A STUDY ON THE TREATMENT PATTERN OF LEPROSY INCLUDING PREVALENCE OF THE DISEASE, ADR MONITORING AND ASSESSMENT OF ADHERENCE TO DRUG THERAPY

A Dissertation submitted to

THE TAMIL NADU Dr. M.G.R. MEDICAL UNIVERSITY

CHENNAI - 600 032

In partial fulfilment of the requirements
for the award of the Degree of

MASTER OF PHARMACY
IN
BRANCH VII - PHARMACY PRACTICE

Submitted by

FAHAD. P

REGISTRATION No. 261640705

Under the Guidance of

Dr. M. KUMAR M.Pharm., Ph.D.

Professor

DEPARTMENT OF PHARMACY PRACTICE

PADMAVATHI COLLEGE OF PHARMACY

& RESEARCH INSTITUTE

PERIYANAHALLI-635 205, DHARMAPURI (DT.),

TAMILNADU.

MAY – 2019

EVALUATION CERTIFICATE

This is to certify that this dissertation work entitled **"A STUDY ON THE TREATMENT PATTERN OF LEPROSY INCLUDING PREVALENCE OF THE DISEASE, ADR MONITORING AND ASSESSMENT OF ADHERENCE TO DRUG THERAPY"** is the Bonafied work carried out by **FAHAD. P, Register No: 261640705** under the guidance of **Dr. M. KUMAR, M Pharm Ph. D.,** Professor, Department of Pharmacy Practice, for the partial fulfilment of the requirement of award for **Master of Pharmacy** and this is forwarded to **The Tamilnadu Dr. M.G.R Medical University, Chennai** during the academic year **2018 – 2019** has been evaluated on_____

Evaluators:

1. 2.

CERTIFICATES

CERTIFICATE

This is to certify that this dissertation work entitled **"A STUDY ON THE TREATMENT PATTERN OF LEPROSY INCLUDING PREVALENCE OF THE DISEASE, ADR MONITORING AND ASSESSMENT OF ADHERENCE TO DRUG THERAPY"** is the Bonafied work carried out by **FAHAD. P, Register No: 261640705** under the guidance of **Dr. M. KUMAR, M Pharm Ph. D.,** Professor, Department of Pharmacy Practice, for the partial fulfilment of the requirement of award for **Master of Pharmacy** and this is forwarded to **The Tamilnadu Dr. M.G.R Medical University, Chennai** during the academic year **2018 – 2019.**

PRINCIPAL

Dr. D.C. PREM ANAND M.Pharm., Ph.D.,

Padmavathi College of Pharmacy & Research Institute,

Periyanahalli, Dharmapuri, Tamilnadu – 635 205.

CERTIFICATE

This is to certify that this dissertation work entitled **"A STUDY ON THE TREATMENT PATTERN OF LEPROSY INCLUDING PREVALENCE OF THE DISEASE, ADR MONITORING AND ASSESSMENT OF ADHERENCE TO DRUG THERAPY"** is the Bonafied work carried out by **FAHAD. P, Register No: 261640705** under the guidance of **Dr. M. KUMAR, M Pharm Ph.D.,** Professor, Department of Pharmacy Practice, for the partial fulfilment of the requirement of award for **Master of Pharmacy** and this is forwarded to **The Tamilnadu Dr. M.G.R Medical University, Chennai** during the academic year **2018 – 2019.**

Dr. G. GOPI M.Pharm., Ph.D.,
HOD
Department of Pharmacy Practice,
Padmavathi College of Pharmacy
& Research Institute
Dharmapuri, Tamilnadu – 635 205.

CERTIFICATE

This is to certify that this dissertation work entitled **"A STUDY ON THE TREATMENT PATTERN OF LEPROSY INCLUDING PREVALENCE OF THE DISEASE, ADR MONITORING AND ASSESSMENT OF ADHERENCE TO DRUG THERAPY"** is the Bonafied work carried out by **FAHAD. P, Register No: 261640705** under the guidance of **Dr. M. KUMAR, M Pharm Ph. D.,** Professor, Department of Pharmacy Practice, for the partial fulfilment of the requirement of award for **Master of Pharmacy** and this is forwarded to **The Tamilnadu Dr. M.G.R Medical University, Chennai** during the academic year **2018 – 2019.**

Dr. M. KUMAR., M. Pharm., Ph.D.,

GUIDE

Department of Pharmacy Practice,
Padmavathi College of Pharmacy
& Research Institute
Dharmapuri, Tamilnadu – 635 205.

DECLARATION

I Hereby I declare that this thesis work **"A STUDY ON THE TREATMENT PATTERN OF LEPROSY INCLUDING PREVALENCE OF THE DISEASE, ADR MONITORING AND ASSESSMENT OF ADHERENCE TO DRUG THERAPY"** is the Bonafied work has been originally carried out by myself under the guidance and supervision of **Dr. M. KUMAR, M. Pharm., Ph.D.,** Assistant Professor, Department of Pharmacy Practice, Padmavathi College of Pharmacy and Research Institute, Periyanahalli, Dharmapuri, Tamilnadu. I also declare that the matter embodied in its original and the same has not previously formed the basis for the award of any degree, diploma, associateship or fellowship of any other university or institution.

Place : Dharmapuri **FAHAD .P**

Date : **Reg. No. 261640705**

ACKNOWLEDGEMENT

ACKNOWLEDGEMENT

The task of preparing this dissertation has been fascinating experience and it is really a movement of great pleasure for me to express my hearty gratitude to those who have helped me in success full completion of this dissertation.

First and foremost, I would like to thank **Almighty God** for showering his immense blessings upon me and granting me the courage, wisdom, health and strength to undertake this thesis work and enabling me to its completion.

