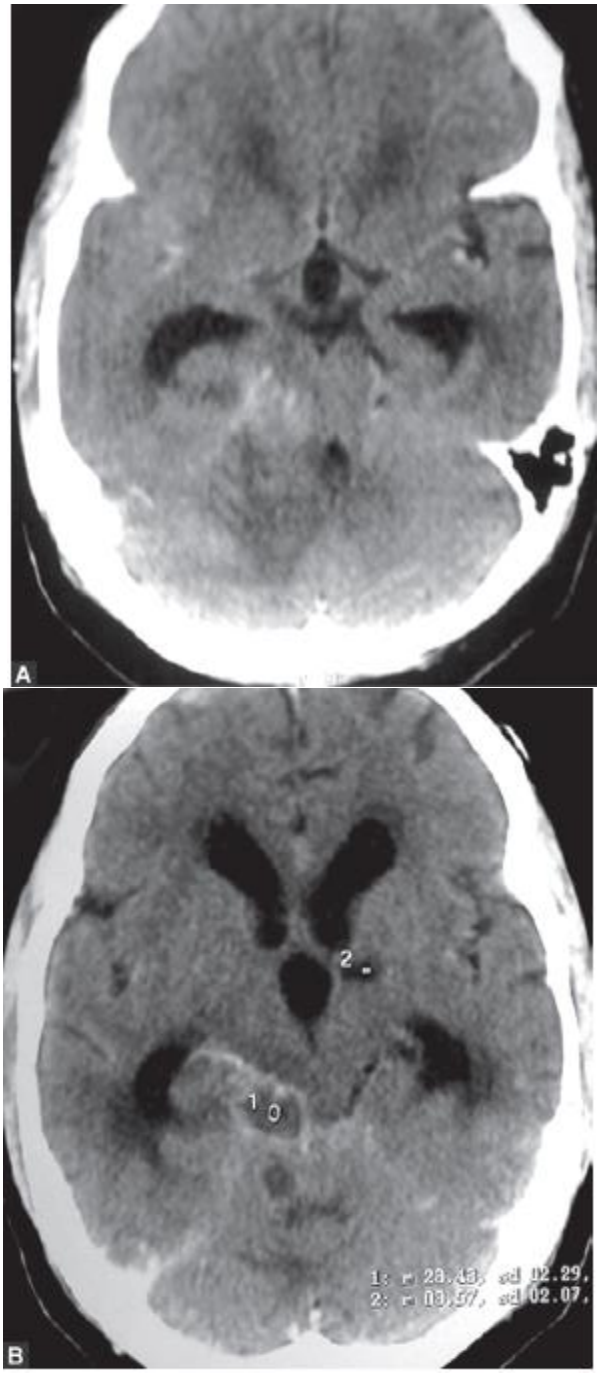
Meningeal enhancement is frequently seen, most commonly in the basal subarachnoid cisterns, Sylvian fissures and around brainstem. There may be associated hydrocephalus or infarction . Hydrocephalus is the single-most common abnormality (50% to 80%), which can be of either communicating or

obstructive type. The radiological features of tuberculoma on CT vary according to its stage. Mature lesions appear as a well-defined round or oval ring enhancing mass with occasionally a target sign. The immature tuberculoma are iso/hypodense on plain CT and show ring or nodular contrast enhancement. In many cases, solitary tuberculoma may be indistinguishable from abscess, tumour and cysticercus granuloma . On MRI, solid caseating granulomas are isointense on T1 and iso/hypointense on T2-weighted images. Occasionally, there may a central hyperintense area with hypointense rim on T2-weighted images. Non-caseating granulomas are usually hypointense in T1 and hyperintense in T2-weighted images, with homogeneous contrast enhancement. Conglomerated lesions are often seen in gadolinium-enhanced MRI. Magnetic resonant spectroscopy (MRS) can provide biochemical information from a tissue. MRS of a tuberculoma usually shows presence of lipid/lactate peak with increased choline:creatine ratio, but usually less than two.

Magnetisation transfer imaging with contrast is a more sensitive imaging modality in tissue characterisation and helpful in differentiating tuberculoma from cysticercus granuloma.[17][19]

Non-invasive MRI has replaced conventional myelographic techniques in detecting spinal diseases. Abnormalities on MRI have included obliteration of the subarachnoid space, clumping of nerve roots, oedema of cord, central and ecentric cavitation of the cord, and extensive signal abnormalities within

the substance of the cord. Intramedullary tuberculoma are hypointense in both T1- and T2-weighted images with marked gadolinium enhancement.



Cect brain showing basal enhancing exudates with obstructive hydrocephalus

In the diagnosis of viral meningitis CSF profile shows pleocytosis, a normal or slightly elevated protein concentration (20–80 mg/dL), a normal glucose concentration, and a normal or mildly elevated opening pressure (100–350 mmH2O). Organisms are *not* seen on Gram's stain of CSF. The total CSF cell count in viral meningitis is typically 25–500/μL, although cell counts of several thousand/μL are occasionally seen, especially with infections due to lymphocytic choriomeningitis virus (LCMV) and mumps virus[21]. Lymphocytes are typically the predominant cell. Rarely, PMNs may predominate in the first 48 h of illness, especially with infections due to echovirus 9, West Nile virus, eastern equine encephalitis (EEE) virus, or mumps. A PMN pleocytosis occurs in 45% of patients with West Nile virus (WNV) meningitis and can persist for a week or longer before shifting to a lymphocytic pleocytosis. PMN pleocytosis with low glucose may also be a feature of cytomegalovirus (CMV) infections in immunocompromised hosts. Despite these exceptions, the presence of a CSF PMN pleocytosis in a patient with suspected viral meningitis in whom a specific diagnosis has not been established should prompt consideration of alternative diagnoses, including bacterial meningitis or parameningeal infections. The CSF glucose concentration is typically normal in viral infections, although it may be decreased in 10–30% of cases due to mumps or LCMV. Rare instances of decreased CSF glucose concentration occur in cases of meningitis due to echoviruses and other enteroviruses, HSV-2, and VZV. As a rule, a lymphocytic pleocytosis with a low glucose concentration should suggest

fungal or tuberculous meningitis, *Listeria* meningoencephalitis, or noninfectious disorders (e.g., sarcoid, neoplastic meningitis).

A number of tests measuring levels of various CSF proteins,enzymes, and mediators—including C-reactive protein, lactic acid, lactate dehydrogenase, neopterin, quinolinate, IL-1β, IL-6, soluble IL-2 receptor, β2-microglobulin, and TNF—have been proposed as potential discriminators between viral and bacterial meningitis or as markers of specific types of viral infection (e.g., infection with HIV),but they remain of uncertain sensitivity and specificity and are not widely used for diagnostic purposes.

Amplification of viral-specific DNA or RNA from CSF using PCR amplification has become the single most important method for diagnosing CNS viral infections. In both enteroviral and HSV infections of the CNS, CSF PCR has become the diagnostic procedure of choice and is substantially more sensitive than viral cultures. HSV CSF PCR is also an important diagnostic test in patients with recurrent episodes of "aseptic" meningitis, many of whom have amplifiable HSV DNA in CSF despite negative viral cultures. CSF PCR is also used routinely to diagnose CNS viral infections caused by CMV, Epstein-Barr virus (EBV), VZV, and human herpesvirus 6 (HHV-6).[21][22] CSF PCR tests are available for WNV but are not as sensitive as detection of WNV specific CSF IgM. PCR is also useful in the diagnosis of CNS infection caused by *Mycoplasma pneumoniae,* which can mimic viral meningitis and encephalitis. PCR of throat washings may assist in diagnosis of enteroviral and mycoplasmal

CNS infections. PCR of stool specimens may also assist in diagnosis of enteroviral infections .[21][22]

The sensitivity of CSF cultures for the diagnosis of viral meningitis and encephalitis, in contrast to its utility in bacterial infections, is generally poor. In addition to CSF, specific viruses may also be isolated from throat swabs, stool, blood, and urine. Enteroviruses and adenoviruses may be found in feces; arboviruses, some enteroviruses, and LCMV in blood; mumps and CMV in urine; and enteroviruses, mumps, and adenoviruses in throat washings. During enteroviral infections, viral shedding in stool may persist for several weeks. The presence of enterovirus in stool is not diagnostic and may result from residual shedding from a previous enteroviral infection; it also occurs in some asymptomatic individuals during enteroviral epidemics.[21]

For many arboviruses including WNV, serologic studies remain important diagnostic tools. Serum antibody determination is less useful for viruses with high seroprevalence rates in the general population such as HSV, VZV, CMV, and EBV. For viruses with low seroprevalence rates, diagnosis of acute viral infection can be made by documenting seroconversion between acute-phase and convalescent sera (typically obtained after 2–4 weeks) or by demonstrating the presence of virus-specific IgM antibodies. For viruses with high seroprevalence such as VZV and HSV, demonstration of synthesis of virus-specific antibodies in CSF, as shown by an increased IgG index or the presence of CSF IgM antibodies, may be useful and can provide presumptive evidence of CNS infection. Although serum and CSF IgM antibodies generally

persist for only a few months after acute infection, there are exceptions to this rule. For example, WNV serum IgM has been shown to persist in some patients for >1 year following acute infection. Unfortunately, the delay between onset of infection and the host's generation of a virus-specific antibody response often means that serologic data are useful mainly for the retrospective establishment of a specific diagnosis, rather than in aiding acute diagnosis or management. In the case of EBV, demonstration of antibody responses consistent with recent/acute infection (e.g., IgM viral capsid antibody, antibody against early antigen, absence of antibody against EBV associated nuclear antigen) may assist in diagnosis. CSF oligoclonal gamma globulin bands occur in association with a number of viral infections.[22] The associated antibodies are often directed against viral proteins. Oligoclonal bands also occur commonly in certain noninfectious neurologic diseases (e.g., multiple sclerosis) and may befound in nonviral infections (e.g., neurosyphilis, Lyme neuroborreliosis).

CSF in cryptococcal meningitis shows a lymphocytic pleocytosis with exceptionally high protein levels. CSF may, however, be normal in exclusively parenchymal disease. CSF India ink preparation shows the polysaccharide capsule of the cryptococcus as a clear 'halo' surrounding the organism. CSF staining and culture may yield positive results if adequate samples are obtained. Cryptococcal latex antigen detection test relies on agglutination tested at differing titres of CSF and has a sensitivity of 90%. Imaging may reveal

meningeal enhancement, abscesses, cryptococcomas, gelatinous ,pseudocysts and hydrocephalus

CSF CHLORIDE :

CSF chloride levels were done in the past about 60 years back and were consistently reduced in cases of TB meningitis.In their basic text on the cerebrospinal fluid,merritt and fremont-smith frequently referred to the work of mestrezat, pointing out that he was the first to emphasize the diagnostic value of the spinal fluid chloride content. but whereas mestrezat implied that the reduction in chloride content of the cerebrospinal fluid in pyogenic and tuberculous meningitis was part of the disease process, merritt regarded the fall in chloride as a reflection of the decline in serum chloride. mestrezat said that very low values were pathognomonic of tuberculous meningitis,but merritt and fremont-smith noted that their results showed this not to be true consistently.

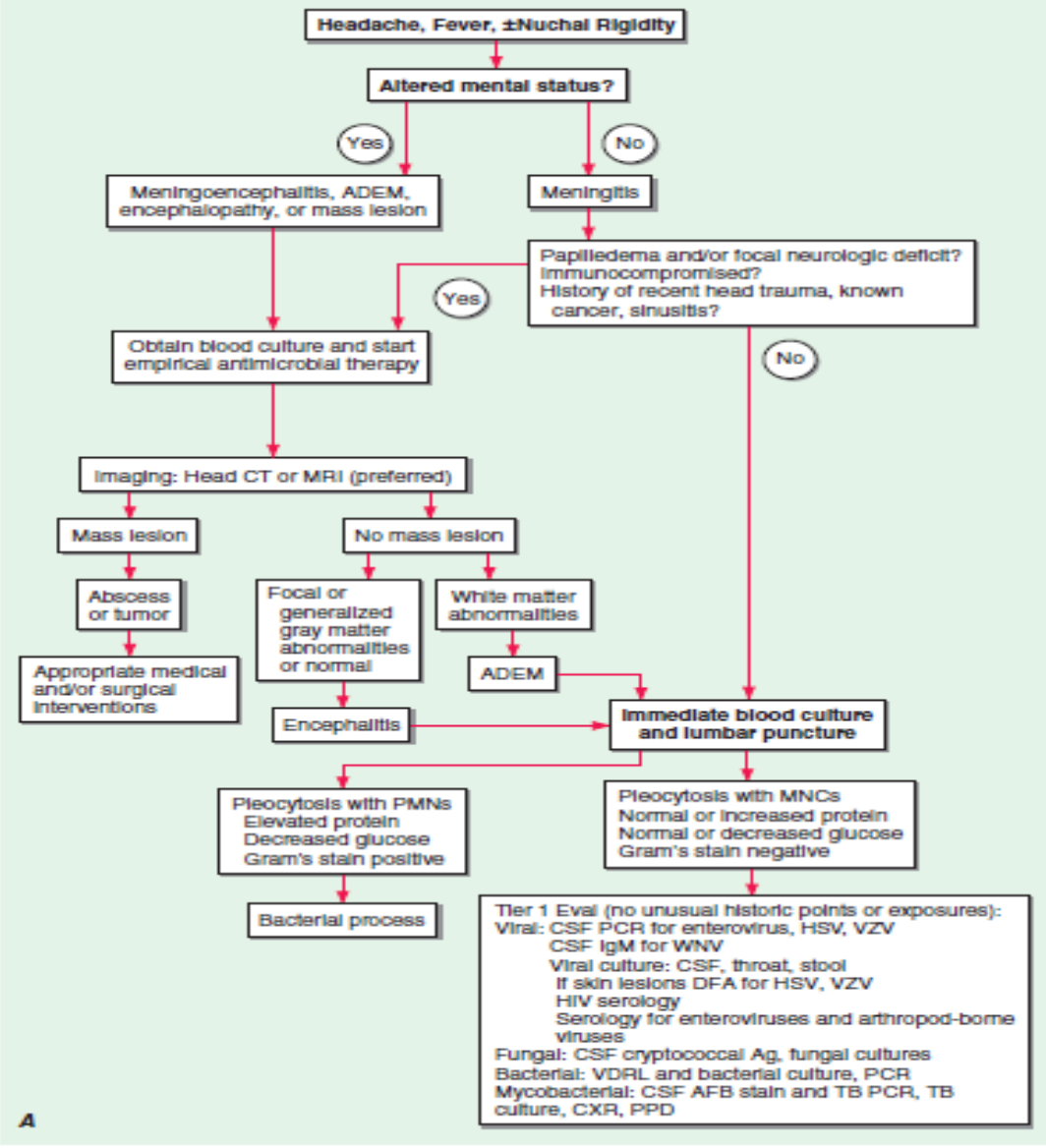
CSF chloride levels normal range was 116 – 127 meq/dl. This was found to be reduced in TB meningitis ranging from low to low normal. In bacterial meningitis it was low normal to the maximum, only a few observations were low. CSF chloride levels and it's relationship with serum chloride remains a point of contention. The mechanism of its reduction whether it can be solely attributed to the alterations in serum chloride values is unanswered. Chloride is measured ion exchange through selective electrodes.

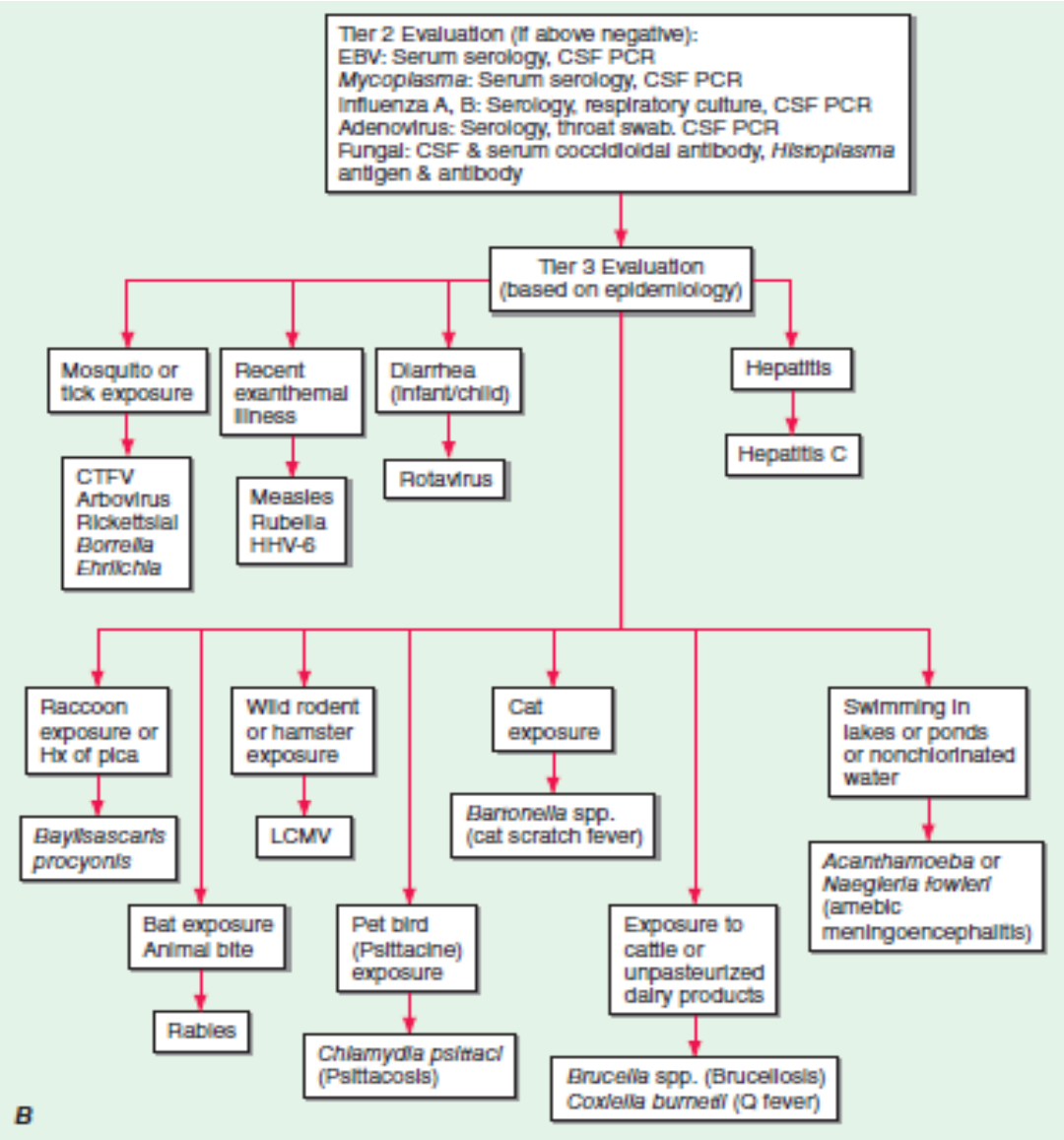
All patients with suspected viral meningitis should have a complete blood count and differential, liver and renal function tests, erythrocyte sedimentation rate (ESR), and C-reactive protein, electrolytes, glucose, creatine

kinase, aldolase, amylase, and lipase. Neuroimaging studies (MRI preferable to CT) are not absolutely necessary in patients with uncomplicated viral meningitis but should be performed in patients with altered consciousness, seizures, focal neurologic signs or symptoms, atypical CSF profiles, or underlying immunocompromising treatments or conditions.