I would like to express my sincere thanks to **Kalvi Kodai Vallal, Mr. M.G. Sekhar**, **B.A., B.L.,** EX.M.L.A., Chairman, Sapthagiri, Padhmavathi & Pee Gee group of institutions for granting me permission to utilize all the facilities and amenities successfully to achieve this task.

It is a delightful moment for me, to put into words all my deep sense gratitude to my beloved and esteemed guide, **Dr. Anish Kumar, Pharm D.,** Assistant Professor, Department of Pharmacy Practice, Padmavathi College of Pharmacy & Research Institute, for her unstinted guidance, innovating ideas, constructive criticism and continuous supervision, and also for making the requisite arrangement to enable me to complete my project work.

I would like to express my sincere thanks to **Prof. Dr. D.C. PREM ANAND., M.Pharm., Ph.D. Principal,** Padmavathi College of Pharmacy and Research Institute, for permitting to carry out the work.

I would like to express my sincere thanks to **Dr. G. Gopi M Pharm Ph.D.,** Head, and Department of Pharmacy Practice for the valuable and right direction to my work.

I would like to express my sincere thanks to **Prof. Dr. R. Anandan, M.Pharm. Ph.D., Professor** Department of Pharmacology, Padmavathi College of Pharmacy & Research Institute.

I would like to thank **Prof. Raja, M.Pharm** and **Mrs. Gnanamabigai, M.Pharm.** Department of Pharmacognosy to give me valuable and right direction to my work.

I would like to thank **Dr. NS Surendiran, M Pharm., Ph. D., Head, Department of Pharmaceutics, Mr. S. Rajesh Kumar, M. Pharm.,** gave me valuable suggestions and encouragement to my project. I would like to thank **Mrs. Usha**., Librarian, Padmavathi College of Pharmacy and Research institute. I place on record, sincere acknowledgement to all teaching and non-teaching staff of Padmavathi College of Pharmacy. I would like to thank **Mr. R. Ramesh, Office Incharge** for esteemed help. I take this opportunity to express gratitude to my dearest classmates for all their help and support when I needed them. Words have no power to pay regards to my most beloved parents and siblings for their prayers, love and inspiration bestowed upon to me without which I would not have accomplished the completion of my thesis work. I greatly acknowledge my friends and my juniors for generous help during my project work. The chain of gratitude would be definitely incomplete if I would forget to thank the first cause of the chain, using Aristotle's words.

A very special gratitude goes out to all down at the Krishnagiri Government District Head Quarters Hospital for helping us and providing their time for our work.

We extend our deepest sense of gratitude to the Institutional Human Ethics Committee of Padmavathi College of Pharmacy and Government District Head Quarters Hospital for granting us the approval to undertake this project.

It is our radiant sentiment to place on record our best regards and gratitude to **Dr. Ashok Kumar, D.Ortho**, Joint Director of Health Service, Govt. District Head Quarters Hospital Krishnagirifor providing us the facilities, support, careful and precious guidance which were extremely valuable for our study both theoretically and practically.

We also thank **Dr Rajkumar, MBBS, MD** government District Head Quarters Hospital Krishnagiri for supervision and co-operation in completion of this work.

Our sincere thanks also goes to all the physicians, Pharmacist, Counselors, Nurses and every other staffs, in Emergency Department, Krishnagiri Government District Quarters Hospital, who provided us an opportunity to join their team and who gave access to the patients and other facilities. Without their precious support, it would not have been possible to conduct this study.

Bearing in mind we use this opportunity to express our deepest gratitude and special thanks to all the physicians at Krishnagiri Government District Quarters Hospital, who in spite of being extraordinarily busy with their duties, took out time to hear, guide and keep us in correct path and extending their support.

We also thank our fellow classmates for the stimulating discussions, for the sleepless nights we were working together before deadlines, and all the support. We also thank our friends in Padmavathi College of Pharmacy.

We would like to thank all those whose assistants proved to be a milestone in the accomplishment of our end goal.

Finally, our deepest gratitude goes to our beloved parents and family for all the love, moral support and the amazing encouragement they have given us over the years.

FAHAD. P

Reg. No: 261640705

DEDICATED TO

MY BELOVED FAMILY,

TEACHERS AND FRIENDS

CONTENTS

CONTENTS

LIST OF TABLES

LIST OF FIGURES

LIST OF ABBREVIATIONS

Abbreviations	Expansions
WHO	World Health Organization
NVBDCP	National Vector Borne Disease Control Programme
CQ	Chloroquine
PV	*Plasmodium vivax*
PF	*Plasmodium falciparum*
CQR	Chloroquine Resistance
AQ	Amodiaquine
MQ	Mefloquine
PQ	Primaquine
SP	Sulphadoxine + Pyrimethamine
AS	Atemisinin
ACT	Antimalarial Combination Therapy
BD	Twice daily
OD	Once daily
GGT	Gamma Glutamine Transferase
ALT	Alanine Amino Transferase
AST	Aspartate Amino Transferase
ALP	Alkaline Phosphatase
ADR	Adverse Drug Reaction
ADEs	Adverse Drug Event
AH&RC	Adhichunchanagiri Hospital & Research Center

CIMS	Current Index of Medical Specialities
G6PD	Glucose 6 Phosphate Deficiency
AO	Acridine Orange
QBC	Quantitative Buffy Coat
RDT	Rapid Diagnostic Test
RR	Risk Ratio
OBG	Obstetrics And Gynaecology

1. INTRODUCTION

Leprosy is a disease of public health concern mainly because of its potential to cause disability in a small proportion of those affected and is a cause for social stigma and discrimination.**[1]** The World Health Organization's (WHO) 2011-2015 global strategy for leprosy control focuses on reducing the rate of new leprosy cases with grade II disabilities per 100,000 people by at least 35% at the end of 2015 taking 2010's occurrence as reference. Leprosy, also known as Hansen's disease (HD) is a chronic infectious disease caused by *Mycobacterium leprae*, principally affecting the peripheral nerve, mucosa of the respiratory tract and the skin of human being. [2]

HISTORY ANDPREVALENCE

Leprosy has affected humanity for over 4,000 years, and was well-recognized in the civilizations of ancient China, Egypt, and India [3].Leprosy was referred to as "Kushtha" in ancient India. The first authentic description of leprosy and its treatment is given in "SushrutaSamhita", a treatise written in India in 600 BC[4]. Hansen's disease named after a physician called GerhadArmaver Hansen who discovered '*Mycobacterium leprae*in 1873 [2]. Till the introduction of the drug Dapsone in 1940s there was no treatment for this disease; patients were kept in isolation. India contributes to more than 50 % of new cases detected globally every year .A total of 1.27 lakh new cases were detected during the year 2011 -2012.A total of 0.83 lakh cases are on record as on 1stApril 2012 given the prevalence rate (PR) of 0.68 per 10,000population.[1]

DETERMINANTS OFLEPROSY

Transmission of Leprosy from source of infection to susceptible host is determined by a number of factors related to agent, host and environment. The causative agent, *Mycobacterium leprae*is an obligate intracellular acid fast bacillus (AFB) multiplying mainly inside the macrophages of the skin (histiocytes) and of the nerves (Schwann cells). Open cases of lepromatous leprosy constitute the principal source of infection. Microorganisms escape from broken nodules and secretion from mouth, nose and pharynx. Upper respiratory tract and skin are the two important routes of entry for the bacilli[4]. Incubation period for leprosy is variable from few weeks to even 20 years. The average incubation period is said to be 5–7 years[1].

Host factors include age, gender, immunity & socio – economic factors. Leprosy is known to occur at all ages ranging from early infancy to very old age.[4] The age at which leprosy occurs depends upon opportunities for exposure to infection [5]. Although leprosy affects both sexes, in most parts of the world males are affected more frequently than females, often in the ratio of 2:1. Higher number of leprosy cases is seen in some hilly, tribal, and other isolated communities. Susceptibility to tuberculoid leprosy is probably related to HLA types.[4]

Leprosy is found more in tropical areas. Large family size and dwellings, especially in urban slums, increase the chance of contact and transmission due to overcrowding. Contact with leprosy infected persons is slightly to be more among the poor and the ignorant. Children of parents suffering from leprosy have higher risk for developing the disease. Because of the increased social stigma associated

with the disease there is a delay in seeking the treatment, thereby increasing the possibility of transmission[5].

PATHOGENESIS OFLEPROSY

Leprosy primarily affects the skin and peripheral nerves. It can also affect the upper respiratory tract eyes, liver, testes, kidney, muscles and bones [4]. Bacilli enter the body through the respiratory system and migrate towards the neural tissue and enter Schwann cells. Bacteria can also be found in macrophages, muscle cells and endothelial cells of blood vessels. Within the cells bacilli start multiplying slowly (12-14 days for one bacterium to divide into two), get liberated from the destroyed cells and enter other unaffected cells. Until this stage person remains free from signs and symptoms of leprosy. Multiplication of bacilli, results in increased bacterial load in the body and the infection is recognized by the immunological system. Lymphocytes and macrophages invade the infected tissue resulting in the appearance of clinical manifestations as involvement of nerves with impairment of sensation and or skin patch. Specific and effective cell mediated immunity offers protection to a person against leprosy [1].

CLASSIFICATION OFLEPROSY

In the National leprosy eradication programme the classification is done according to whether leprosy is of multi -bacillary or pauci -bacillary type. [1]

Table:-1

Characteristics of PB and MB form of Leprosy

Sl.NO.	Characteristics	PB(Pauci bacillary)	MB(Multi bacillary)
1.	Skin lesions	1-5 lesions	6 and above
2.	Peripheral nerve involvement	No nerve/only one nerve with or without 1-5 lesions.	More than 1 nerveirrespectiveof number of skin lesions
3.	Skin smear	Negative at all sites	Positive at any sites.

Table 2

Characteristics of sub-types of borderline leprosy [4]

Characteristics	**Borderline-Tuberculoid (BT)**	**Mid- Borderline (BB)**	**Borderline Lepromatous (BL)**
Skin lesions: Number	Few	Some	Many
Distribution	Asymmetrical	Asymmetrical	Roughly symmetrical
Description	Usually well-demarcated, Somewhat dry. May be annular with clearly defined outer Border. Surface may Be scaly.	Less well-demarcated, Somewhat shiny lesions. often annular lesions with characteristic, punched-out appearance (the outer border is vague, whilethe inner border is clearly Defined).	Shiny macules, papules, nodules and plaques with sloping edges
Sensory impairment in lesions	Marked	Moderate	Slight
Peripheral nerve involvement	Widespread or asymmetrical	Widespread or asymmetrical	Widespread and less Asymmetrical
Pauci- bacillary or multi – bacillary	Pauci – bacillary	Multi – bacillary	Multi – bacillary
Reactions	Reversal (Type 1)	Reversal (Type 1)	Reversal and/or ENL (Type 2)