MANAGEMENT

Management of patient suspected with CNS infection





Bacterial meningitis is a medical emergency. The goal is to begin antibiotic therapy within 60 min of a patient's arrival in the emergency room. Empirical antimicrobial therapy is initiated in patients with suspected bacterial meningitis before the results of CSF Gram's stain and culture are known. *S. pneumoniae* and *N. meningitidis* are the most common etiologic organisms of community-acquired bacterial meningitis.

Due to the emergence of penicillin- and cephalosporin-resistant *S. pneumoniae*, empirical therapy of community-acquired suspected bacterial meningitis in children and adults should include a combination of dexamethasone, a third- or fourth-generation cephalosporin(e.g., ceftriaxone, cefotaxime, or cefepime), and vancomycin, plus acyclovir, as HSV encephalitis is the leading disease in the differential diagnosis, and doxycycline during tick season to treat tick-borne bacterial infections. Ceftriaxone or cefotaxime provides good coverage for susceptible *S. pneumoniae*, group B streptococci, and *H.influenzae* and adequate coverage for *N. meningitidis*.[3][4][5] Cefepime is a broad-spectrum fourth-generation cephalosporin with in vitro activity similar to that of cefotaxime or ceftriaxone against *S. pneumonia* and *N. meningitidis* and greater activity against *Enterobacter* species and *Pseudomonas aeruginosa*. In clinical trials, cefepime has been demonstrated to be equivalent to cefotaxime in the treatment of penicillin-sensitive pneumococcal and meningococcal meningitis, and it has been used successfully in some patients with meningitis due to *Enterobacter* species and *P. aeruginosa*. Ampicillin should be added to the empirical regimen for coverage of *L. monocytogenes* in individuals <3 months of age, those >55, or those with suspected impaired cell-mediated immunity because of chronic illness, organ transplantation, pregnancy, malignancy, or immunosuppressive therapy. Metronidazole is added to the empirical regimen to cover gram-negative anaerobes in patients with otitis, sinusitis, or mastoiditis.[12][13]

In hospital-acquired meningitis, and particularly meningitis following neurosurgical procedures, staphylococci and gram-negative organisms including *P. aeruginosa* are the most common etiologic organisms. In these patients, empirical therapy should include a combination of vancomycin and ceftazidime, cefepime, or meropenem. Ceftazidime, cefepime, or meropenem should be substituted for ceftriaxone or cefotaxime in neurosurgical patients and in neutropenic patients, because ceftriaxone and cefotaxime do not provide adequate activity against CNS infection with *P. aeruginosa*. Meropenem is a carbapenem antibiotic that is highly active in vitro against *L.monocytogenes*, has been demonstrated to be effective in cases of meningitis caused by *P. aeruginosa*, and shows good activity against penicillin-resistant pneumococci. In experimental pneumococcal meningitis, meropenem was comparable to ceftriaxone and inferior to vancomycin in sterilizing CSF cultures. The number of patients with bacterial meningitis enrolled in clinical trials of meropenem has not been sufficient to definitively assess the efficacy of this antibiotic.

In cases of *N. meningitides* infection, penicillin G remains the antibiotic of choice for meningococcal meningitis caused by susceptible strains. Isolates of *N. meningitides* with moderate resistance to penicillin have been identified and are increasing in incidence worldwide. CSF isolates of *N. meningitides* should be tested for penicillin and ampicillin susceptibility, and if resistance is found, cefotaxime or ceftriaxone should be substituted for penicillin. A 7-day course of intravenous antibiotic therapy is adequate for uncomplicated meningococcal meningitis.[6] The index case and all close contacts should

receive chemoprophylaxis with a 2-day regimen of rifampin (600 mg every 12 h for 2 days in adults and 10 mg/kg every 12 h for 2 days in children >1 year). Rifampin is not recommended in pregnant women. Alternatively, adults can be treated with one dose of azithromycin (500 mg) or one intramuscular dose of ceftriaxone (250 mg). Close contacts are defined as those individuals who have had contact with oropharyngeal secretions, either through kissing or by sharing toys, beverages, or cigarettes[11].

Antimicrobial therapy of pneumococcal meningitis is initiated with a cephalosporin (ceftriaxone, cefotaxime, or cefepime) and vancomycin. All CSF isolates of *S. pneumoniae* should be tested for sensitivity to penicillin and the cephalosporins. Once the results of antimicrobial susceptibility tests are known, therapy can be modified accordingly . For *S. pneumoniae* meningitis, an isolate of *S. pneumoniae* is considered to be susceptible to penicillin with a minimal inhibitory concentration (MIC) <0.06 μg/mL and to be resistant when the MIC is >0.12 μg/mL. Isolates of *S. pneumoniae* that have cephalosporin MICs ≤0.5 μg/mL are considered sensitive to the cephalosporins (cefotaxime, ceftriaxone, cefepime). Those with MICs of 1 μg/mL are considered to have intermediate resistance, and those with MICs ≥2 μg/mL are considered resistant. For meningitis due to pneumococci, with cefotaxime or ceftriaxone MICs ≤0.5 μg/mL, treatment with cefotaxime or ceftriaxone is usually adequate. For MIC >1 μg/mL, vancomycin is the antibiotic of choice. Rifampin can be added to vancomycin for its synergistic effect but is inadequate as monotherapy because resistance develops rapidly when it is used alone. A 2-week course of

intravenous antimicrobial therapy is recommended for pneumococcal meningitis[5][7].

Patients with *S. pneumoniae* meningitis should have a repeat LP performed 24–36 h after the initiation of antimicrobial therapy to document sterilization of the CSF. Failure to sterilize the CSF after 24–36 h of antibiotic therapy should be considered presumptive evidence of antibiotic resistance. Patients with penicillin- and cephalosporin- resistant strains of *S. pneumoniae* who do not respond to intravenous vancomycin alone may benefit from the addition of intraventricular vancomycin. The intraventricular route of administration is preferred over the intrathecal route because adequate concentrations of vancomycin in the cerebral ventricles are not always achieved with intrathecal administration.

Meningitis due to *L. monocytogenes* is treated with ampicillin for at least 3 weeks . Gentamicin is added in critically ill patients (2 mg/kg loading dose, then 7.5 mg/kg per day given every 8 h and adjusted for serum levels and renal function).The combination of trimethoprim (10–20 mg/kg per day) and sulfamethoxazole (50–100 mg/kg per day) given every 6 h may provide an alternative in penicillin-allergic patients.[7][9][11]

Meningitis due to susceptible strains of *S. aureus* or coagulase-negative staphylococci is treated with nafcillin. Vancomycin is the drug of choice for methicillin resistant staphylococci and for patients allergic to penicillin. In these patients, the CSF should be monitored during therapy. If the CSF is not

sterilized after 48 h of intravenous vancomycin therapy, then either intraventricular or intrathecal vancomycin, 20 mg once daily, can be added. Third-generation cephalosporins—cefotaxime, ceftriaxone, and ceftazidime—are equally efficacious for the treatment of gram-negative bacillary meningitis, with the exception of meningitis due to *P. aeruginosa*, which should be treated with ceftazidime, cefepime, or meropenem . A 3-week course of intravenous antibiotic therapy is recommended for meningitis due to gram-negative bacilli.

ADJUNCTIVE THERAPY

The release of bacterial cell-wall components by bactericidal antibiotics leads to the production of the inflammatory cytokines IL-1βand TNF-α in the subarachnoid space. Dexamethasone exerts its beneficial effect by inhibiting the synthesis of IL-1β and TNF-α at the level of mRNA, decreasing CSF outflow resistance, and stabilizing the blood-brain barrier. The rationale for giving dexamethasone 20 min before antibiotic therapy is that dexamethasone inhibits the production of TNF-α by macrophages and microglia only if it is administered before these cells are activated by endotoxin[22].Dexamethasone does not alter TNF-α production once it has been induced. The results of clinical trials of dexamethasone therapy in meningitis due to *H. influenzae, S. pneumoniae,* and *N. meningitides* have demonstrated its efficacy in decreasing meningeal inflammation and neurologic sequelae such as the incidence of sensorineural hearing loss. The benefits were most striking in patients with pneumococcal meningitis. Dexamethasone (10 mg intravenously) was

administered 15–20 min before the first dose of an antimicrobial agent, and the same dose was repeated every 6 h for 4 days. These results were confirmed in a second trial of dexamethasone in adults with pneumococcal meningitis. Therapy with dexamethasone should ideally be started 20 min before, or not later than concurrent with, the first dose of antibiotics. It is unlikely to be of significant benefit if started >6 h after antimicrobial therapy has been initiated. Dexamethasone may decrease the penetration of vancomycin into CSF, and it delays the sterilization of CSF in experimental models of *S. pneumoniae* meningitis[6][9].

Available antituberculosis drugs are divided on the basis of efficacy and toxicity into first-line [isoniazid (H), rifampicin (R),ethambutol (E), pyrazinamide (Z) and streptomycin (S)] and second-line (para-aminosalicylic acid, ethanolamine, cycloserine, kanamycin, capreomycin and amikacin) agents. Newer second-line drugs like fluoroquinolones (ciprofloxacin or ofloxacin) and macrolides (azithromycin and clarythromycin) are used in multidrug resistant (MDR) cases or when first-line drugs are not tolerated. Isoniazid and rifampicin are bactericidal and other first-line drugs are bacteriostatic. Isoniazid, pyrazinamide and ethambutol have good CSF penetration and others have poor CSF concentration [15][17].

World Health Organization (WHO) recommends use of 4 drugs (HRZE) for 2 months followed by 2 drugs (HR) for 6 to 7 months for the treatment of TBM. The same drug regimen is prescribed for tuberculoma and spinal disease. In spite of WHO recommendations, universal consensus regarding duration of

treatment has not developed. The current UK guidelines recommend 12 months of anti-tuberculosis treatment (ATT) in uncomplicated cases of TBM (including tuberculoma without meningitis) extending to 18 months if pyrazinamide is omitted.[19] The American Thoracic Society's recent recommendation is a course of 2 months of HRZ, followed by 4 months of HR for adults and 10 months HR for children. In a recent study from South India by Venugopal and co-workers, it has been seen that directly observed treatment, short-course (DOTS) intermittent regimen is an effective treatment for neurotuberculosis. A paradoxical worsening of clinical and laboratory parameters has been noted by many clinicians immediately after starting ATT, including enlargement of tuberculoma. Addition of corticosteroids may lessen this paradoxical response.

Multidrug-Resistant Neurotuberculosis

Drug resistance may be primary or secondary. Exact incidence of MDR of neurotuberculosis is not known due to difficulty in isolating mycobacteria from the CSF. In other forms of tuberculosis, prevalence of resistance to any drug is 13% to 25% and of MDR is about 13%. Most case reports of MDR TBM from India are among immunocompromised patients due to HIV infection. There is no standard protocol for the treatment. Every attempt should be made to isolate the organism and test for sensitivity. At least two agents to which the organism is sensitive are to be continued for a full 18 to 20 months[19]. Despite a substantial literature accumulated over the past 40years,

the place of corticosteroids in the treatment of TBM remains unclear. It is most beneficial when complications appear. These include raised intra-cranial pressure, cerebral oedema, stupor, focal neurological signs, spinal block, hydrocephalus and basal opto-chiasmatic arachnoiditis

Treatment of almost all cases of viral meningitis is primarily symptomatic and includes use of analgesics, antipyretics, and antiemetics. Fluid and electrolyte status should be monitored. Patients with suspected bacterial meningitis should receive appropriate empirical therapy pending culture results . Hospitalization may not be required in immunocompetent patients with presumed viral meningitis and no focal signs or symptoms, no significant alteration in consciousness, and a classic CSF profile (lymphocytic pleocytosis, normal glucose, negative Gram's stain) if adequate provision for monitoring at home and medical follow-up can be ensured.

Immunocompromised patients, patients with significant alteration in consciousness, seizures, or the presence of focal signs and symptoms suggesting the possibility of encephalitis or parenchymal brain involvement; and patients who have an atypical CSF profile should be hospitalized. Oral or intravenous acyclovir may be of benefit in patients with meningitis caused by HSV-1 or -2 and in cases of severe EBV or VZV infection. Data concerning treatment of HSV, EBV, and VZV meningitis are extremely limited. Seriously ill patients should probably receive intravenous acyclovir (15–30 mg/kg per day in three divided doses), which can be followed by an oral drug such as acyclovir (800 mg five times daily), famciclovir (500 mg tid), or valacyclovir

(1000 mg tid) for a total course of 7–14 days. Patients who are less ill can be treated with oral drugs alone. Patients with HIV meningitis should receive highly active antiretroviral therapy. There is no specific therapy of proven benefit for patients with arboviral encephalitis, including that caused by WNV. Patients with viral meningitis who are known to have deficient humoral immunity (e.g., X-linked agammaglobulinemia) and who are not already receiving either intramuscular gamma globulin or intravenous immunoglobulin (IVIg) should be treated with these agents. Intraventricular administration of immunoglobulin through an Ommaya reservoir has been tried in some patients with chronic enteroviral meningitis who have not responded to intramuscular or intravenous immunoglobulin. Vaccination is an effective method of preventing the development of meningitis and other neurologic complications associated with poliovirus, mumps, measles, rubella, and varicella infection. A live attenuated VZV vaccine (Varivax) is available in the United States. Clinical studies indicate an effectiveness rate of 70–90% for this vaccine, but a booster may be required after ~10 years to maintain immunity. A related vaccine (Zostavax) is recommended for prevention of herpes zoster (shingles) in adults over the age of 60. An inactivated varicella vaccine is available for transplant recipients and others for whom live viral vaccines are contraindicated.

Treatment of cryptococcal meningitis involves combination chemotherapy with conventional amphotericin B and flucytosine for 2 to 4 weeks and then

switching to fluconazole for 8 weeks. Lifelong flucanazole therapy is indicated in patients with AIDS.

Amphotericin B is an effective agent for most CNS mycoses. Amphotericin B is a polyene antibiotic that binds to ergosterols in the fungal cell wall and disrupts the cell wall integrity leading to increased permeabilty, K + leakage and cell death. Depending on its concentration, it can be fungistatic or fungicidal. It is used in a dose of 0.3 to 1.5 mg/kg body weight per day intravenously daily as a 1 to 4 hour infusion. It has poor penetration of bloodbrain barrier, reducing its ability to achieve effective fungicidal levels in the brain. Side effects include renal toxicity, hypokalaemia, hypomagnesaemia, normocytic normochromic anaemia and 'flu-like' allergic reaction during or after intravenous infusion. Lipid-based amphotericin B compounds although costlier have lesser adverse effects. Most CNS fungal infections require long treatment periods of 4 to 10 weeks often guided by CSF culture reports.

Oral flucytosine, a cytosine analogue, commonly used as an adjunct to amphotericin B in case of invasive infections with *Cryptococcus, Candida* and *Aspergillus,* is usually well tolerated but may rarely cause bone marrow suppression, especially with concomitant use of amphotericin B.

Azoles (ketoconazole, fluconazole, itraconazole, voriconazole) although broad-spectrum are weak antifungals. They have good bioavailability on oral administration and are usually well tolerated.

MATERIALS AND METHODS

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STUDY CENTRE:

Madras Medical College and Rajiv Gandhi Government General Hospital, Chennai – 600003.

STUDY DESIGN:

Single centre observational study

SAMPLE SIZE:

100 meningitis patients admitted in medical wards based on inclusion and exclusion criteria.

STUDY DURATION:

July 2017 – June 2018

ETHICAL ISSUES:

Approval from Institutional Ethics Committee was taken before starting the study. Prior informed consent was obtained from all the patients and controls.

INCLUSION CRITERIA:

1.Fever,headache with neckstiffness,altered mental status

2. Age > 14 years

EXCLUSION CRITERIA:

1. Patients with vomiting,diarrhoea,dka

2. Patients on drugs like diuretics,corticosteroids and laxatives

STUDY PLAN:

Sample size was calculated using the formula **4*pq/d**, where **p** denotes the prevalence of the disease, **q = 1-p** and **d** denotes the error range. About 100 patients admitted to the medical wards with the diagnosis of meningitis were chosen. A complete history was taken from the patients and the attenders including history of chronic kidney disease, previous history of treatment for diabetes, hypertension , history of immunocompromised states .Through physical examination done looking specifically for clinical signs of meningitis and documented. Basic blood investigations were done including a complete blood count, liver function test, PT/INR, renal function test, CSF studies like sugar, protein, LDH, culture and sensitivity, Gram staining, AFB staining, fungal culture, india ink, Gene expert for MTB, CSF chloride level and Serum chloride levels done. Imaging studies like CT Brain AND MRI Brain with contrast and MRS done.

STATISTICAL ANALYSIS:

Data analysed using statistical package - SPSS Software

CONSENT:

Written informed consent was obtained from the participating patients/attenders.

OBSERVATION AND RESULTS

OBSERVATION AND RESULTS

Frequency Table

Age group	Frequency	Percent
up to 20 years	13	13.0
21-30 years	22	22.0
31-40 years	24	24.0
41-50 years	21	21.0
51-60 years	16	16.0
60-70 years	4	4.0
Total	100	100.0

SEX	Frequency	Percent
Male	51	51.0
Female	49	49.0
Total	100	100.0

PAST HISTORY	Frequency	Percent
DM	25	25.0
DM/HT	3	3.0
DM/HT/CAD	1	1.0
HEAD INJURY	1	1.0
HEAD INJURY/ DM	1	1.0
HIV	5	5.0
NIL	64	64.0
Total	100	100.0

CSF CYTOLOGY	Frequency	Percent
Acellular	45	45.0
Predominantly Lymphocytes	37	37.0
Predominantly PMN	18	18.0
Total	100	100.0

CSF GRAM STAIN	Frequency	Percent
Gram Negative Coccobacillus	1	1.0
Gram Negative Diplococcus	1	1.0
Gram Positive Coccus	8	8.0
Nil	90	90.0
Total	100	100.0

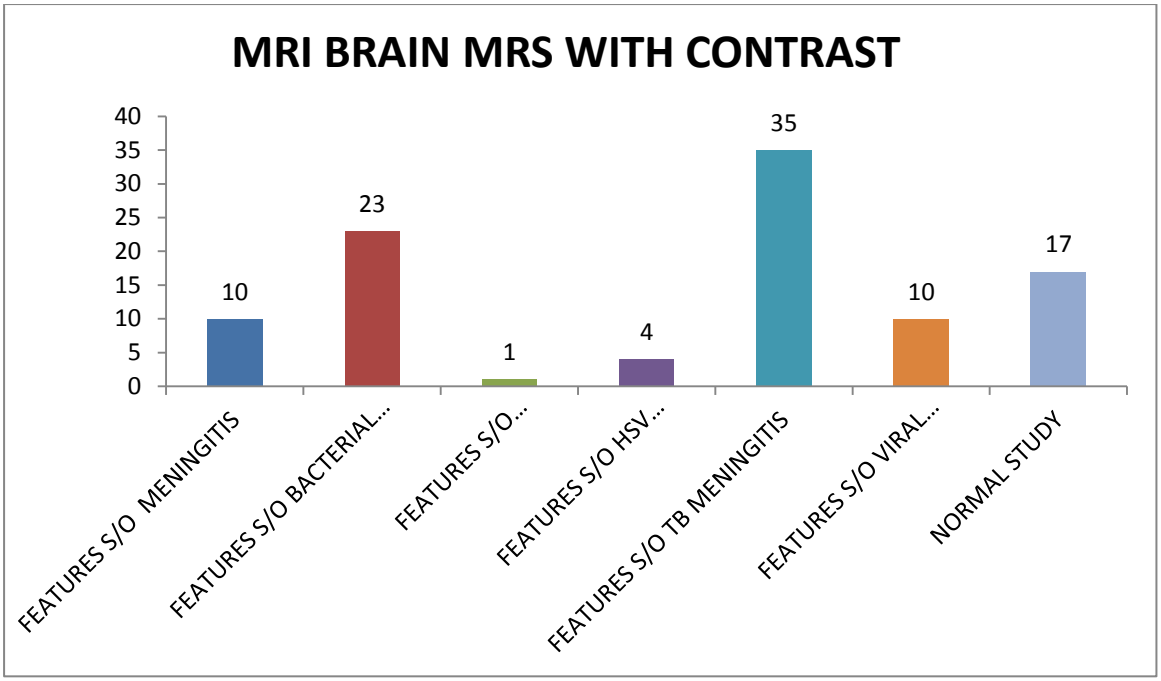
CSF CUL&SENSITIVITY	Frequency	Percent
No growth	95	95.0
S.pneumoniae	5	5.0
Total	100	100.0

CSFGENE EXPERT	Frequency	Percent
MTB DETECTED	22	22.0
MTB NOT DETECTED	78	78.0
Total	100	100.0

CSF INDIA INK	Frequency	Percent
Negative	3	3.0
Not done	96	96.0
Positive	1	1.0
Total	100	100.0

SERUM CHLORIDE meq/l	Frequency	Percent
90.00	1	1.0
91.00	2	2.0
92.00	3	3.0
93.00	2	2.0
94.00	5	5.0
95.00	4	4.0
96.00	8	8.0
97.00	5	5.0
98.00	5	5.0
99.00	15	15.0
100.00	9	9.0
101.00	6	6.0
102.00	3	3.0
103.00	8	8.0
104.00	11	11.0
105.00	8	8.0
106.00	4	4.0
107.00	1	1.0
Total	100	100.0

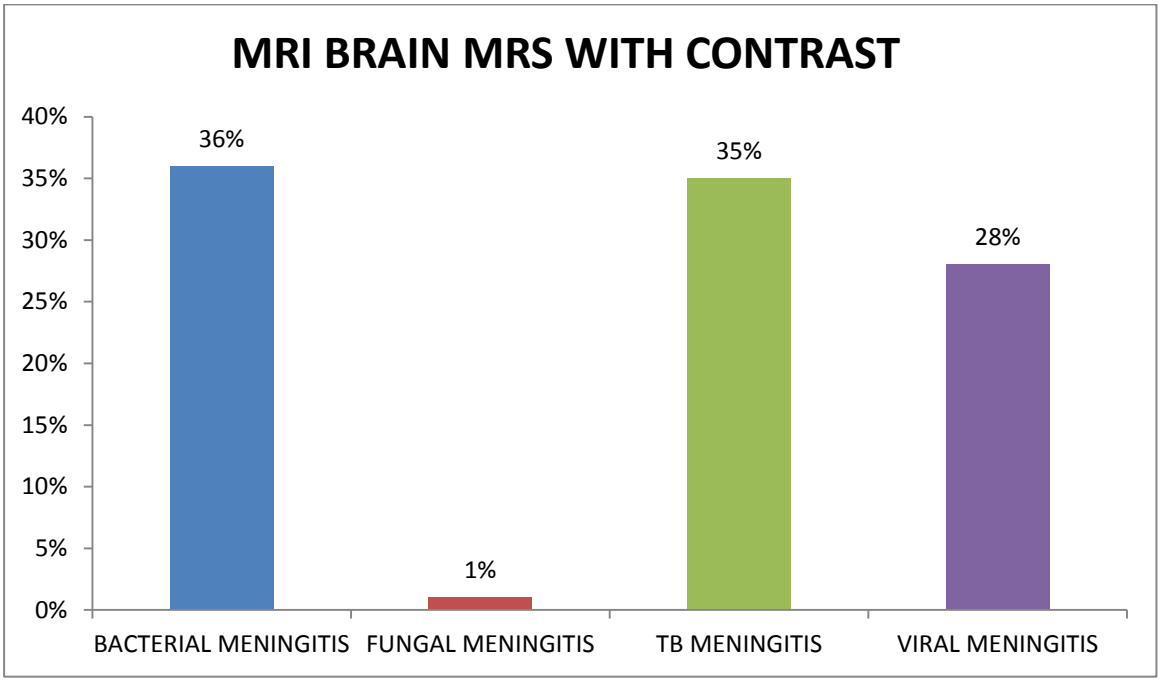
MRI BRAIN MRS WITH CONTRAST	Frequency	Percent
FEATURES S/O MENINGITIS	10	10.0
FEATURES S/O BACTERIAL MENINGITIS	23	23.0
FEATURES S/O CRYPTOCOCCAL MENINGOENCEPHALITIS	1	1.0
FEATURES S/O HSV MENINGOENCEPHALITIS	4	4.0
FEATURES S/O TB MENINGITIS	35	35.0
FEATURES S/O VIRAL MENINGITIS	10	10.0
NORMAL STUDY	17	17.0
Total	100	100.0



Interpretation:

The above table depicts the percentage of distribution of features suggestive of meningitis is 10%,of bacterial meningitis is 23%,of cryptococcal meningoencephalitis is 1%,of meningoencephalitis is 4%, of TB meningitis is 35%,of viral meningitis is 10%,of normal study is 17% in MRI of brain and MRS with contrast.

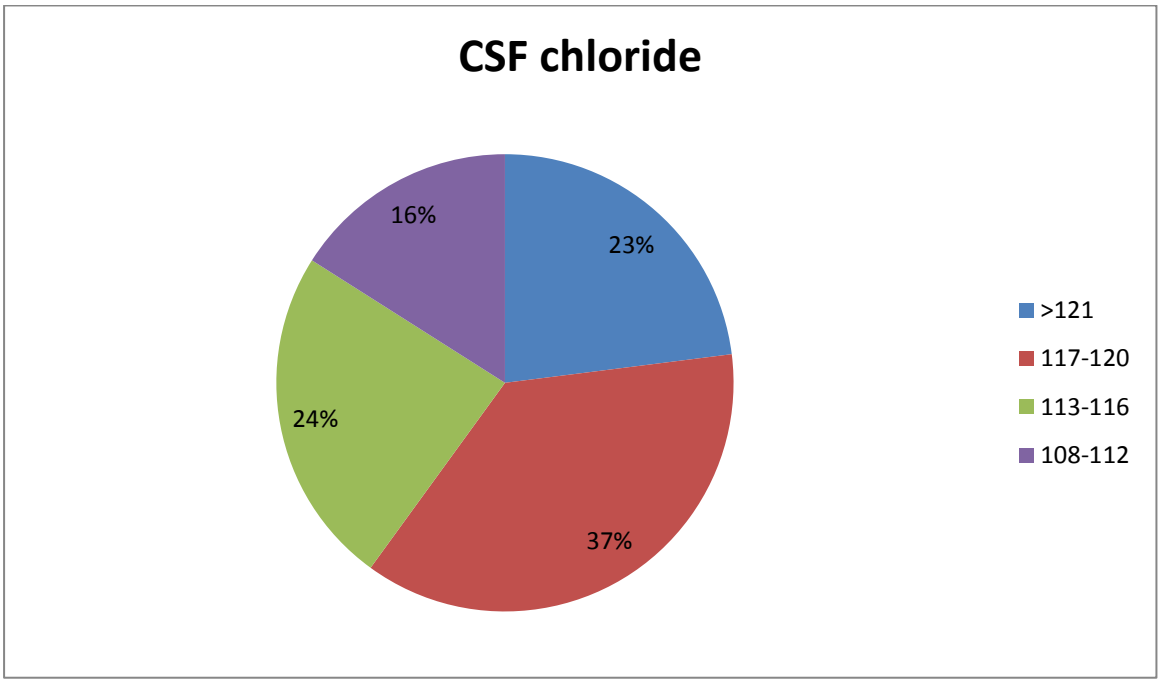
DIAGNOSIS	Frequency	Percent
BACTERIAL MENINGITIS	36	36.0
FUNGAL MENINGITIS	1	1.0
TB MENINGITIS	35	35.0
VIRAL MENINGITIS	28	28.0
Total	100	100.0



Interpretation:

The above table depicts the diagnosis of meningitis percentage bacterial meningitis is 36% and fungal meningitis is 1% ,TB meningitis is 35%,and viral meningitis is 28%.

CSF chloride	Frequency	Percent
>121	23	23.0
117-120	37	37.0
113-116	24	24.0
108-112	16	16.0
Total	100	100.0

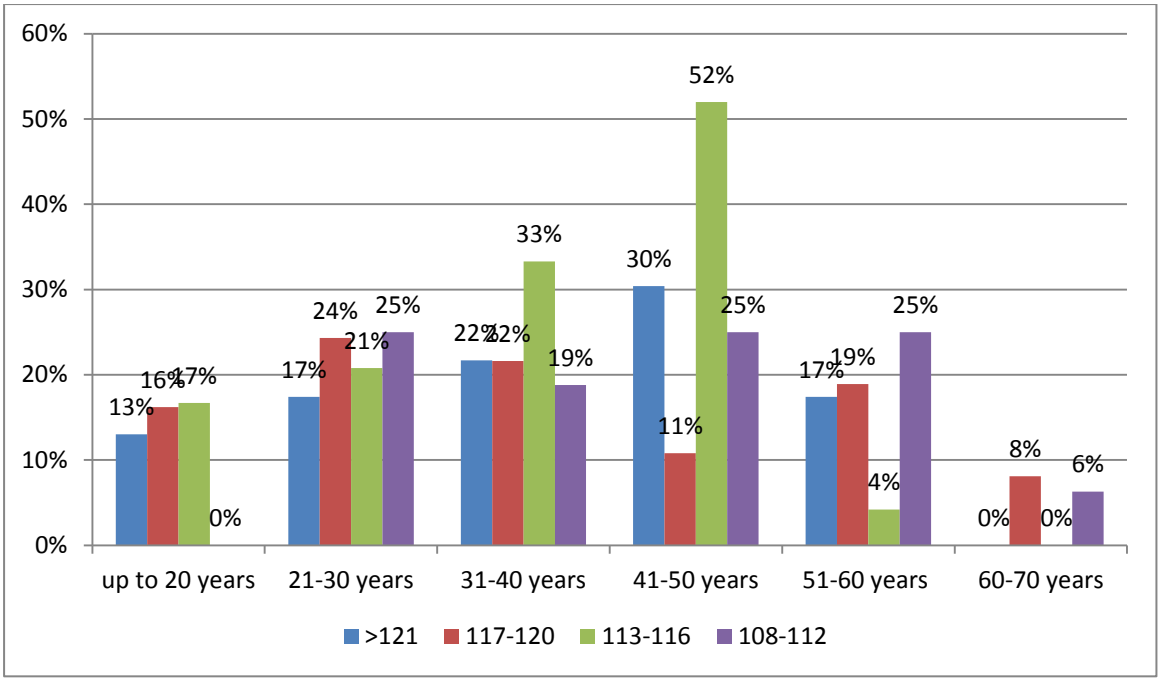


Interpretation:

The above table depicts the CSF chloride levels frequency along with percentage >121 is 23%,117-120 is 37%.113-116 is 24%,108-112 is 16%.

Cross tab							
			CSF chloride				Total
			>121	117-120	113-116	108-112	
Age group	up to 20 years	Count	3	6	4	0	13
		%	13.0%	16.2%	16.7%	.0%	13.0%
	21-30 years	Count	4	9	5	4	22
		%	17.4%	24.3%	20.8%	25.0%	22.0%
	31-40 years	Count	5	8	8	3	24
		%	21.7%	21.6%	33.3%	18.8%	24.0%
	41-50 years	Count	7	4	6	4	21
		%	30.4%	10.8%	25.0%	25.0%	21.0%
	51-60 years	Count	4	7	1	4	16
		%	17.4%	18.9%	4.2%	25.0%	16.0%
	60-70 years	Count	0	3	0	1	4
		%	.0%	8.1%	.0%	6.3%	4.0%
Total		Count	23	37	24	16	100
		%	100.0%	100.0%	100.0%	100.0%	100.0%

Pearson Chi-Square=14.095 p=0.518



Interpretation:

The above table depicts the age group of the patients according to their CSF chloride group from 20 years to 70 years .

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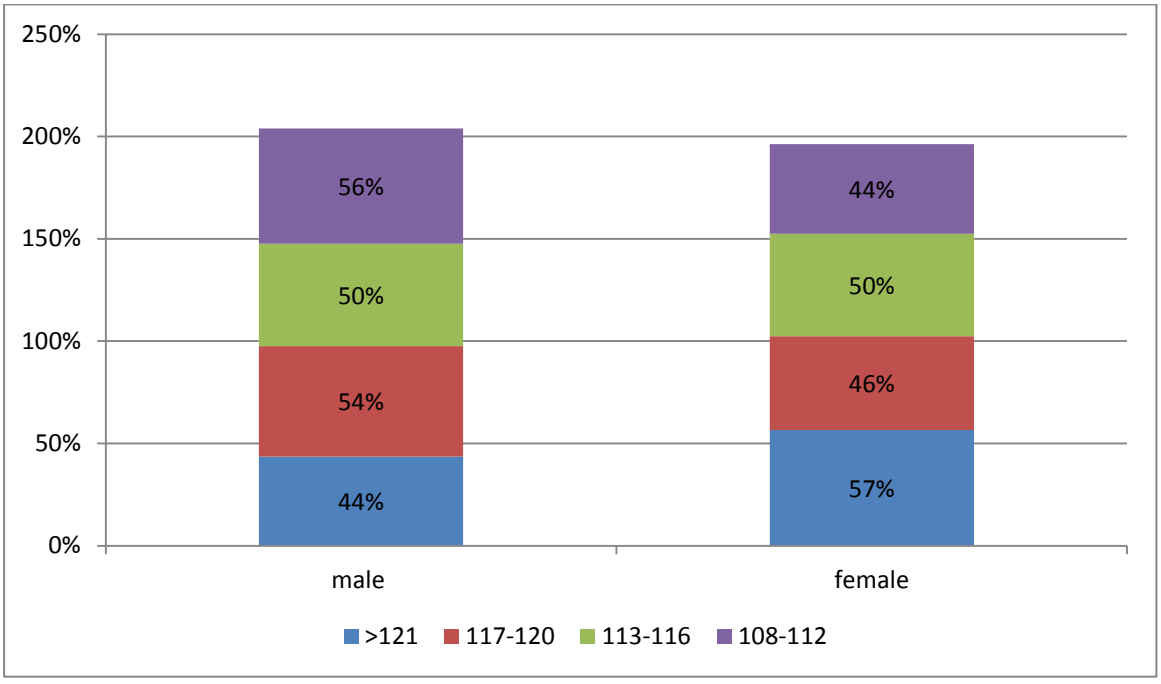
Cross tab							
			CSF chloride				Total
			>121	117-120	113-116	108-112	
SEX	Male	Count	10	20	12	9	51
		%	43.5%	54.1%	50.0%	56.3%	51.0%
	Female	Count	13	17	12	7	49
		%	56.5%	45.9%	50.0%	43.8%	49.0%
Total		Count	23	37	24	16	100
		%	100.0%	100.0%	100.0%	100.0%	100.0%

Pearson Chi-Square=0.845 p=0.839

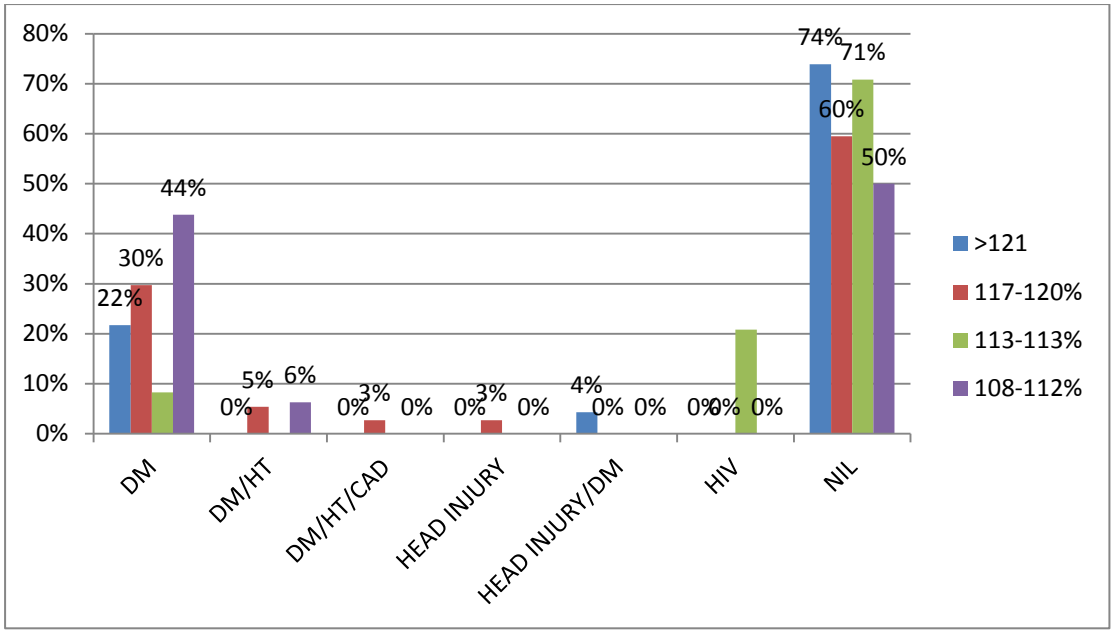


Interpretation:

The above table depicts the sex of patients according to their CSF chloride levels (>121,117-120,113-116,108-112).