CLINICAL FEATURES OFLEPROSY

Leprosy symptoms generally appear three to five years after a person becomes infected with bacteria that cause the disease. The symptoms include :Hypo- pigmented or reddish skin lesions with decreased sensation to touch, heat, or pain and lesions do not heal after several weeks to months; Numbness or absent sensation in the hands, arms, feet, and legs; Muscle weakness; Eye problems; Skin rash; Skin stiffness ; Infiltration/thickening of skin:- Reddish or skin colored nodules or smooth shiny diffuse thickening of skin without loss of sensation ; Involvement of peripheral nerves:- Cord like thickening of nerves with or without pain and tenderness: especially behind the ear, around elbow, wrist, knee and ankle joints.Disabilities and deformities of hands, feet and eyes [3]

DIAGNOSIS

Cardinal Signs of Leprosy include

1. Hypo - pigmented or erythematous, well-defined skin lesions, e.g. macules or plaques, with definite loss ofsensation.
2. Signs of peripheral nerve damage, such as sensory loss, paralysis or pseudomotor dysfunction with or without nerveenlargement.
3. Finding acid-fast bacilli in the skin smears and/or biopsies taken from the skin lesions.

At least one of the above three must be present for the diagnosis of leprosy. Other investigations that can be used for diagnosis of Leprosy are:-Examination of nerves, Bacteriological examination, Biopsy and Histo-pathological examination, sweat function test[4]

GRADING OFDISABILITIES

Immunological reactions are the main cause of nerve damage, which in turn is the main risk factor for long term disability in leprosy [6]. Peripheral nerve involvement is the chief cause of permanent disability in leprosy .The problem of disabilitiesassumesincreasing importance not only in terms of evolving better methods of treatment, correction of deformities and rehabilitation of the disabled, but also with regard to better medical management of patients under anti - leprosy therapy [7]. The major risk factors known for leprosy disability and physical deformity are delay in diagnosis, delay in provision of proper care for the disease, multiple nerve enlargements, and the type of leprosy (pauci or multi bacillary), smear result and age (6-8) [8]. Patients developing reactions are at a higher risk of developing disabilities and deformities compared to people who do not develop reaction [1] The EHF score is used to grade the disability of the individual organ separately and to give an overall disability grade to the person. The highest grade of disability given in any of the part is used as the Disability Grade forthat patient. EHF score i.e. sum of all the individual disability grades for two eyes, two hands and two feet (0–12).[4]

DG 0 - no disability caused by leprosy in eyes, hands and feet

DG 1 – Anaesthesia present, over palm / sole but no visible deformitiy or damage...

DG 2 – Visible deformity or damage present [1]

Table 3

Deformities occurring in leprosy [4]

Face	lagophthalmos, loss of eyebrows (superciliarymadarosis) and eyelashes , corneal ulcers and opacities, perforated nose, depressed nose,
Hand	Claw hand, wrist-drop, ulcers, absorption of digits, thumb-web contracture, hollowing of the inter - osseous spaces and swollen hand.
Feet	Plantar ulcers, foot-drop, inversion of the foot, clawing of the toes, absorption of the toes, collapsed foot, swollen foot and callosities

LEPRAREACTIONS

It occurs due to sudden alteration in the immunological status of the host against the living or dead bacilli. It can occur at any time either during the course of disease, during treatment or even after the completion of treatment with MDT .There are two types of lepra reactions:-

1) Type 1Reactions

2) Type 11Reactions

Type 1 Reactions:-

It is a delayed hypersensitivity response which is also called as Reversal reactions. It presents as inflammation of the existing skin lesions i.e. increase in redness, swelling, tenderness/discomfort and rarely ulceration appearance of few new inflamed skin lesion and/or neuritis.

Type 2 Reactions:-

It is also called Erythema NodosmLeprosum (ENL).It usually occurs in MB type of leprosy. During the course of treatment a large number of bacilli are killed

and its antigen is been produced .It combines with the antibodies and form immune complexes.These immune complexes deposit within the tissue and result in inflammation .The organs that involved in these type of reaction are eyes ,testis, kidney, liver, nerve, endocardium and joints. Neuritis is always accompanied with type2 reactions. [1]

TREATMENT

The development of multidrug therapy (MDT) changed the face of leprosy dramatically. The treatment consists of combination of three drugs, Rifampicin, Dapsone, and Clofazimine. MDT made it possible to cure patients, interrupt the transmission of leprosy, and thus – most important for the social perception of the illness and to prevent disabilities. Even patients with the severest form of the disease show visible clinical improvement within weeks of starting treatment. In 1981, the WorldHealthOrganization(WHO)recommendedMDT as the standard treatmentagainst leprosy [4].

MDT introduction came with additional benefits such as an intense monitoring of patients, coverage of affected populations, and improvement of the closeness between leprosy patients and medical care, and that leprosy changed into a curable disease [9].

PB leprosy is treated with with Dapsone and rifampicin for a period of six months while MB leprosy is treated with Dapsone, Rifampicine and Clofazimine for a period of 12 months [10] .WHO has designed blister pack medication kits for both PB and MB leprosy. Each easy-to use kit contains medication for 28 days [11]Advantages of Multidrug Therapy [1] includeReduces chances of development

of resistance to the drugs. Duration of treatment is short and fixed.

MDT is safe, has minimal side effects and has increased patient compliance. Available in blister pack; easy to dispense, store and take.

Assessing fitness of a Leprosy patient for MDT

Treatment of leprosy under MDT depends upon the clinical group to which thepatient belongs [10]

Jaundice: If the patient is jaundiced, wait till jaundice subsides.

Anemia: If the patient is anaemic, treat it simultaneously along with MDT.

Tuberculosis: If the patient is taking rifampicin, ensure that he/she continues to take rifampicin in the dose required for the treatment of tuberculosis along with other drugs regimen required for the treatment ofLeprosy.

Allergy to sulpha drugs: If the patient is known to be allergic to sulpha drugs, dapsone should be avoided [1].