Cross tab							
			CSF chloride				Total
			>121	117-120	113-116	108-112	
PAST HISTORY	DM	Count	5	11	2	7	25
		%	21.7%	29.7%	8.3%	43.8%	25.0%
	DM/HT	Count	0	2	0	1	3
		%	.0%	5.4%	.0%	6.3%	3.0%
	DM/HT/CAD	Count	0	1	0	0	1
		%	.0%	2.7%	.0%	.0%	1.0%
	HEAD INJURY	Count	0	1	0	0	1
		%	.0%	2.7%	.0%	.0%	1.0%
	HEAD INJURY/ DM	Count	1	0	0	0	1
		%	4.3%	.0%	.0%	.0%	1.0%
	HIV	Count	0	0	5	0	5
		%	.0%	.0%	20.8%	.0%	5.0%
	NIL	Count	17	22	17	8	64
		%	73.9%	59.5%	70.8%	50.0%	64.0%
Total		Count	23	37	24	16	100
		%	100.0%	100.0%	100.0%	100.0%	100.0%

Pearson Chi-Square=37.757* p=0.023

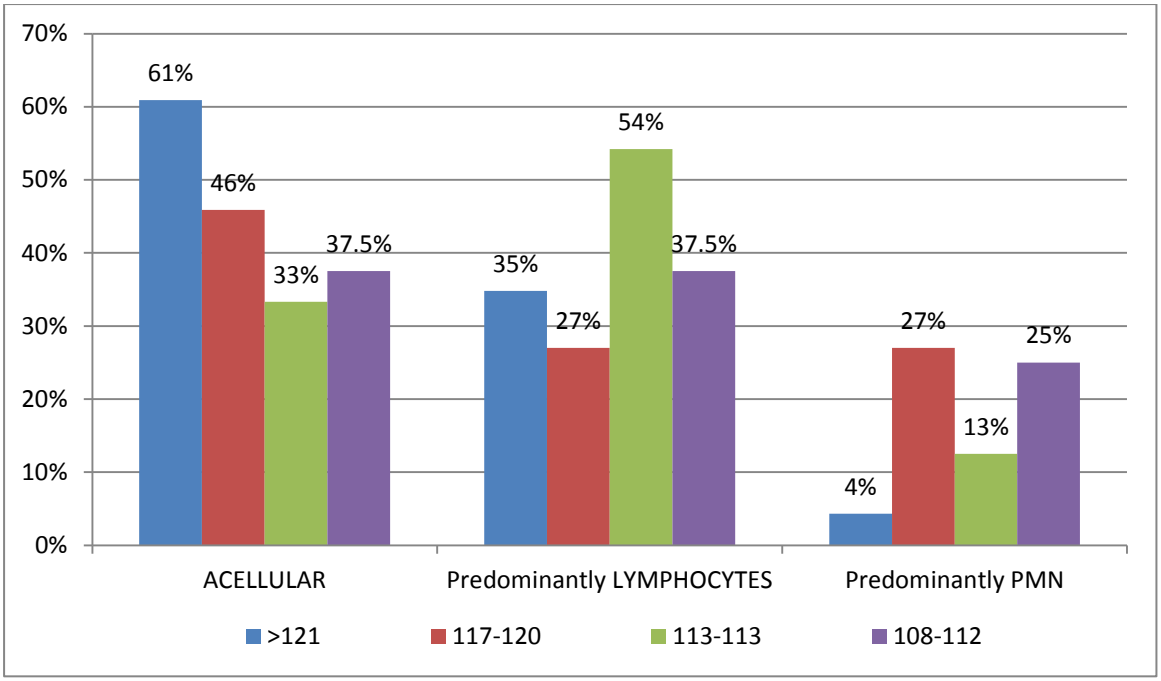


Interpretation:

The above table depicts the past history of patients like DM,DM/HT,DM/HT/CAD,HEAD INJURY,HEAD INJURY/DM, HIV. NIL according to their CSF chloride levels.

Cross tab							
			CSF chloride				Total
			>121	117-120	113-116	108-112	
CSF CYTOLOGY	Acellular	Count	14	17	8	6	45
		%	60.9%	45.9%	33.3%	37.5%	45.0%
	Predominantly Lymphocytes	Count	8	10	13	6	37
		%	34.8%	27.0%	54.2%	37.5%	37.0%
	Predominantly PMN	Count	1	10	3	4	18
		%	4.3%	27.0%	12.5%	25.0%	18.0%
Total		Count	23	37	24	16	100
		%	100.0%	100.0%	100.0%	100.0%	100.0%

Pearson Chi-Square=10.054 p=0.122

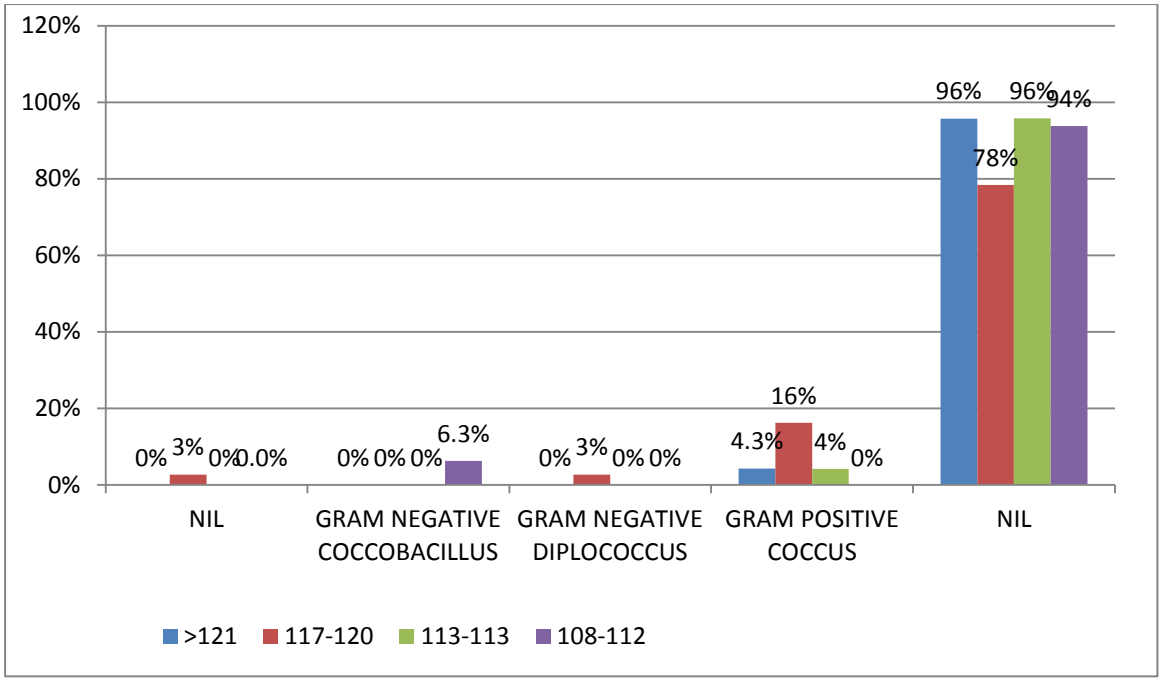


Interpretation:

The above table depicts the CSF cytology like acellular,predominant lymphocytes, predominantly PMN's percentage according to its CSF chloride levels.

Cross tab							
			CSF chloride				Total
			>121	117-120	113-116	108-112	
CSF GRAM STAIN	NIL	Count	0	1	0	0	1
		%	.0%	2.7%	.0%	.0%	1.0%
	Gram Negative Coccobacillus	Count	0	0	0	1	1
		%	.0%	.0%	.0%	6.3%	1.0%
	Gram Negative Diplococcus	Count	0	1	0	0	1
		%	.0%	2.7%	.0%	.0%	1.0%
	Gram Positive Coccus	Count	1	6	1	0	8
		%	4.3%	16.2%	4.2%	.0%	8.0%
	Nil	Count	22	29	23	15	89
		%	95.7%	78.4%	95.8%	93.8%	89.0%
Total		Count	23	37	24	16	100
		%	100.0%	100.0%	100.0%	100.0%	100.0%

Pearson Chi-Square=14.632 p=0.262

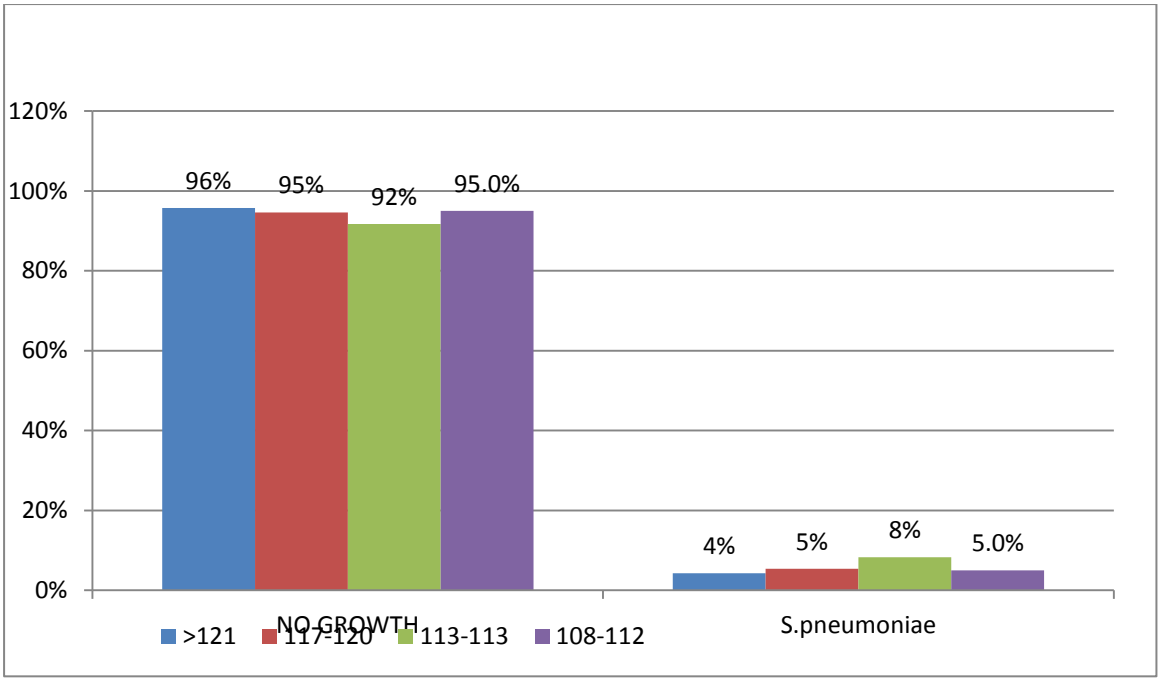


Interpretation:

The above table depicts the CSF gram stain of the patients compared to CSF chloride levels.

Cross tab							
			CSF chloride				Total
			>121	117-120	113-116	108-112	
CSF CUL&SENSITIVITY	No Growth	Count	22	35	22	16	95
		%	95.7%	94.6%	91.7%	100.0%	95.0%
	S.pneumoniae	Count	1	2	2	0	5
		%	4.3%	5.4%	8.3%	.0%	5.0%
Total		Count	23	37	24	16	100
		%	100.0%	100.0%	100.0%	100.0%	100.0%

Pearson Chi-Square=1.437 p=0.697

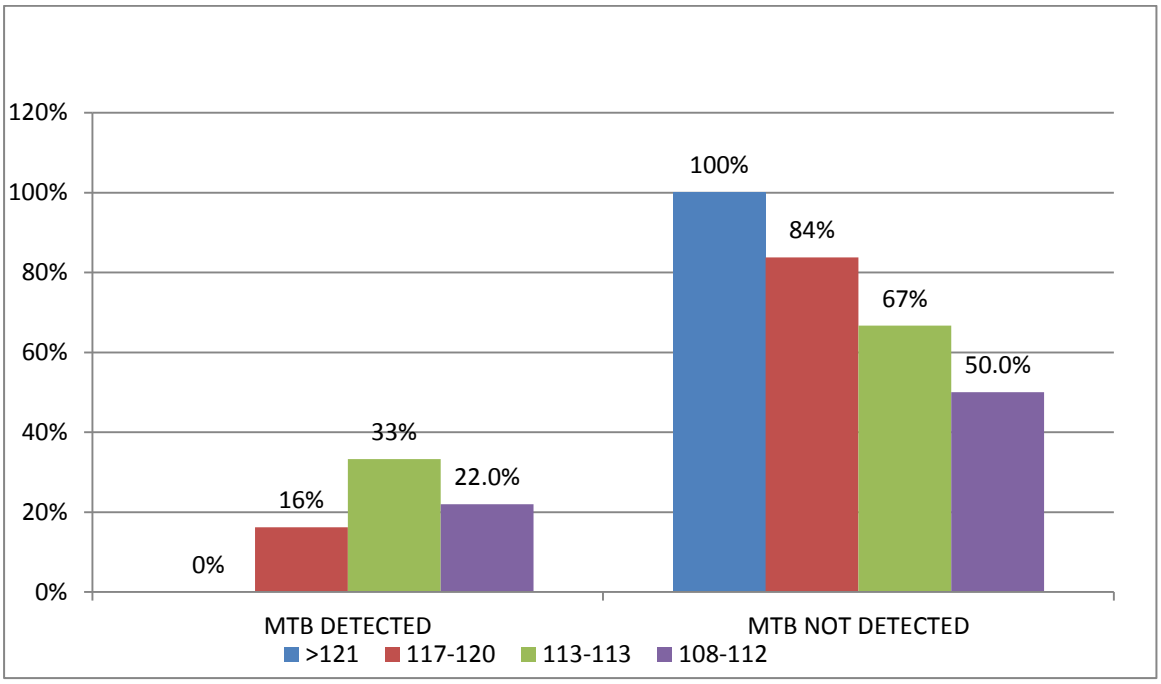


Interpretation:

The above table depicts the CSF culture & sensitivity of the patients with no growth and S.pneumoniae according to their CSF chloride levels.

Cross tab							
			CSF chloride				Total
			>121	117-120	113-116	108-112	
CSF GENE EXPERT	MTB DETECTED	Count	0	6	8	8	22
		%	.0%	16.2%	33.3%	50.0%	22.0%
	MTB NOT DETECTED	Count	23	31	16	8	78
		%	100.0%	83.8%	66.7%	50.0%	78.0%
Total		Count	23	37	24	16	100
		%	100.0%	100.0%	100.0%	100.0%	100.0%

Pearson Chi-Square=16.315**p=0.001

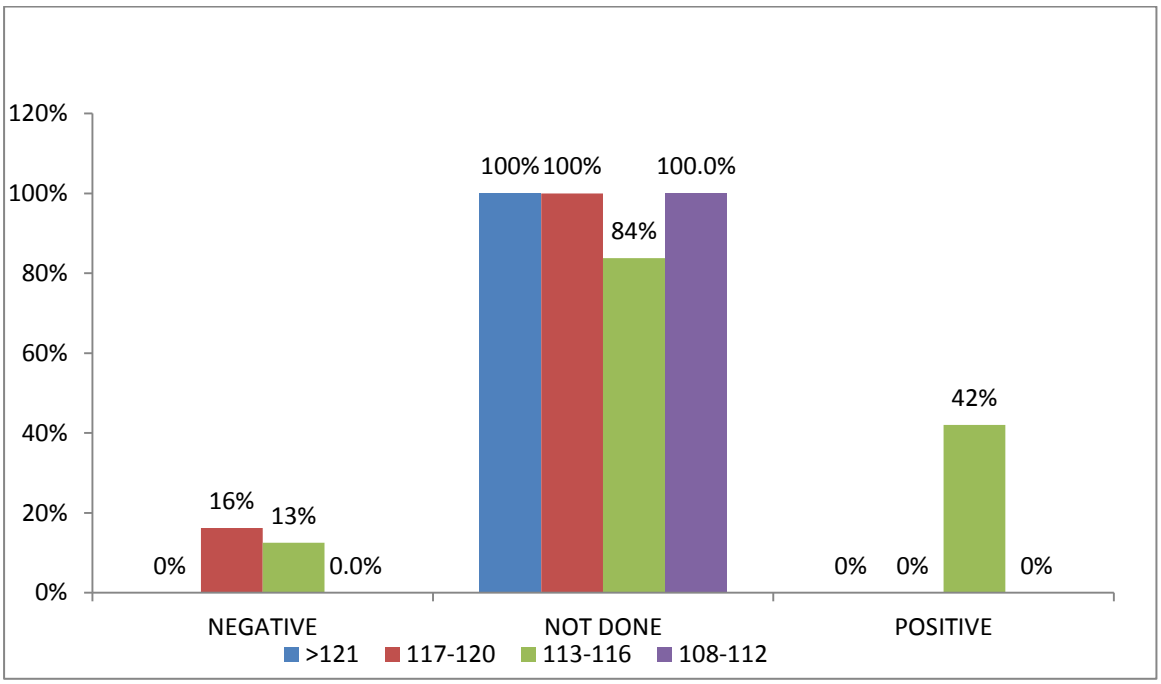


Interpretation:

The above table depicts the CSF gene expert of the patients with MTB and without MTB compared to their CSF chloride levels.