Table 4

WHO recommended treatment regimens [11]

Type of leprosy	Drugs used	Frequency of administration Adults(children inbracket)	Dosage (adult)15 years and above	Dosage children between 10-14 years	Dosage children Below
MB Leprosy	Rifampicin	Once monthly	600mg	450mg	300mg
	Clofazimine	Monthly	300mg	150mg	100mg
	Dapsone	Daily once	100mg	50mg	25mg
	Clofazimine	Daily for adults(every other day for children)	50mg	50mg(alternate day, not daily)	50mg (weekly twice)
PB Leprosy	Rifampicin	Once monthly	600mg	450mg	300mg
	Dapsone	Daily	100mg	50mg	25mg daily or 50mg alternate day

COMMON DRUGS USED FOR THE TREATMENT OF LEPROSY

CLOFAZIMINE:-

It is a dye with leprostatic and anti-inflammatory properties; which is a major advantage of clofazimine over other antileprosy drugs and therefore it has a vital role in the management of lepra reactions [12, 13]. Clofazimine is used for dapsone resistant leprosy in patients intolerant to dapsone[13]. Clofazimine acts by blocking the template function of DNA by binding to its guanine bases and there by inhibits bacterial proliferation [5]. Adverse Effects include: discoloration of skin, hair, cornea, conjunctiva, tears, sweat, and sputum. Dose related gastrointestinal symptoms include pain, nausea, vomiting and diarrhea[11].

DAPSONE:-

Dapsone was introduced as the standard chemotherapy for leprosy in 1950s and it is the most widely used sulphone for the long term therapy of both MB and PB types of leprosy [13, 14]. It is a bacteriostatic agent and acts by inhibiting the De Novo synthesis of folic acid [15]. Haemolyticanaemia is the most important toxicity and it is common in patients with G6PD deficiency. Others adverse effects include anorexia, nausea, methaemoglobinemia,headache, paresthesias, mental symptoms, hepatitis, agranulocytosis, lepra reaction and sulphone syndrome [12].

RIFAMPICIN:-

It is an important drug used in MDT regimen because of its ability to shorten the treatment duration when given in combination with dapsone. It is a bactericidal agent and acts by inhibiting the DNA dependent RNA synthesis. Adverse effects include: - Hepatitis is the major dose related adverse effect (liver damage). Other serious but rarereactionsincluderespiratorysyndrome,haemolysis, purpura,cutaneoussyndrome, flu syndrome, abdominal syndrome, renal failure [12].

OFLOXACIN

It is usually used if rifampicin is not used in the therapy or those patients who refuse to take clofazimine or to shorten the duration of the treatment.99.9% of bacteria are usually killed by 22 daily doses of monotherapy of ofloxacin. Inhibits bacterial DNA gyrase and ultimately resulting in the bacterial cell death. Usual dose: 400mg/day.Adverse effects include:-Aplastic anaemia, Hepatitis, toxic epidermal necrosis, Agranulocytosisetc[12]

MINOCYCLINE

Minocycline is a semisynthetis tetracycline. It is used in PB cases in combination with rifampicin and ofloxacin. In MB case it is used when patients refuse to take clofazimine or those patients who could not take rifampicin. It mainly helps to inhibit the protein synthesis thus by producing a bacteriostatic effect. For adults single dose of 100mg was preferred. Adverse effects include:-Vestibular disturbances, Dizziness, Vertigo GI irritations, Phototoxic reaction, hypersensitivity reaction etc[12].

MANAGEMENT OF LEPRA REACTIONS PREDNISOLONE:-

It is a synthetic glucocorticoid with weak mineralocorticoid properties. It is used for the treatment of lepra reactions or neuritis or inflammation in the eyes of the leprosy patients. It prevents the inflammation by suppressing the migration of fibroblast and reversing capillary permeability and also by controlling the rate of protein synthesis. An adverse effect mainly depends upon the dosage and duration of therapy. Common sideeffects include moon face, acne, bruising, muscle wasting,amenorrhea,hirsutismetc[4, 11].

ANALGESICS:-

Aspirin (acetyl salicylic acid) is still the cheapest effective drug for controlling the moderate degrees of pain and inflammation and it is also commonly used in cases of leprosy supportive management. 600mg given 4 times daily with meals .Dosage is reduced as signs and symptoms are being controlled. Inhibits the synthesis of prostaglandin by cyclo-oxygenase; inhibits platelet aggregation and has analgesics activity. Adverse effects include vomiting, epigastric distress, increased

occultbloodloss in stools, gastric mucosal damage, peptic ulceration, angioedema, anaphylactic reaction, vertigo, electrolyte imbalance etc[4].

THALIDOMIDE

It was banned in 160 for its teratogenic effects. But now days it is used to manage lepra reactions. It down modulates the cell surface adhesion molecules involved in leukocyte migration. Its half life is about 5-7 hour .Adverse effects:- photosensitivity, bradycardia, neuropathy, vertigo etc. Treatment with thalidomide is only recommended in tertiary care hospitals after taking necessary consent. Since this drug is teratogenic, it is contraindicated for use in women of reproductive age group [1,4].

The burden of leprosy can be measured in terms of the occurrence of reported new cases, or of the number of cases registered for treatment, or the number of cases with disabilities [8]. The consequent lack of treatment or delayed treatment resulted in an

increased risk of disabilities, which in turn strengthened and perpetuated the stigma of the disease .The principle of reducing the load of infection in society, to break the chain of infection, is the cornerstone of leprosy control work today. It implies early diagnosis and early adequate drug treatment to make the patient non-infectious [4].

SIGNIFICANCE OF THE STUDY

Current situation in Tamilnadu showed an increase in number of leprosy patients with several fresh cases being reported during the past one year. The health department data showed that 796 fresh cases of leprosy have been reported in the

state in 2014 -2015period. The highest number of fresh cases has been reported at Chennai – 111, Erode - 91, Coimbatore – 90 and Madurai -84.The rise in leprosy cases has been blamed on the growing migrant population in the state [16]. Return of this old curserevealed that Tamilnadu is no longer immune to leprosy. Multi drug therapy (MDT), which is the treatment recommended by WHO has been associated with problems like undesirable side effects, poor compliance, drug resistance and high relapse rates. Thus the present study was undertaken to assess the current prevalence of leprosy in two districts in Tamilnadu (Dharmapuri and Krishnagiri) and to analyze the treatment patterns & drug related problems like adverseeffectsassociatedwiththedisease.

LITERATURE REVIEW

B.L. Ajibade, Okunlade, Olawale Femi, O.P. Adisa, M.O.A Adeyemo[(2)]

Conducted a retrospective and cross-sectional carried out to determine the yearly prevalence, most prevalent type of leprosy ,perceived psychological impacts and modes of treatment of leprosy for a period of 5 years(January 2005 – December 2010)Sample size consisted of 77 respondents that were selected randomly. Self designed questionnaire was used to assess the perceived psychological impacts of leprosy. The study results showed a decline in yearly prevalence of leprosy. Most prevalent type of leprosy was multibacillary which accounted for 97.8 %. The issue of leprosy was pronounced in males than females with the pick recorded in the year 2005.Treatment of multibacillary leprosy were through the use of combination of rifampicin, dapsone and clofazimine. Paucibacillary was treated with combination of rifampicin and dapsone.

Harmindersingh, bithikanel, Vivekdey, pawantiwari& Naveen dulhani (2008)[(17)]

Conducted a prospective observational study carried out in the department of dermatology, Jagdalpur, to assess the adverse effects of multidrug therapy (MDT) in leprosy patients.Theadvers effects were recorded on the personal record of every individual patient, filled during the course of treatment.176 patients were included in the study, 97(55 %) were males and 79(45%) were females. 106 (60%) were treated with MDT MB and 70(40 %) were given MDT PB. Among the 176 patients, 79 had adverse effects due to one or more components of MDT, 73 had

adverse effects due to dapsone, 8 due to rifampicin and 16due to clofazimine .Mean duration for the development of adverse effects from the startoftherapy was 1.99 +/- 0.69 months for dapsone, 3.6 +/- 0.68 months for rifampicin and7.13+/- 0.79 months for clofazimine.

SileshiBaye (2011) [18]

Conducted a form of longitudinal ecological study design was employed to describe the epidemiological trends and changes of leprosy in Ethiopia from 2000 to 2011. Data on variables of interest were collected from health and health related indicator reports and database of the FMoH. Health institutions across the country routinely collect the data using a standardized Health Management Information System (HMIS) reporting format. On average, 5,034 leprosy cases were recorded nationally every year. Out of these, the average number of new cases of leprosy was 4,475 (88.9%).Multi-bacillary cases of leprosy were the predominant 3,963 (88.7%) form of the disease. Overall childhood leprosy rate and grade-2-disability rate respectively were 7.1 and 9.3 per 100 new cases. The treatment success rate was more than 86 per 100 registered cases. A yearly average relapse rate of 4.8 per 100 total cases (242 on average per year) was recorded while a total of 188 leprosy patients (3.7 per 100 total cases) defaulted from follow-up between 2000 and2011.

PSS Rao (2008) [19]

This study was done in two phases: In the first phase , a representative sample of Six leprosy mission hospitals in UP , Delhi, West Bengal , Maharashtra were chosen for estimating the defaulter rates and their association with selected socio-demographic factors. For the second phase, three of these centers were

randomly chosen for ascertaining the reasons for defaulting. A total of 6291 new untreated cases of leprosy who received MDTin the six TLM hospitals were followed up. Including the 1st dose, the overall defaulter rate for patients within the district was 46%, and for those outside the district, 60%. Patients from outside the district had significantly higher defaulter rates for both MB and PB ($p<0.05$). Of those who were contacted , the reasons for defaulting was found to be psychosocial in 176 patients (43.3 %) , health related in 102 patients(25.2 %) & medical reasons in 54 patients. Generally, the women patients defaulted more due to medical problems.

Huan-Ying Li, Lu-Fang Hu, Pei-Wei Wu, Jiu-Si Luo, and Xue-Ming Liu2 (1992) [20]

A prospective cohort study conducted to study the relapse rates after fixed duration-MDT, the critical bacterial index (BI) before MDT which is necessary to prevent relapse.657 active MB leprosy patients were put on fixed duration –MDT between 1985 & 1992 and were followed for 5 years after therapy. The study results showed that male/female ratio is 4:1 (323/79) for MB patients without & 6:1(218/37) for MB with previous dapsone therapy. Reactions occurred more frequently during the first 6 months (12%), decreasing gradually from months 7to 24 of MDT. Significantly more reactions occurred in the 20-39 age group than in the 40-59 age groups in the present study. Reactions were treated with prednisone (30-60 mg/day), gradually tapering off within 6 months. Some ENL reactions received thalidomide 200-300mg/day in addition to prednisone. Eleven patients developed hypersensitivity reactions to dapsone. Three patients developed liver damage with abnormal liver function tests after 3-20 months' administration of

MDT. They received palliative therapy for liver damage and MDT was continued after a temporarybreak.