Cross tab							
			CSF chloride				Total
			>121	117-120	113-116	108-112	
CSF INDIA INK	Negative	Count	0	0	3	0	3
		%	.0%	.0%	12.5%	.0%	3.0%
	Not done	Count	23	37	20	16	96
		%	100.0%	100.0%	83.3%	100.0%	96.0%
	Positive	Count	0	0	1	0	1
		%	.0%	.0%	4.2%	.0%	1.0%
Total		Count	23	37	24	16	100
		%	100.0%	100.0%	100.0%	100.0%	100.0%

Pearson Chi-Square=13.194* p=0.040

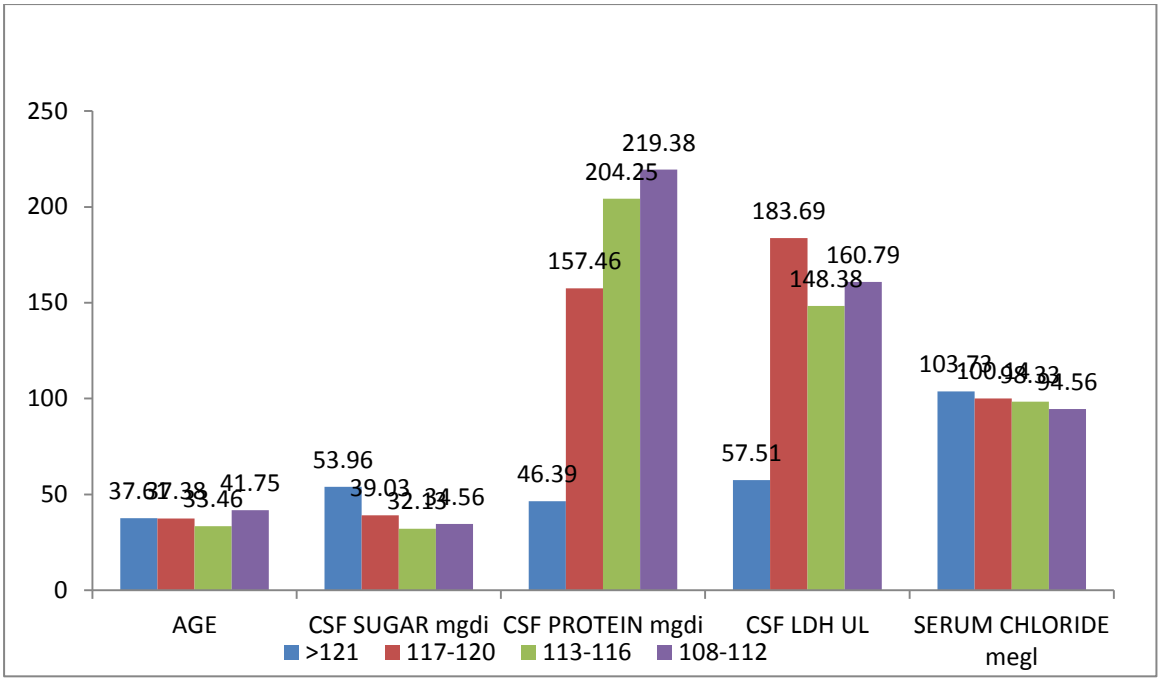


Interpretation:

The above table depicts patients in whom CSF india ink was negative, positive & not done according to their CSF chloride levels.

Descriptives											
		N	Mean	Std. Deviation	Std. Error	95% Confidence Interval for Mean		Minimum	Maximum		
						Lower Bound	Upper Bound			F value	P value
AGE	>121	23	37.61	12.02	2.51	32.41	42.81	18.00	55.00	1.264	.291
	117-120	37	37.38	15.24	2.51	32.30	42.46	16.00	69.00		
	113-116	24	33.46	10.66	2.18	28.96	37.96	16.00	52.00		
	108-112	16	41.75	13.81	3.45	34.39	49.11	21.00	65.00		
	Total	100	37.19	13.37	1.34	34.54	39.84	16.00	69.00		
CSF SUGAR mg/dl	>121	23	53.96	11.64	2.43	48.92	58.99	26.00	73.00	18.594**	.p<0001
	117-120	37	39.03	11.52	1.89	35.18	42.87	23.00	66.00		
	113-116	24	32.13	5.71	1.16	29.72	34.53	25.00	53.00		
	108-112	16	34.56	13.26	3.31	27.50	41.63	22.00	66.00		
	Total	100	40.09	13.34	1.33	37.44	42.74	22.00	73.00		
CSF PROTEIN mg/dl	>121	23	46.39	62.43	13.02	19.39	73.39	20.00	323.00	21.912**	.p<0001
	117-120	37	157.46	84.24	13.85	129.37	185.55	30.00	375.00		
	113-116	24	204.25	82.04	16.75	169.61	238.89	99.00	455.00		
	108-112	16	219	73.84	18.	180	258	115.0	356.0		

			.38		46	.03	.72	0	0		
	Total	100	153.05	99.16	9.92	133.37	172.73	20.00	455.00		
CSF LDH U/L	>121	23	57.51	62.15	12.96	30.64	84.39	21.90	266.40	6.338**	.p<0001
	117-120	37	183.69	145.64	23.94	135.13	232.25	33.50	631.70		
	113-116	24	148.38	85.86	17.53	112.12	184.63	52.00	421.60		
	108-112	16	160.79	106.09	26.52	104.26	217.32	53.00	454.30		
	Total	100	142.53	119.85	11.98	118.75	166.31	21.90	631.70		
SERUM CHLORIDE meq/l	>121	23	103.70	2.16	.45	102.76	104.63	99.00	107.00	31.863**	.p<0001
	117-120	37	100.14	3.16	.52	99.08	101.19	92.00	105.00		
	113-116	24	98.33	3.16	.64	97.00	99.67	92.00	105.00		
	108-112	16	94.56	3.18	.80	92.87	96.26	90.00	103.00		
	Total	100	99.63	4.13	.41	98.81	100.45	90.00	107.00		



Interpretation:

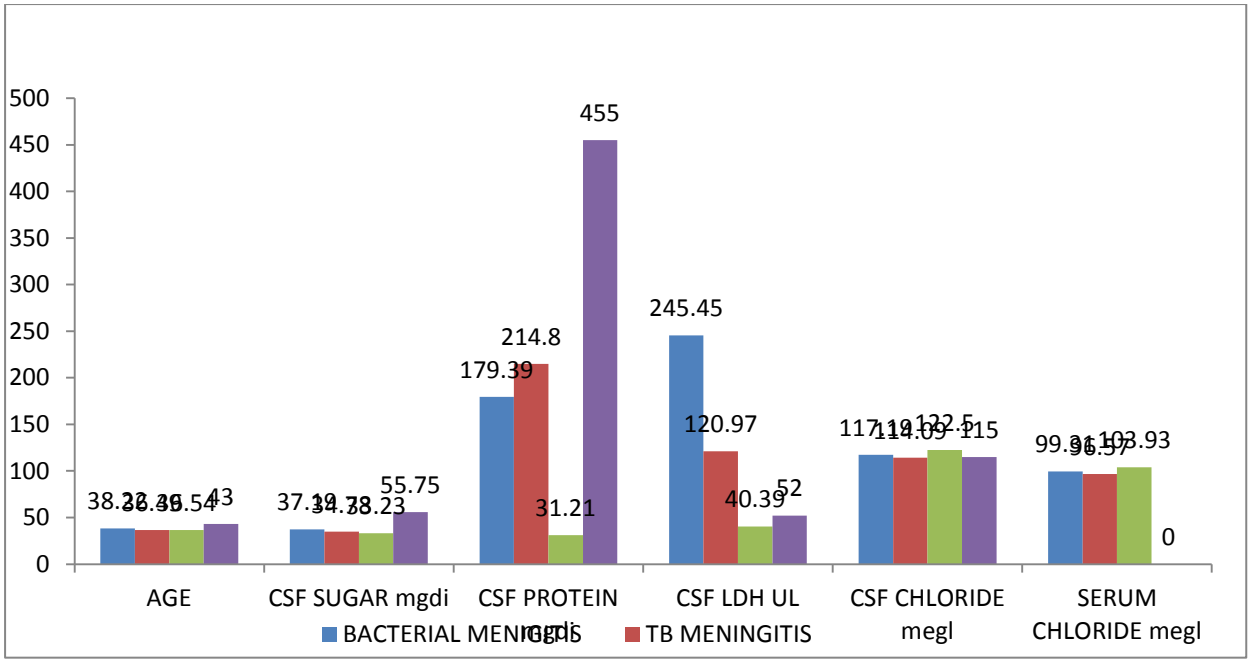
The above table depicts the age, CSF sugar mg/dl, CSF protein mg/dl, CSF LDH U/L, Serum chloride meq/L of the patients and compares it with CSF chloride and provides mean,standard deviation along with standard error. The table also shows significant p value in CSF Sugar,CSF Protein, CSF LDH compared to CSF chloride levels.

Descriptives											
		N	Mean	Std. Deviation	Std. Error	95% Confidence Interval for Mean		Minimum	Maximum		
						Lower Bound	Upper Bound				
AGE	BACTERIAL MENINGITIS	36	38.22	13.79	2.30	33.55	42.89	16.00	69.00	.185	.907
	TB MENINGITIS	35	36.49	14.46	2.44	31.52	41.45	16.00	65.00		
	VIRAL MENINGITIS	28	36.54	11.90	2.25	31.92	41.15	18.00	57.00		
	FUNGAL MENINGITIS	1	43.00	.	.	.	.	43.00	43.00		
	Total	100	37.19	13.37	1.34	34.54	39.84	16.00	69.00		
CSF SUGAR mg/dl	BACTERIAL MENINGITIS	36	34.78	10.16	1.69	31.34	38.22	22.00	66.00	38.133**	<.001
	TB MENINGITIS	35	33.23	8.44	1.43	30.33	36.13	24.00	56.00		
	VIRAL MENI	28	55.75	8.62	1.63	52.41	59.09	41.00	73.00		

	NGITIS										
	FUNGAL MENINGITIS	1	33.00	.	.	.	.	33.00	33.00		
	Total	100	40.09	13.34	1.33	37.44	42.74	22.00	73.00		
CSF PROTEIN mg/dl	BACTERIAL MENINGITIS	36	179.39	66.45	11.07	156.91	201.87	88.00	356.00	69.058**	.p<0001
	TB MENINGITIS	35	214.80	67.12	11.35	191.74	237.86	126.00	390.00		
	VIRAL MENINGITIS	28	31.21	4.48	.85	29.48	32.95	20.00	38.00		
	FUNGAL MENINGITIS	1	455.00	.	.	.	.	455.00	455.00		
	Total	100	153.05	99.16	9.92	133.37	172.73	20.00	455.00		
CSF LDH U/L	BACTERIAL MENINGITIS	36	245.45	135.34	22.56	199.66	291.24	55.80	631.70	30.839**	.p<0001
	TB MENINGITIS	35	120.97	48.27	8.16	104.39	137.55	53.00	251.10		
	VIRAL MENI	28	40.39	11.98	2.26	35.75	45.04	21.90	69.90		

	NGITIS										
	FUNGAL MENINGITIS	1	52.00	.	.	.	.	52.00	52.00		
	Total	100	142.53	119.85	11.98	118.75	166.31	21.90	631.70		
CSF CHLORIDE meq/l	BACTERIAL MENINGITIS	36	117.19	3.53	.59	116.00	118.39	109.00	126.00	43.206**	.p<0001
	TB MENINGITIS	35	114.09	2.70	.46	113.16	115.01	109.00	119.00		
	VIRAL MENINGITIS	28	122.50	2.30	.43	121.61	123.39	118.00	126.00		
	FUNGAL MENINGITIS	1	115.00	.	.	.	.	115.00	115.00		
	Total	100	117.57	4.43	.44	116.69	118.45	109.00	126.00		
SERUM CHLORIDE meq/l	BACTERIAL MENINGITIS	36	99.31	3.27	.54	98.20	100.41	90.00	105.00	32.659**	.p<0001
	TB MENINGITIS	35	96.57	3.29	.56	95.44	97.70	91.00	105.00		

	VIRAL MENINGITIS	28	103.93	1.84	.35	103.21	104.64	99.00	107.00		
	FUNGAL MENINGITIS	1	98.00	.	.	.	.	98.00	98.00		
	Total	100	99.63	4.13	.41	98.81	100.45	90.00	107.00		



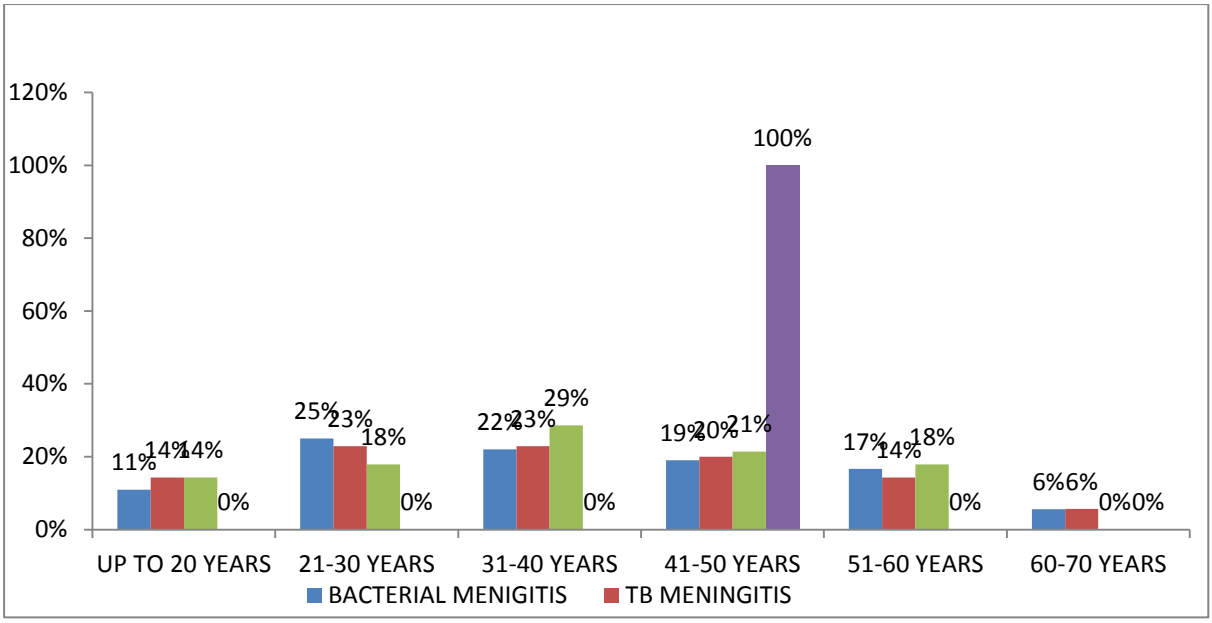
Interpretation:

The above table depicts the age, CSF sugar mg/dl, CSF protein mg/dl, CSF LDH U/L,CSF chloride meq/L ,Serum chloride meq/L of the patients and each compared with diagnosis of bacterial meningitis ,TB meningitis, viral meningitis and fungal meningitis.

Cross tab

			MENINGITIS				Total
			BACTERIAL MENINGITIS	TB MENINGITIS	VIRAL MENINGITIS	FUNGAL MENINGITIS	
Age group	up to 20 years	Count	4	5	4	0	13
		% within MENINGITIS	11.1%	14.3%	14.3%	.0%	13.0%
	21-30 years	Count	9	8	5	0	22
		% within MENINGITIS	25.0%	22.9%	17.9%	.0%	22.0%
	31-40 years	Count	8	8	8	0	24
		% within MENINGITIS	22.2%	22.9%	28.6%	.0%	24.0%
	41-50 years	Count	7	7	6	1	21
		% within MENINGITIS	19.4%	20.0%	21.4%	100.0%	21.0%
	51-60 years	Count	6	5	5	0	16
		% within MENINGITIS	16.7%	14.3%	17.9%	.0%	16.0%
	60-70 years	Count	2	2	0	0	4
		% within MENINGITIS	5.6%	5.7%	.0%	.0%	4.0%
Total		Count	36	35	28	1	100
		% within MENINGITIS	100.0%	100.0%	100.0%	100.0%	100.0%

Pearson Chi-Square=6.419 P=0.972



Interpretation:

The above table depicts the age group of the patients from 20-70 years compared to final diagnosis (bacterial meningitis, TB meningitis, viral meningitis and fungal meningitis).