ShivlalRawlani*, Adarshlata Singh, Rahul Bhowte*, ShirishDegwekar*et-al (2012)[21]**

Cross-sectional study to assess cutaneous and mucocutaneous lesions in leprosy patients taking multidrug Therapy .The study population comprised of 30 admitted leprosy patients for taking multidrug treatment .The study was conducted over a period of 7 days. The recorded data were tabulated and analyzed using chi square test and student t- test. Patches were the most common type of cutaneous lesions (90%) observed in leprosy patients taking multi drug therapy, followed by ichthyosis/dryness of skin (60%), atrophy (26.75%), and hair loss (20%) while only 13.4% patients showed papules and infiltrated lesions. There was multiple nerve involvement in patients taking multi drug therapy; out of that ulnar nerve is most commonly affected followed by radial nerve and post auricular nerve. Deformities found in these patients were in the form of claw hand (16.7%), lagophthalmos (13.4%), ulcer (6.7%) and absorption(3.3%).

Patricia d. deps *, Sofia Nasser *, Patricia guerra *, Marisa Simon*et-al (2007)[9]

Conducted a retrospective, descriptive study in Brazil to assess the, adverse effects from Multi-drug therapy in leprosy. 194 patients were included in this study, 78 (40%) male and 116 (60%) female. 40% were MB and 60% were PB; 34% of the patients were under 30 years old, 51% 31-60 year old and 15% over 60 year old. Side-effects were attributed to at least one MDT component in 88 (45%) patients;

85 had side-effects due to dapsone, 24 due to rifampicin and 18 due to clofazimine. Eighty-five patients had adverse effects from dapsone such as hemolytic anemia, gastrointestinal manifestations, hepatic abnormalities, dizziness, headache, and leucopenia. The present study shows side-effects in 88 (45%)patients and an alternative treatment regimen was needed in 47 out of 88 (24%).Alternative regimens should be administered under direct supervision : Daily administration of 50mg of clofazimine, together with 400 mg of ofloxacin and 100 mg of minocycline for 6 months; followed by daily administration of 50 mg of clofazimine, together with 100 mg of minocycline or 400 mg of ofloxacin for at least an additional 18 months could be used to replace rifampicin in adult MBpatients.

S. Karat, P. S. S. Rao and A. B. A. Karat (1971) [(7)]

Conducted an epidemiological study to assess the Prevalence of Deformities and Disabilities and nerve involvement Among Leprosy Patients in an Endemic Area (GudiyathamTaluk,, South India. The prevalence of leprosy was 29 per 1,000 populations. Of 1,780 patients, 1,721 or 97% could be assessed, these consisted of 716 men, 498womenand 507 children (under 15 years of age) .343 were lepromatous, 1,052 tuberculoid, 155 borderline, 168 indeterminate and 3 were purely neural cases. The nerves considered were the ulnar, median, radial, lateral popliteal, and facial. Lepromatous and borderline cases were the most affected (nearly two-thirds) as compared to only 23% among tuberculoid and 18% among indeterminate. The differences were highly significant ($P < .01$) the motor nerve most affected was the ulnar nerve and the least was the radial nerve. There was a significantly higher percentage of disability among patients with bacillated types.

Tigist S. et al (2010) [8]

Conducted A cross sectional retrospective study to determine the Prevalence of Disability and Associated Factors among Registered Leprosy Patients in All African Tb andLeprosyRehabilitation and Training Centre Medical records of leprosy patients registered from September 11, 2010 to September 10 , were reviewed. The calculated sample size was 513. Out of those involved in this study, 98.1% reported by themselves; of these, 328(63.9%) were male and 185(36.1%) were females patients. 25 (4.9%) of the leprosy patients were aged less than or equal to 14 years. 225 (43.9%) were aged 15 to 30 years. 172 (33.5%) were in the age group of 30-50. The remaining 91 (17.7%) were above 50 years old. 379(73.9%) of the patients were newly diagnosed cases of leprosy, 11(2.1%) were returnees after default, 35(6.8%) were relapse and the remaining 88(17.2%) were in other categories. Almost all of the patients were multi-bacillary (MB) leprosy cases, 509/513(99.2%). This study revealed that 65.9% of the leprosy patients studied had disability Grade I or II. Among those with disability, 40.2% had grade I and 25.7% had grade II disabilities. Age, duration of symptoms, sensory loss and nerve damage and reversal reaction are the factors found to be associated withdisability.

Henry et al (2014) [22]

Conducted explorative, Quantitative, Questionnaire Based Study 56 participants were recruited from ILSL: 43 outpatients, 7 inpatients and 6 residents. This exploratory study used a self-constructed, quantitative questionnaire which was delivered to participants over a seven-week recruitment period in September/October 2018. In the questionnaire, participants were asked to report the

time elapsed between first noting leprosy symptoms and visiting a medical doctor for these symptoms. This was labeled as patient delay. Participants were also asked to report the time that elapsed between their first visit to a medical doctor and them receiving a diagnosis of leprosy/Hansen's disease. This was labeled as health systemdelay. One hundred and twenty one participants, (99.2%), reported presenting to a medical doctor within 5 years of symptom onset and no patient delay exceeded 10 years.

Nitin.J.Nadkarni*Antonio Grugni*and Manjunath S Kini (1992) [24]

Conducted a fixed duration of MDT in paucibacillary patients. They analyzed the records of 1022 patients of PB leprosy who had received 6 doses of WHO-MDT alone or had post- dapsone for 6 months Monthly clinical assessments, random tablet counting, as well as urine tile testing for dapsone are done routinely to ensure compliance. The duration of post therapy surveillance ranged from 6 months to 7 years. They found that the incidence of unfavorable events was significantly higher with the classical regimen when patients were gradedasactiveattheendofthefixeddurationregimen,especiallywhenpatientswith>2les ions were considered.6 doses of MDT is adequate in the majority of patients who have few lesion or who have become inactive at the end of the treatment.