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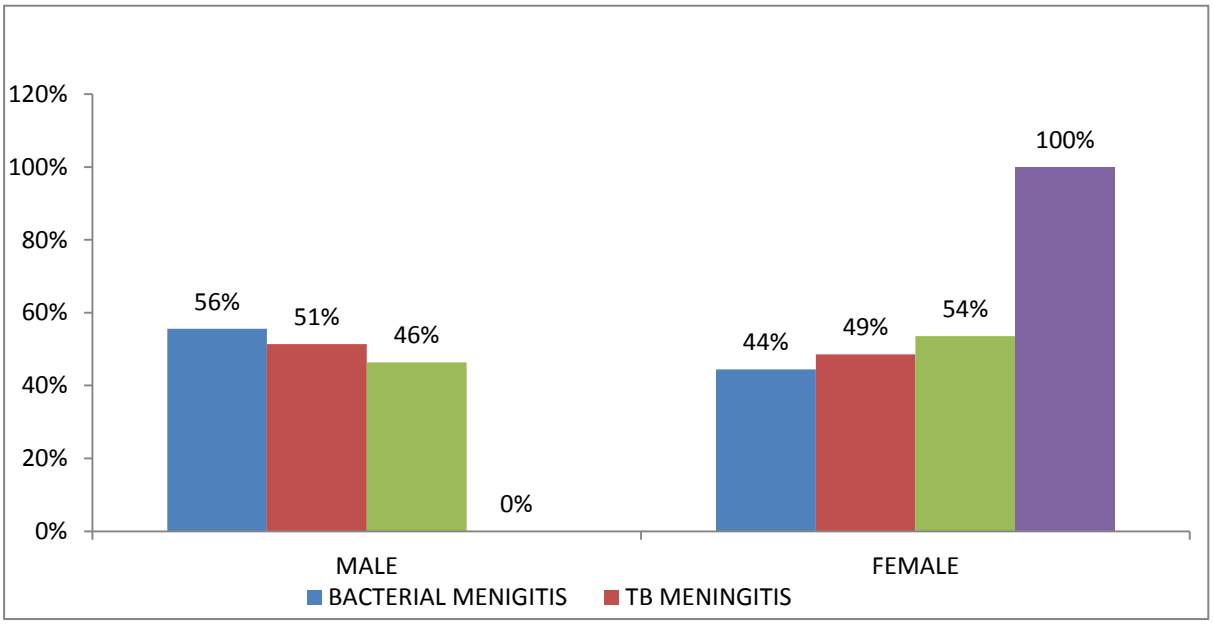
Cross tab

			MENINGITIS				Total
			BACTERIAL MENINGITIS	TB MENINGITIS	VIRAL MENINGITIS	FUNGAL MENINGITIS	
SEX	Male	Count	20	18	13	0	51
		% within MENINGITIS	55.6%	51.4%	46.4%	.0%	51.0%
	Female	Count	16	17	15	1	49
		% within MENINGITIS	44.4%	48.6%	53.6%	100.0%	49.0%
Total		Count	36	35	28	1	100
		% within MENINGITIS	100.0%	100.0%	100.0%	100.0%	100.0%

Pearson Chi-Square=1.577 P=0.666



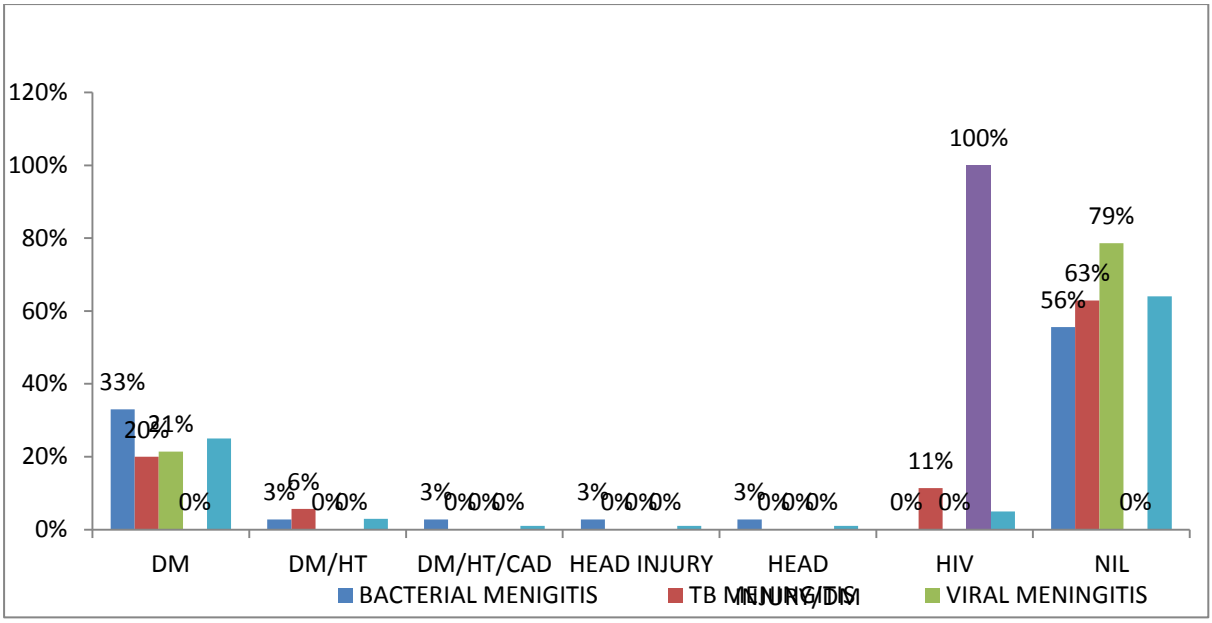
Interpretation:

The above table depicts the sex of the patients compared with the diagnosis of bacterial meningitis ,TB meningitis,viral meningitis or fungal meningitis.

Cross tab

			MENINGITIS				Total
			BACTERIAL MENINGITIS	TB MENINGITIS	VIRAL MENINGITIS	FUNGAL MENINGITIS	
PAST HISTORY	DM	Count	12	7	6	0	25
		% within MENINGITIS	33.3%	20.0%	21.4%	.0%	25.0%
	DM/HT	Count	1	2	0	0	3
		% within MENINGITIS	2.8%	5.7%	.0%	.0%	3.0%
	DM/HT/CAD	Count	1	0	0	0	1
		% within MENINGITIS	2.8%	.0%	.0%	.0%	1.0%
	HEAD INJURY	Count	1	0	0	0	1
		% within MENINGITIS	2.8%	.0%	.0%	.0%	1.0%
	HEAD INJURY / DM	Count	1	0	0	0	1
		% within MENINGITIS	2.8%	.0%	.0%	.0%	1.0%
	HIV	Count	0	4	0	1	5
		% within MENINGITIS	.0%	11.4%	.0%	100.0%	5.0%
	NIL	Count	20	22	22	0	64
		% within MENINGITIS	55.6%	62.9%	78.6%	.0%	64.0%
Total		Count	36	35	28	1	100
		% within MENINGITIS	100.0%	100.0%	100.0%	100.0%	100.0%

Pearson Chi-Square = 34.932* P=0.010



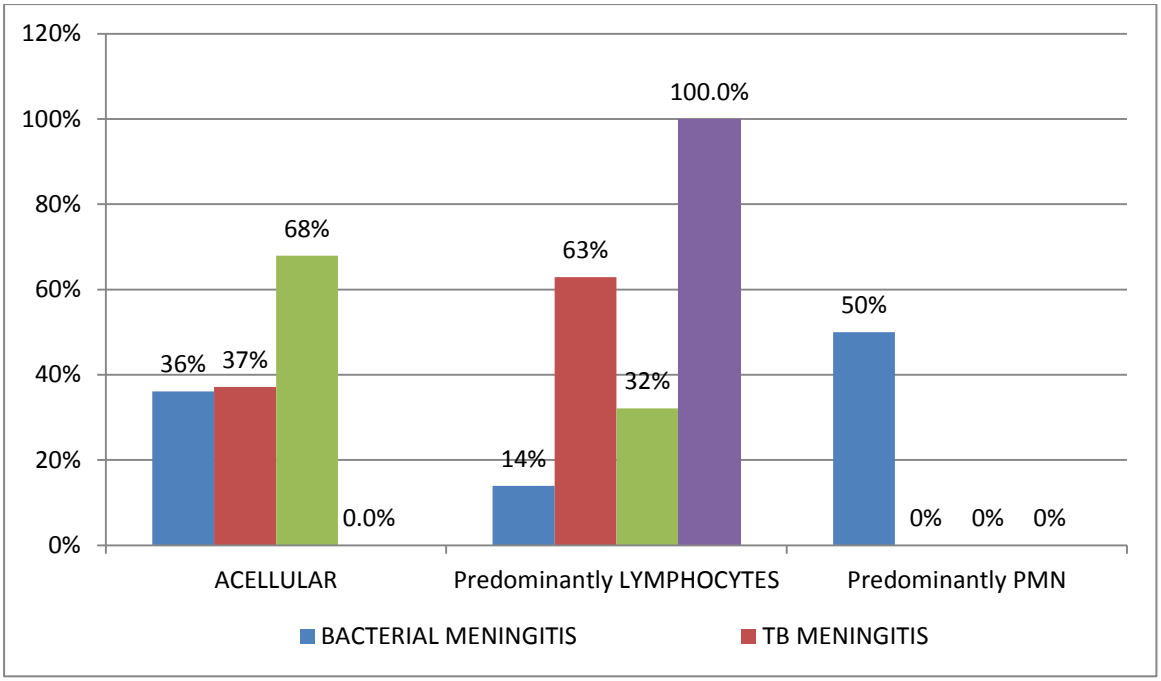
Interpretation:

The above table depicts the past history of the patients and noted like DM,DM/HT,DM/HT/CAD, HEAD INJURY,HEAD INJURY/DM, HIV. NIL compared with the diagnosis of bacterial meningitis ,TB meningitis, viral meningitis or fungal meningitis.

Cross tab

			MENINGITIS				Total
			BACTERIAL MENINGITIS	TB MENINGITIS	VIRAL MENINGITIS	FUNGAL MENINGITIS	
CSF CYTOLOGY	Acellular	Count	13	13	19	0	45
		% within MENINGITIS	36.1%	37.1%	67.9%	.0%	45.0%
	Predominantly Lymphocytes	Count	5	22	9	1	37
		% within MENINGITIS	13.9%	62.9%	32.1%	100.0%	37.0%
	Predominantly PMN	Count	18	0	0	0	18
		% within MENINGITIS	50.0%	.0%	.0%	.0%	18.0%
Total		Count	36	35	28	1	100
		% within MENINGITIS	100.0%	100.0%	100.0%	100.0%	100.0%

Pearson Chi-Square=49.586** P<0.001



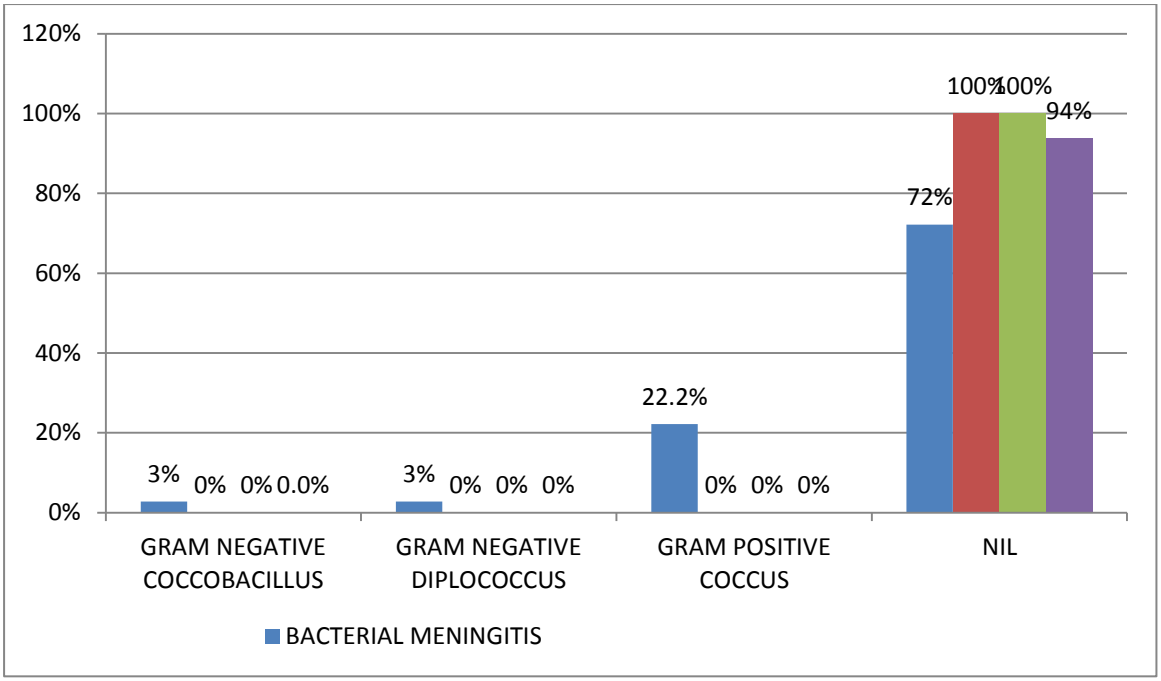
Interpretation:

The above table depicts the CSF cytology compared with diagnosis of bacterial meningitis, TB meningitis, viral meningitis or fungal meningitis.

Cross tab

			MENINGITIS				Total
			BACTERIAL MENINGITIS	TB MENINGITIS	VIRAL MENINGITIS	FUNGAL MENINGITIS	
CSF GRAM STAIN	Gram Negative Coccobacillus	Count	1	0	0	0	1
		% within MENINGITIS	2.8%	.0%	.0%	.0%	1.0 %
	Gram Negative Diplococcus	Count	1	0	0	0	1
		% within MENINGITIS	2.8%	.0%	.0%	.0%	1.0 %
	Gram Positive Coccus	Count	8	0	0	0	8
		% within MENINGITIS	22.2%	.0%	.0%	.0%	8.0 %
	Nil	Count	26	35	28	1	90
		% within MENINGITIS	72.2%	100.0%	100.0%	100.0%	90.0 %
Total		Count	36	35	28	1	100
		% within MENINGITIS	100.0%	100.0%	100.0%	100.0%	100.0%

Pearson Chi-Square=19.753* P=0.019



Interpretation:

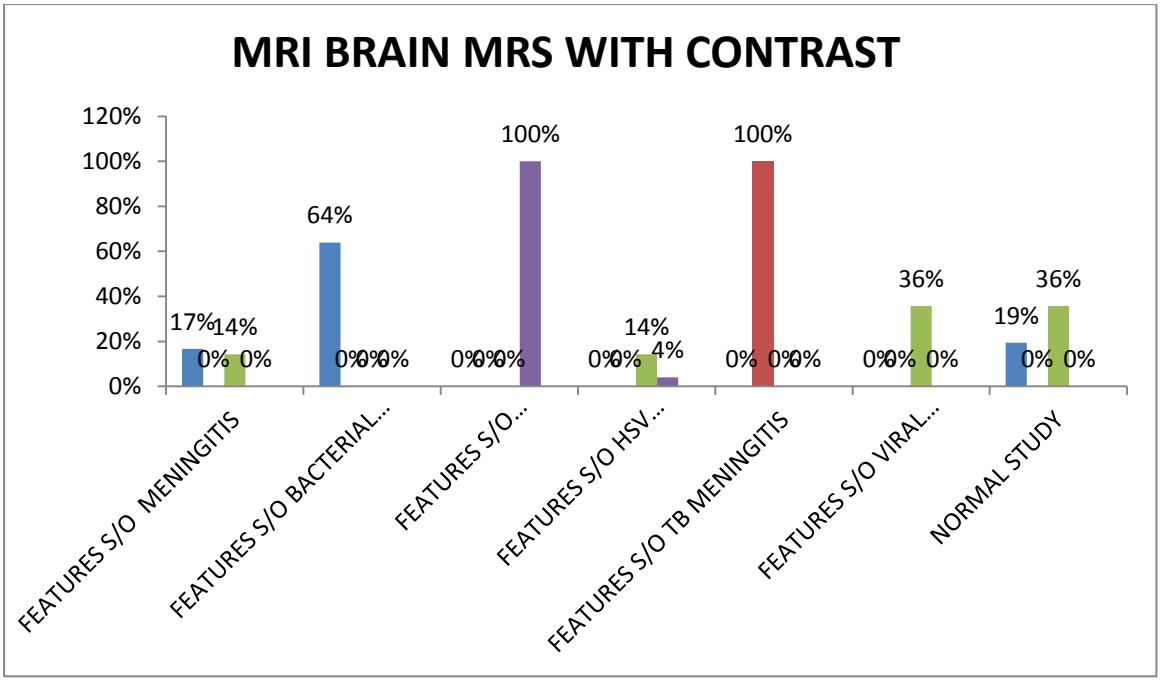
The above table depicts the CSF gram stain compared with diagnosis of bacterial meningitis ,TB meningitis, viral meningitis and fungal meningitis.

Cross tab

			MENINGITIS				Total
			BACTERIAL MENINGITIS	TB MENINGITIS	VIRAL MENINGITIS	FUNGAL MENINGITIS	
MRI BRAIN MRS WITH CONTRAST	FEATURES S/O MENINGITIS	Count	6	0	4	0	10
		% within MENINGITIS	16.7%	.0%	14.3%	.0%	10.0%
	FEATURES S/O BACTERIAL MENINGITIS	Count	23	0	0	0	23
		% within MENINGITIS	63.9%	.0%	.0%	.0%	23.0%
	FEATURES S/O CRYPTOCOCCAL MENINGOENCEOHALITIS	Count	0	0	0	1	1
		% within MENINGITIS	.0%	.0%	.0%	100.0%	1.0%
	FEATURES S/O HSV MENINGOENCEPHALITIS	Count	0	0	4	0	4
		% within MENINGITIS	.0%	.0%	14.3%	.0%	4.0%
	FEATURES S/O TB MENINGITIS	Count	0	35	0	0	35
		% within MENINGITIS	.0%	100.0%	.0%	.0%	35.0%
	FEATURES S/O VIRAL MENINGITIS	Count	0	0	10	0	10
		% within MENINGITIS	.0%	.0%	35.7%	.0%	10.0%
	NORMAL	Count	7	0	10	0	17

	STUDY	% within MENINGITIS	19.4%	.0%	35.7%	.0%	17.0%
Total		Count	36	35	28	1	100
		% within MENINGITIS	100.0%	100.0%	100.0%	100.0%	100.0%

Pearson Chi-Square=255.618** P<0.001



Interpretation:

The above table depicts the MRI of brain and MRS with contrast ‘s features and its percentage of features s/o meningitis is 17%,features s/o bacterial meningitis is 64%,features s/o cryptococcal meningoencephalitis is 1%,features s/o HSV meningoencephalitis is 4%,features s/o TB meningitis is 35%,features s/o viral meningitis is 10%,normal study is 17%. According to their bacterial meningitis, TB meningitis, viral meningitis, fungal meningitis..

DISCUSSION

DISCUSSION

The present study was undertaken to compare the cerebrospinal fluid chloride levels in bacterial, tuberculous , viral and fungal meningitis. It also compares the cerebrospinal fluid chloride levels along with other investigations like CSF sugar, CSF protein, CSF LDH,CSF gram stain, CSF AFB staining, CSF culture& sensitivity, CSF fungal culture, CSF gene expert and MRI brain with contrast & MRS of 100 meningitis patients in a tertiary care centre.

After getting informed consent from the patients or their relatives routine investigations were done which included complete blood hemogram, renal function, liver function, serum electrolytes ,CSF studies and imaging were done. After ensuring that patient did not have any confounding factors, the data was analysed for comparison of the cerebrospinal fluid chloride levels in bacterial, tuberculous , viral and fungal meningitis.

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The present study among a total of hundred patients 51 were males and 49 were females. 36 patients carried risk factors/predisposing factors for CNS infection.45 % of meningitis patients whose CSF cytology were found to be acellular had clinical, laboratory ,microbiological and/or imaging confirmation of the presence of meningitis. Gram stain helped in the isolation of 10 cases of bacterial meningitis i.e., 27.78 % patients had microbiological confirmation of bacterial meningitis. A total of 5 cases were culture positive all the 5 cases had *S.pneumoniae* isolated suggesting only 13.89% of bacterial meningitis were identified by cultures among the 36 cases.

Among the 100 meningitis patients studied age and sex had no significant co relation with the CSF chloride levels. This is in similar lines to studies conducted by Dr. Arthi Ramkissoon in 1985. Gram stain positive or Culture & sensitive positive patients were not found to significantly related to

CSF chloride levels. Cryptococcal meningoencephalitis were significantly related to fall in CSF chloride levels but the total number of cases is just 1 so this needs further study as the statistical significance could be baised. The gene expert positive patients had a significant lower chloride levels with a p value of less than 0.001. CSF chloride levels were found to low/low normal in more than half of the subjects studied proving to be statistically significant when compared with CSF protein values, a depiction in lines with Califmed study by Dr H. W. Gierson, M.D., and Dr.G. J. Owens. . CSF LDH co relates with the CSF chloride levels with a significant p value of< 0.001 found in patients with bacterial and TB meningitis

The study depicted the time tested facts of raised CSF protein and low CSF sugar in bacterial and tuberculous meningitis. Viral meningitis the CSF protein ,CSF sugar tend to be within normal range. Serum chloride levels trend were similar to CSF chloride levels with low to low normal levels documented . CSF chloride level in bacterial meningitis patients tend to show a statistical significant p value found to be <0.001 by having mean CSF chloride level to be 117.19 meq/dl. CSF chloride levels in tuberculous meningitis were found to be statistically significant with a mean CSF chloride 114. The serum chloride levels in comparison to all the types of meningitis were reduced more in tuberculous meningitis followed by bacterial meningitis. Similar findings were observed in a study conducted in 2003 in Chinese PLA hospital by Dr. Q.C.Tan. The comparison ends there as this study excluded bacterial meningitis altogether so the trends and whether it could be used as a diagnostic test of value cannot be categorically stated. The Chinese PLA hospital study also observed a rapid fall in serum chloride levels in cryptococcal meningitis. Cases of viral meningitis had normal CSF chloride levels in the present study. The same was observed in the Chinese PLA hospital study Different age group compared with types of meningitis showed no statistical significance with the CSF chloride levels. There was no co relation between sex and different types of meningitis with both the sexes almost clocking similar

disease pattern with no statistical significance. CSF AFB staining was all in all zero also the gram stain and culture yielded much less than reported worldwide reasons for which could be this being tertiary care referral centre patients might already be exposed to antibiotics ,given antibiotics prior to lumbar puncture, errors in sampling and laboratory errors.

Among 35 cases of TB meningitis 62.9% were found to be CSF gene expert positive against the remaining 31.1% confirmed by other means .MRI brain with contrast and MRS was done which detected features of tuberculous meningitis in all the cases,it detected 29 cases of bacterial meningitis i.e., 81.6% and 18 cases of all viral meningitis patients accounting to i.e., 81.6%.

The present study provides confirmation of the studies in the past like Dr. Arthi Ramkissoon study, califmed study and Chinese PLA hospital study that CSF chloride levels are decreased more in tuberculous meningitis than in bacterial meningitis but whether this could be of diagnostic significance cannot be concretely stated. It could be at large be taken as indicative. Further corrabation and studies could be valuable in throwing light. In this era of evidence based medicine this could add to a valuable piece of evidence if not the sole evidence.

CONCLUSION

CONCLUSION

In this study the CSF chloride levels are reduced in TB meningitis greater than bacterial meningitis.

In viral meningitis CSF chloride levels were found to be normal.

CSF chloride levels can be measured in cases of meningitis which could give an indication of the etiology considering the cost- effectiveness of the investigation.

LIMITATIONS

LIMITATIONS

The study was conducted in a single center -tertiary care referral hospital.

The CSF profile could have been altered by prior antibiotic usage before referral from secondary and primary health care providers.

The possibility of study containing sick patients since study being conducted in a tertiary referral centre.

The study is a cross sectional observational study and follow up details were not evaluated. Hence the change in the CSF chloride values after treatment could not be documented.

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BIBLIOGRAPHY

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ANNEXURE

ANNEXURES

- PROFORMA
- ETHICAL COMMITTEE APPROVAL FORM
- PLAGIARISM SCREENSHOT
- PLAGIARISM CERTIFICATE
- INFORMATION SHEET
- CONSENT FORM
- MASTER CHART

A STUDY OF CEREBROSPINAL FLUID CHLORIDE LEVELS IN MENINGITIS - PROFORMA

Name :

Age/Sex :

OP/IP No :

Occupation :

Address :

Contact No. :

SYMPTOMS

◊ Fever

◊ Altered sensorium

◊ Neck stiffness

◊ Altered behaviour

PATIENT CHARACTERISTICS

◊ Age

◊ Alcoholic

◊ Diabetic

◊ Immunocompromised state

◊ Previous history of neurosurgery / head injury

◊ Socioeconomic status

◊ Tuberculosis

CT BRAIN/ MRI BRAIN WITH CONTRAST AND MRS

CEREBROSPINAL FLUID ANALYSIS INCLUDING CHLORIDE

SERUM CHLORIDE

INSTITUTIONAL ETHICS COMMITTEE
MADRAS MEDICAL COLLEGE, CHENNAI 600 003

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

CERTIFICATE OF APPROVAL

To

Dr.C.Gobinath
I Year PG in MD General Medicine
Institute of Internal Medicine
Madras Medical College
Chennai 600 003

Dear Dr.C.Gobinath,

The Institutional Ethics Committee has considered your request and approved your study titled "**A STUDY OF COREBROSPINAL FLUID CHLORIDE LEVELS IN MENINGITIS "** - **NO.16062017(A)**

The following members of Ethics Committee were present in the meeting hold on **20.06.2017** conducted at Madras Medical College, Chennai 3

1. Prof.Dr.C.Rajendran, MD.,	:Chairperson
2. Prof.R.Narayana Babu, MD.,DCH., Dean,MMC,Ch-3	: Deputy Chairperson
3. Prof.Sudha Seshayyan,MD., Vice Principal,MMC,Ch-3	:Member Secretary
4. Prof.S.Mayilvahanan,MD,Director,Inst. of Int.Med,MMC, Ch-3	: Member
5. Prof.A.Pandiya Raj,Director, Inst. of Gen.Surgery,MMC	: Member
6. Prof.Rema Chandramohan,Prof.of Paediatrics,ICH,Chennai	: Member
7. Prof. Susila, Director, Inst. of Pharmacology,MMC,Ch-3	: Member
8.Thiru S.Govindasamy, BA.,BL,High Court,Chennai	: Lawyer
9.Tmt.Arnold Saulina, MA.,MSW.,	:Social Scientist
10.Tmt.J.Rajalakshmi, JAO,MMC, Ch-3	: Lay Person

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

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

Member Secretary – Ethics Committee

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

URKUND

Urkund Analysis Result

Analysed Document: A STUDY OF CSF CHLORIDE LEVEL IN MENINGITIS FINAL.docx (D42544785)
Submitted: 10/14/2018 10:55:00 PM
Submitted By: c_gobinath@yahoo.in
Significance: 3 %

Sources included in the report:

THESIS FINAL.docx (D31029054)
DR.S.VIMALA DISSERTATION (5).docx (D31130566)
https://emedicine.medscape.com/article/232915-workup
https://en.wikipedia.org/wiki/Acute_viral_meningitis

Instances where selected sources appear:

23

CERTIFICATE – II

This is to certify that this dissertation work titled **"A STUDY OF CEREBROSPINAL FLUID LEVELS IN MENINGITIS"** of the candidate **Dr.C.GOBINATH** with registration Number **201611006** for the award of **M.D.** in the branch of **GENERALMEDICINE**. I personally verified the urkund.com website for plagiarism Check. I found that the uploaded thesis file contains from introduction to conclusion pages and result shows **3 percentage** of plagiarism in the dissertation.

Guide & Supervisor sign with Seal.

INFORMATION SHEET

We are conducting a study on **"A STUDY OF CEREBROSPINAL FLUID CHLORIDE LEVELS IN MENINGITIS"** among patients attending Rajiv Gandhi Government General Hospital, Chennai and for that your specimen may be valuable to us.

The purpose of this study is to identify the chloride levels in meningitis .

We are selecting certain cases and if you are found eligible, we may perform extra tests and special studies which in any way do not affect your final report or management.

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

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

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

Signature of Investigator Signature of Participant

Date :

Place :

PATIENT CONSENT FORM

Study Detail : **A STUDY OF CEREBROSPINAL FLUID CHLORIDE LEVEL IN MENINGITIS**

Study Centre : Rajiv Gandhi Government General Hospital, Chennai.

Patient's Name :

Patient's Age :

Identification Number :

Patient may check (☑) these boxes

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

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

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

data or results that arise from this study.

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

I hereby consent to participate in this study. ☐

I hereby give permission to undergo complete clinical examination and diagnostic tests including hematological, biochemical, radiological tests. ☐

Signature/thumb impression

Patient's Name and Address

Signature of Investigator

Dr.C.GOBINATH

S.No	AGE	SEX	PAST HISTORY	CSF SUGAR mg/dl	CSF PROTEIN mg/dl	CSF CYTOLOGY	CSF GRAM STAIN	CSF CUL.& SENSITIVITY	CSF AFB	CSF FUNGAL CUL & SENSITIVITY	CSF GENE EXPERT	CSF INDIA INK	CSF LDH U/L	CSF CHLORIDE meq/l	SERUM CHLORIDE meq/l	MRI BRAIN MRS WITH CONTRAST	DIAGNOSIS
1	26	F	NIL	30	103	ACELLULAR	NIL	NO GROWTH	NO AFB	NO GROWTH	MTB NOT DETECTED	NOT DONE	366.7	118	103	NORMAL STUDY	BACTERIAL MENINGITIS
2	52	M	DM	44	115	predominantly PMN	GRAM NEGATIVE COCCOBACILLUS	NO GROWTH	NO AFB	NO GROWTH	MTB NOT DETECTED	NOT DONE	277	111	95	FEATURES S/O BACTERIAL MENINGITIS	BACTERIAL MENINGITIS
3	17	M	NIL	35	169	Predominantly LYMPHOCYTES	NIL	NO GROWTH	NO AFB	NO GROWTH	MTB DETECTED	NOT DONE	146	115	97	FEATURES S/O TB MENINGITIS	TB MENINGITIS
4	33	M	NIL	44	35	Predominantly LYMPHOCYTES	NIL	NO GROWTH	NO AFB	NO GROWTH	MTB NOT DETECTED	NOT DONE	33.5	120	101	FEATURES S/O HSV MENINGOENCEPHALITIS	VIRAL MENINGITIS
5	39	F	NIL	40	108	ACELLULAR	NIL	NO GROWTH	NO AFB	NO GROWTH	MTB NOT DETECTED	NOT DONE	421.6	116	100	NORMAL STUDY	BACTERIAL MENINGITIS
6	49	M	AD INJURY/ I	28	105	predominantly PMN	GRAM POSITIVE COCCUS	S.pneumoniae	NO AFB	NO GROWTH	MTB NOT DETECTED	NOT DONE	266.4	122	99	FEATURES S/O BACTERIAL MENINGITIS	BACTERIAL MENINGITIS
7	55	M	NIL	33	135	ACELLULAR	NIL	NO GROWTH	NO AFB	NO GROWTH	MTB DETECTED	NOT DONE	201.9	112	91	FEATURES S/O TB MENINGITIS	TB MENINGITIS
8	43	M	DM	58	30	ACELLULAR	NIL	NO GROWTH	NO AFB	NO GROWTH	MTB NOT DETECTED	NOT DONE	25.9	121	105	NORMAL STUDY	VIRAL MENINGITIS
9	21	F	NIL	24	150	Predominantly LYMPHOCYTES	NIL	NO GROWTH	NO AFB	NO GROWTH	MTB DETECTED	NOT DONE	139.7	109	94	FEATURES S/O TB MENINGITIS	TB MENINGITIS
10	33	F	NIL	38	219	ACELLULAR	NIL	NO GROWTH	NO AFB	NO GROWTH	MTB NOT DETECTED	NOT DONE	105.6	113	99	FEATURES S/O TB MENINGITIS	TB MENINGITIS
11	42	M	HIV	32	142	Predominantly LYMPHOCYTES	NIL	NO GROWTH	NO AFB	NO GROWTH	MTB NOT DETECTED	NEGATIVE	82.5	116	104	FEATURES S/O TB MENINGITIS	TB MENINGITIS
12	20	M	NIL	55	32	ACELLULAR	NIL	NO GROWTH	NO AFB	NO GROWTH	MTB NOT DETECTED	NOT DONE	43.3	119	100	FEATURES S/O VIRAL MENINGITIS	VIRAL MENINGITIS
13	29	F	NIL	23	132	predominantly PMN	GRAM POSITIVE COCCUS	NO GROWTH	NO AFB	NO GROWTH	MTB NOT DETECTED	NOT DONE	199.7	120	99	FEATURES S/O MENINGITIS	BACTERIAL MENINGITIS
14	38	F	DM	32	99	ACELLULAR	NIL	NO GROWTH	NO AFB	NO GROWTH	MTB NOT DETECTED	NOT DONE	230.6	115	100	FEATURES S/O BACTERIAL MENINGITIS	BACTERIAL MENINGITIS
15	53	F	DM	29	256	Predominantly LYMPHOCYTES	NIL	NO GROWTH	NO AFB	NO GROWTH	MTB DETECTED	NOT DONE	125.6	117	96	FEATURES S/O TB MENINGITIS	TB MENINGITIS
16	34	F	NIL	41	37	ACELLULAR	NIL	NO GROWTH	NO AFB	NO GROWTH	MTB NOT DETECTED	NOT DONE	55.9	119	105	FEATURES S/O VIRAL MENINGITIS	VIRAL MENINGITIS

17	22	M	NIL	33	126	Predominantly LYMPHOCYTES	NIL	NO GROWTH	NO AFB	NO GROWTH	MTB DETECTED	NOT DONE	88.2	109	93	FEATURES S/O TB MENINGITIS	TB MENINGITIS
18	33	M	DM	24	199	predominantly PMN	NIL	NO GROWTH	NO AFB	NO GROWTH	MTB NOT DETECTED	NOT DONE	152.7	112	97	FEATURES S/O BACTERIAL MENINGITIS	BACTERIAL MENINGITIS
19	19	F	NIL	29	143	ACELLULAR	NIL	NO GROWTH	NO AFB	NO GROWTH	MTB NOT DETECTED	NOT DONE	143.1	120	101	NORMAL STUDY	BACTERIAL MENINGITIS
20	22	M	NIL	31	211	Predominantly LYMPHOCYTES	NIL	NO GROWTH	NO AFB	NO GROWTH	MTB DETECTED	NOT DONE	67.8	114	98	FEATURES S/O TB MENINGITIS	TB MENINGITIS
21	38	M	NIL	47	38	ACELLULAR	NIL	NO GROWTH	NO AFB	NO GROWTH	MTB NOT DETECTED	NOT DONE	33.7	123	104	FEATURES S/O VIRAL MENINGITIS	VIRAL MENINGITIS
22	55	F	NIL	55	35	Predominantly LYMPHOCYTES	NIL	NO GROWTH	NO AFB	NO GROWTH	MTB NOT DETECTED	NOT DONE	28.6	126	102	NORMAL STUDY	VIRAL MENINGITIS
23	38	F	DM	36	156	predominantly PMN	GRAM POSITIVE COCCUS	NO GROWTH	NO AFB	NO GROWTH	MTB NOT DETECTED	NOT DONE	66.4	118	99	NORMAL STUDY	BACTERIAL MENINGITIS
24	46	M	HIV	27	244	Predominantly LYMPHOCYTES	NIL	NO GROWTH	NO AFB	NO GROWTH	MTB DETECTED	NEGATIVE	176	114	96	FEATURES S/O TB MENINGITIS	TB MENINGITIS
25	18	F	NIL	44	28	ACELLULAR	NIL	NO GROWTH	NO AFB	NO GROWTH	MTB NOT DETECTED	NOT DONE	66.2	122	104	FEATURES S/O VIRAL MENINGITIS	VIRAL MENINGITIS
26	23	F	NIL	28	177	predominantly PMN	NIL	NO GROWTH	NO AFB	NO GROWTH	MTB NOT DETECTED	NOT DONE	556.7	119	101	FEATURES S/O BACTERIAL MENINGITIS	BACTERIAL MENINGITIS
27	39	M	NIL	36	193	predominantly PMN	NIL	NO GROWTH	NO AFB	NO GROWTH	MTB NOT DETECTED	NOT DONE	327.8	120	103	FEATURES S/O MENINGITIS	BACTERIAL MENINGITIS
28	34	M	DM	29	301	Predominantly LYMPHOCYTES	NIL	NO GROWTH	NO AFB	NO GROWTH	MTB DETECTED	NOT DONE	85.2	110	96	FEATURES S/O TB MENINGITIS	TB MENINGITIS
29	44	F	NIL	50	34	ACELLULAR	NIL	NO GROWTH	NO AFB	NO GROWTH	MTB NOT DETECTED	NOT DONE	43.7	121	99	NORMAL STUDY	VIRAL MENINGITIS
30	52	M	NIL	66	30	Predominantly LYMPHOCYTES	NIL	NO GROWTH	NO AFB	NO GROWTH	MTB NOT DETECTED	NOT DONE	52.5	125	104	FEATURES S/O VIRAL MENINGITIS	VIRAL MENINGITIS
31	28	M	NIL	48	34	ACELLULAR	NIL	NO GROWTH	NO AFB	NO GROWTH	MTB NOT DETECTED	NOT DONE	39.7	120	105	NORMAL STUDY	VIRAL MENINGITIS
32	16	F	NIL	30	255	Predominantly LYMPHOCYTES	NIL	NO GROWTH	NO AFB	NO GROWTH	MTB DETECTED	NOT DONE	188.4	115	98	FEATURES S/O TB MENINGITIS	TB MENINGITIS
33	27	M	NIL	26	161	ACELLULAR	NIL	NO GROWTH	NO AFB	NO GROWTH	MTB NOT DETECTED	NOT DONE	278.9	113	95	FEATURES S/O BACTERIAL MENINGITIS	BACTERIAL MENINGITIS
34	41	F	DM	50	287	predominantly PMN	NIL	NO GROWTH	NO AFB	NO GROWTH	MTB NOT DETECTED	NOT DONE	349.5	119	100	FEATURES S/O BACTERIAL MENINGITIS	BACTERIAL MENINGITIS

35	59	F	DM/HT	53	188	ACELLULAR	NIL	NO GROWTH	NO AFB	NO GROWTH	MTB DETECTED	NOT DONE	97	112	94	FEATURES S/O TB MENINGITIS	TB MENINGITIS
36	62	M	DM/HT/CAD	45	105	predominantly PMN	GRAM POSITIVE COCCUS	S.pneumoniae	NO AFB	NO GROWTH	MTB NOT DETECTED	NOT DONE	631.7	119	104	FEATURES S/O BACTERIAL MENINGITIS	BACTERIAL MENINGITIS
37	46	F	NIL	32	144	Predominantly LYMPHOCYTES	NIL	NO GROWTH	NO AFB	NO GROWTH	MTB NOT DETECTED	NOT DONE	98.6	115	97	FEATURES S/O TB MENINGITIS	TB MENINGITIS
38	36	F	NIL	28	233	ACELLULAR	NIL	NO GROWTH	NO AFB	NO GROWTH	MTB NOT DETECTED	NOT DONE	53	111	91	FEATURES S/O TB MENINGITIS	TB MENINGITIS
39	41	M	DM	55	32	ACELLULAR	NIL	NO GROWTH	NO AFB	NO GROWTH	MTB NOT DETECTED	NOT DONE	33.5	126	104	FEATURES S/O VIRAL MENINGITIS	VIRAL MENINGITIS
40	28	M	NIL	33	121	predominantly PMN	NIL	NO GROWTH	NO AFB	NO GROWTH	MTB NOT DETECTED	NOT DONE	55.8	116	99	NORMAL STUDY	BACTERIAL MENINGITIS
41	21	F	NIL	26	190	ACELLULAR	NIL	NO GROWTH	NO AFB	NO GROWTH	MTB NOT DETECTED	NOT DONE	248.1	117	100	FEATURES S/O BACTERIAL MENINGITIS	BACTERIAL MENINGITIS
42	36	F	NIL	58	28	ACELLULAR	NIL	NO GROWTH	NO AFB	NO GROWTH	MTB NOT DETECTED	NOT DONE	31.3	125	105	NORMAL STUDY	VIRAL MENINGITIS
43	45	M	DM	30	88	predominantly PMN	GRAM POSITIVE COCCUS	S.pneumoniae	NO AFB	NO GROWTH	MTB NOT DETECTED	NOT DONE	249	117	92	FEATURES S/O MENINGITIS	BACTERIAL MENINGITIS
44	32	F	NIL	28	136	ACELLULAR	NIL	NO GROWTH	NO AFB	NO GROWTH	MTB DETECTED	NOT DONE	197	114	96	FEATURES S/O TB MENINGITIS	TB MENINGITIS
45	19	F	NIL	30	188	Predominantly LYMPHOCYTES	NIL	NO GROWTH	NO AFB	NO GROWTH	MTB NOT DETECTED	NOT DONE	153.8	117	99	FEATURES S/O TB MENINGITIS	TB MENINGITIS
46	57	M	DM	55	35	ACELLULAR	NIL	NO GROWTH	NO AFB	NO GROWTH	MTB NOT DETECTED	NOT DONE	55.2	120	105	FEATURES S/O MENINGITIS	VIRAL MENINGITIS
47	27	M	NIL	66	32	Predominantly LYMPHOCYTES	NIL	NO GROWTH	NO AFB	NO GROWTH	MTB NOT DETECTED	NOT DONE	47	118	104	FEATURES S/O VIRAL MENINGITIS	VIRAL MENINGITIS
48	33	F	DM	26	168	ACELLULAR	NIL	NO GROWTH	NO AFB	NO GROWTH	MTB DETECTED	NOT DONE	99.9	119	98	FEATURES S/O TB MENINGITIS	TB MENINGITIS
49	42	M	NIL	32	257	ACELLULAR	NIL	NO GROWTH	NO AFB	NO GROWTH	MTB NOT DETECTED	NOT DONE	176.6	115	105	FEATURES S/O BACTERIAL MENINGITIS	BACTERIAL MENINGITIS
50	26	M	NIL	26	323	Predominantly LYMPHOCYTES	NIL	NO GROWTH	NO AFB	NO GROWTH	MTB NOT DETECTED	NOT DONE	233.7	126	100	FEATURES S/O BACTERIAL MENINGITIS	BACTERIAL MENINGITIS
51	18	F	NIL	45	30	ACELLULAR	NIL	NO GROWTH	NO AFB	NO GROWTH	MTB NOT DETECTED	NOT DONE	41.6	123	103	NORMAL STUDY	VIRAL MENINGITIS
52	55	F	DM	36	129	Predominantly LYMPHOCYTES	GRAM POSITIVE COCCUS	NO GROWTH	NO AFB	NO GROWTH	MTB NOT DETECTED	NOT DONE	187.4	119	99	NORMAL STUDY	BACTERIAL MENINGITIS

53	35	M	NIL	30	199	Predominantly LYMPHOCYTES	NIL	NO GROWTH	NO AFB	NO GROWTH	MTB NOT DETECTED	NOT DONE	154.4	115	96	FEATURES S/O TB MENINGITIS	TB MENINGITIS
54	16	M	NIL	36	288	Predominantly LYMPHOCYTES	NIL	NO GROWTH	NO AFB	NO GROWTH	MTB DETECTED	NOT DONE	87.1	117	97	FEATURES S/O TB MENINGITIS	TB MENINGITIS
55	22	F	NIL	53	33	ACELLULAR	NIL	NO GROWTH	NO AFB	NO GROWTH	MTB NOT DETECTED	NOT DONE	32	123	104	NORMAL STUDY	VIRAL MENINGITIS
56	29	F	NIL	25	390	Predominantly LYMPHOCYTES	NIL	NO GROWTH	NO AFB	NO GROWTH	MTB DETECTED	NOT DONE	59.9	113	92	FEATURES S/O TB MENINGITIS	TB MENINGITIS
57	46	M	DM	30	183	ACELLULAR	NIL	NO GROWTH	NO AFB	NO GROWTH	MTB NOT DETECTED	NOT DONE	57.7	119	103	FEATURES S/O BACTERIAL MENINGITIS	BACTERIAL MENINGITIS
58	53	M	NIL	66	28	ACELLULAR	NIL	NO GROWTH	NO AFB	NO GROWTH	MTB NOT DETECTED	NOT DONE	69.9	122	105	FEATURES S/O MENINGITIS	VIRAL MENINGITIS
59	58	F	DM	22	166	predominantly PMN	NIL	NO GROWTH	NO AFB	NO GROWTH	MTB NOT DETECTED	NOT DONE	454.3	109	90	FEATURES S/O BACTERIAL MENINGITIS	BACTERIAL MENINGITIS
60	48	F	HIV	29	228	Predominantly LYMPHOCYTES	NIL	NO GROWTH	NO AFB	NO GROWTH	MTB NOT DETECTED	NEGATIVE	169.8	115	105	FEATURES S/O TB MENINGITIS	TB MENINGITIS
61	36	M	NIL	50	30	ACELLULAR	NIL	NO GROWTH	NO AFB	NO GROWTH	MTB NOT DETECTED	NOT DONE	28.9	122	103	NORMAL STUDY	VIRAL MENINGITIS
62	41	M	NIL	27	156	ACELLULAR	NIL	NO GROWTH	NO AFB	NO GROWTH	MTB DETECTED	NOT DONE	98.7	117	99	FEATURES S/O TB MENINGITIS	TB MENINGITIS
63	38	F	NIL	31	201	predominantly PMN	NIL	NO GROWTH	NO AFB	NO GROWTH	MTB NOT DETECTED	NOT DONE	154.7	119	100	FEATURES S/O BACTERIAL MENINGITIS	BACTERIAL MENINGITIS
64	17	M	NIL	34	123	ACELLULAR	NIL	NO GROWTH	NO AFB	NO GROWTH	MTB NOT DETECTED	NOT DONE	188.9	117	102	FEATURES S/O BACTERIAL MENINGITIS	BACTERIAL MENINGITIS
65	29	F	NIL	57	28	ACELLULAR	NIL	NO GROWTH	NO AFB	NO GROWTH	MTB NOT DETECTED	NOT DONE	49.6	125	106	FEATURES S/O HSV MENINGOENCEPHALITIS	VIRAL MENINGITIS
66	43	F	HIV	33	455	Predominantly LYMPHOCYTES	NIL	NO GROWTH	NO AFB	NO GROWTH	MTB NOT DETECTED	POSITIVE	52	115	98	FEATURES S/O CRYPTOCOCCAL MENINGOENCEOHALITIS	FUNGAL MENINGITIS
67	58	M	DM	51	375	Predominantly LYMPHOCYTES	NIL	NO GROWTH	NO AFB	NO GROWTH	MTB DETECTED	NOT DONE	91	118	98	FEATURES S/O TB MENINGITIS	TB MENINGITIS
68	37	F	NIL	35	253	ACELLULAR	NIL	NO GROWTH	NO AFB	NO GROWTH	MTB NOT DETECTED	NOT DONE	79.3	115	96	FEATURES S/O TB MENINGITIS	TB MENINGITIS
69	20	M	NIL	29	178	predominantly PMN	GRAM POSITIVE COCCUS	S.pneumoniae	NO AFB	NO GROWTH	MTB NOT DETECTED	NOT DONE	146.5	116	96	FEATURES S/O BACTERIAL MENINGITIS	BACTERIAL MENINGITIS
70	29	F	NIL	33	199	ACELLULAR	NIL	NO GROWTH	NO AFB	NO GROWTH	MTB NOT DETECTED	NOT DONE	99.4	120	99	FEATURES S/O MENINGITIS	BACTERIAL MENINGITIS

71	33	F	NIL	63	37	Predominantly LYMPHOCYTES	NIL	NO GROWTH	NO AFB	NO GROWTH	MTB NOT DETECTED	NOT DONE	44.7	125	104	NORMAL STUDY	VIRAL MENINGITIS
72	27	M	NIL	37	156	ACELLULAR	NIL	NO GROWTH	NO AFB	NO GROWTH	MTB NOT DETECTED	NOT DONE	75	118	100	FEATURES S/O TB MENINGITIS	TB MENINGITIS
73	45	F	DM	73	30	ACELLULAR	NIL	NO GROWTH	NO AFB	NO GROWTH	MTB NOT DETECTED	NOT DONE	33.2	124	102	FEATURES S/O MENINGITIS	VIRAL MENINGITIS
74	35	M	HIV	32	177	Predominantly LYMPHOCYTES	NIL	NO GROWTH	NO AFB	NO GROWTH	MTB DETECTED	NOT DONE	251.1	116	99	FEATURES S/O TB MENINGITIS	TB MENINGITIS
75	42	M	NIL	26	356	Predominantly LYMPHOCYTES	NIL	NO GROWTH	NO AFB	NO GROWTH	MTB NOT DETECTED	NOT DONE	88.4	111	95	FEATURES S/O BACTERIAL MENINGITIS	BACTERIAL MENINGITIS
76	57	F	NIL	30	146	ACELLULAR	GRAM POSITIVE COCCUS	NO GROWTH	NO AFB	NO GROWTH	MTB NOT DETECTED	NOT DONE	192.6	119	101	FEATURES S/O BACTERIAL MENINGITIS	BACTERIAL MENINGITIS
77	28	F	NIL	25	221	Predominantly LYMPHOCYTES	NIL	NO GROWTH	NO AFB	NO GROWTH	MTB DETECTED	NOT DONE	136.3	112	93	FEATURES S/O TB MENINGITIS	TB MENINGITIS
78	20	M	NIL	56	32	ACELLULAR	NIL	NO GROWTH	NO AFB	NO GROWTH	MTB NOT DETECTED	NOT DONE	40	125	104	NORMAL STUDY	VIRAL MENINGITIS
79	48	F	DM	70	35	Predominantly LYMPHOCYTES	NIL	NO GROWTH	NO AFB	NO GROWTH	MTB NOT DETECTED	NOT DONE	25.8	124	103	FEATURES S/O HSV MENINGOENCEPHALITIS	VIRAL MENINGITIS
80	53	M	DM	45	244	predominantly PMN	NIL	NO GROWTH	NO AFB	NO GROWTH	MTB NOT DETECTED	NOT DONE	337.4	117	100	FEATURES S/O MENINGITIS	BACTERIAL MENINGITIS
81	65	F	NIL	30	193	ACELLULAR	NIL	NO GROWTH	NO AFB	NO GROWTH	MTB NOT DETECTED	NOT DONE	77.2	111	94	FEATURES S/O TB MENINGITIS	TB MENINGITIS
82	46	F	DM	24	274	Predominantly LYMPHOCYTES	NIL	NO GROWTH	NO AFB	NO GROWTH	MTB DETECTED	NOT DONE	201.2	112	99	FEATURES S/O TB MENINGITIS	TB MENINGITIS
83	24	M	HEAD INJURY	32	188	Predominantly LYMPHOCYTES	NIL	NO GROWTH	NO AFB	NO GROWTH	MTB NOT DETECTED	NOT DONE	332.8	118	97	FEATURES S/O BACTERIAL MENINGITIS	BACTERIAL MENINGITIS
84	39	M	NIL	55	36	Predominantly LYMPHOCYTES	NIL	NO GROWTH	NO AFB	NO GROWTH	MTB NOT DETECTED	NOT DONE	21.9	123	107	FEATURES S/O VIRAL MENINGITIS	VIRAL MENINGITIS
85	26	M	NIL	36	277	ACELLULAR	NIL	NO GROWTH	NO AFB	NO GROWTH	MTB DETECTED	NOT DONE	145.7	110	94	FEATURES S/O TB MENINGITIS	TB MENINGITIS
86	24	F	NIL	47	20	ACELLULAR	NIL	NO GROWTH	NO AFB	NO GROWTH	MTB NOT DETECTED	NOT DONE	31	122	106	FEATURES S/O VIRAL MENINGITIS	VIRAL MENINGITIS
87	16	F	NIL	29	164	Predominantly LYMPHOCYTES	NIL	NO GROWTH	NO AFB	NO GROWTH	MTB NOT DETECTED	NOT DONE	102.2	115	95	FEATURES S/O TB MENINGITIS	TB MENINGITIS
88	44	M	DM	66	243	predominantly PMN	NIL	NO GROWTH	NO AFB	NO GROWTH	MTB NOT DETECTED	NOT DONE	297.4	110	103	NORMAL STUDY	BACTERIAL MENINGITIS

89	69	M	DM/HT	55	133	Predominantly LYMPHOCYTES	NIL	NO GROWTH	NO AFB	NO GROWTH	MTB NOT DETECTED	NOT DONE	173.2	119	96	FEATURES S/O BACTERIAL MENINGITIS	BACTERIAL MENINGITIS
90	55	F	NIL	52	22	Predominantly LYMPHOCYTES	NIL	NO GROWTH	NO AFB	NO GROWTH	MTB NOT DETECTED	NOT DONE	41.5	122	106	FEATURES S/O VIRAL MENINGITIS	VIRAL MENINGITIS
91	16	M	NIL	60	215	predominantly PMN	GRAM NEGATIVE DIPLOCOCCUS	NO GROWTH	NO AFB	NO GROWTH	MTB NOT DETECTED	NOT DONE	98.6	120	101	FEATURES S/O MENINGITIS	BACTERIAL MENINGITIS
92	47	M	DM	56	333	ACELLULAR	NIL	NO GROWTH	NO AFB	NO GROWTH	MTB NOT DETECTED	NOT DONE	77.4	111	94	FEATURES S/O TB MENINGITIS	TB MENINGITIS
93	38	F	NIL	33	189	predominantly PMN	NIL	S.pneumoniae	NO AFB	NO GROWTH	MTB NOT DETECTED	NOT DONE	111.4	115	99	FEATURES S/O BACTERIAL MENINGITIS	BACTERIAL MENINGITIS
94	22	M	NIL	27	228	ACELLULAR	NIL	NO GROWTH	NO AFB	NO GROWTH	MTB DETECTED	NOT DONE	76.3	113	99	FEATURES S/O TB MENINGITIS	TB MENINGITIS
95	41	F	DM	67	23	Predominantly LYMPHOCYTES	NIL	NO GROWTH	NO AFB	NO GROWTH	MTB NOT DETECTED	NOT DONE	47.2	125	106	FEATURES S/O MENINGITIS	VIRAL MENINGITIS
96	34	F	NIL	65	30	ACELLULAR	NIL	NO GROWTH	NO AFB	NO GROWTH	MTB NOT DETECTED	NOT DONE	33.7	120	104	FEATURES S/O HSV MENINGOENCEPHALITIS	VIRAL MENINGITIS
97	63	M	DM/HT	43	166	Predominantly LYMPHOCYTES	NIL	NO GROWTH	NO AFB	NO GROWTH	MTB DETECTED	NOT DONE	112.4	117	92	FEATURES S/O TB MENINGITIS	TB MENINGITIS
98	56	M	DM	38	304	ACELLULAR	NIL	NO GROWTH	NO AFB	NO GROWTH	MTB NOT DETECTED	NOT DONE	326.5	118	99	FEATURES S/O BACTERIAL MENINGITIS	BACTERIAL MENINGITIS
99	37	F	NIL	34	199	ACELLULAR	NIL	NO GROWTH	NO AFB	NO GROWTH	MTB NOT DETECTED	NOT DONE	356.9	120	103	FEATURES S/O BACTERIAL MENINGITIS	BACTERIAL MENINGITIS
100	52	M	DM	53	175	Predominantly LYMPHOCYTES	NIL	NO GROWTH	NO AFB	NO GROWTH	MTB NOT DETECTED	NOT DONE	132.7	116	101	FEATURES S/O TB MENINGITIS	TB MENINGITIS