Luzivander S Soares*Rodrigo De O* Vanesa V. Vilela*et-al (2000) [25]

They investigated the impact of MDT on the epidemiological pattern of leprosy in juiz de for a, Brazil, from 1978 to 1995.Evaluation of 1283 medical charts was performed according to the treatment regimen used in two different periods. They were analyzed to determine annual incidence and prevalence of the

disease. The results show that multibacillary forms of leprosy predominate over the paucibacillary in both study periods. The number of new cases recorded in juiz de for an exceeded the number of discharge of patients on active file from city health units, such that the total number of registered casesincreased every year. They also found that there is increased incidence of leprosy at extreme ages.

A.K.Das*, J.C.Das*, A.Roy*, B.De (1993) (26)

Conducted study on the effect of multi drug therapy on leprosy: Analysis based on a study in west Tripura district. The period of study was from 1981-1993, to find the treatment pattern of leprosy. The data of all leprosy patients were been collected. The background information was collected from department of statistics government of Tripura. Statistical test of significance was done by "Z"test. The main finding of the study includes a clear decrease in number of leprosy cases and prevalence rate was also been found to be decreased with the introduction of MDT.

AIMS AND OBJECTIVES

AIM

Study the treatment pattern of leprosy in two districts in Tamilnadu.

OBJECTIVE

1) To study the prevalence of the disease.

2) Monitor presence of adverse drugreaction,

3) To study the treatment pattern of leprosy including leprareactions

4) Assess adherence to drugtherapy

METHODOLOGY

STUDYSETTING

Participants for this study were selected from various regions of Dharmapuri and Krishnagiri Districts. In KrishnagiriDistrict, the study was carried out in the dermatology department of Krishnagiri Government District Head Quarters Hospital located in the city of Krishnagiri that has grown into the premier center of treatment for several diseases in Tamilnadu. The medical college campus houses several departments like super -specialty blocks and department of chest diseases etc. The various specialities includes general medicine, radiotherapy, surgical gastroenterology, dermatology &venerology,ENT, orthopedics, preventive clinics, psychiatry, plastic surgery, ophthalmology, general surgery etc.

In Dharmapuri district data was collected from Govt. Primary Health Centre, Chinnankuppam, Dharmapuri, Govt Primary health Centre, Vellagoundanpalayam. Govt Primary health centre Chinnanguppam is a primary center for people are more depending for all types of diseases as well as Government primary health center Vellagoundanpalayam. As it is a village area, most of the population are uneducated. The literacy rate is very low in old age people.

STUDYPERIOD

A prospective observational study was carried out over a period of six months from July 2018 to December 2018among the leprosy patients who receives care from Krishnagiri and Dharmapuri districts.

STUDYDESIGN

An observational cross – sectional study was conducted in the leprosy centers in Krishnagiri and DharmapuriDistricts. Cross- sectional studies can be thought of as providing a snap shot of the frequency of health related characteristics in a population at a single point of time.

SOURCE OFDATA

Sources of data include patient's medical records; NLEP cards (National Leprosy Eradication Program) obtained from leprosy centers & filled questionnaires through personal interviews

FORMS USED IN THESTUDY

A well designed patient data collection form and medication adherence questionnaire were developed by the team members with the help of guide for recording the patient case details.

DATA COLLECTIONFORM

A data collection form was designed after assessing different standard forms that mainly covers aspects like,

- Patient demographic details - which includes the basic information of patient

along with sex, age, date ofadmission.

- SocialHistory
- Reason for consultation – which includes the clinicalfeatures
- Past medical & medication history – Co -morbidities of patient along with the drugs the patient was taking for long back was documentedhere.
- Diagnosis - it includes provisional conclusion of patient regarding the signs & symptoms and skin biopsyreports.
- Assessment of disability and nervefunction
- Treatment pattern- detailed information regarding the medication including the dose, frequency, route of administration wasrecorded.
- Adverse drug reactions – adverse reactions experienced by the patient while taking multi-drugtherapy
- Relevant laboratory parameters

MEDICATION ADHERANCEQUESTIONNAIRE

A well designed medication adherence questionnaire was developed to assess patient's adherence to drug therapy.

Medication adherence- the questionnaire consists of 12 questions evaluating the medication adherence of patients with two options to answer i.e.; yes or no .the positive results were given a score of +1 and negative results a score of -1 .the medication adherence is graded into three categories; highly adherent (>6)

moderately adherent (0-6)and non-adherent (<6).

PATIENTSELECTION

Based on the inclusion and exclusion criteria of the protocol reviewed by the ethics committee (Department of pharmacy Practice, Padmavathi college of pharmacy,and Krishnagiri Government District Head Quarters Hospital), 104 leprosy were include and enrolled for the study.

Inclusion Criteria:

- All patients diagnosed with leprosy (old and new cases)
- No age limit
- Both genders are included

Exclusion Criteria:

- Immigrantpatients
- Patients in whom the relevant data notavailable

4.6. ETHICAL COMMITTEE APPROVAL

The protocol was reviewed by the ethics committee of Department of pharmacy Practice, Padmavathi college of pharmacy and a consent was provided by the authority for the purpose of conducting the study. It was reviewed by the institutional ethics committee and approved the proposal of the dissertation.Alsoethicalcommitteeclearancewas obtained by Institutional Research Committee of Krishnagiri Government District Head Quarters Hospital and

approved the proposal dissertation.

STUDYPROCEDURE

This observational cross sectional was conducted at Krishnagiri and Dharmapuri districts over a period of six months. Study title was selected based on our area of interest and under the guidance of our project guide. We reviewed around 15 literatures related to the topic and prepared study protocol. A well designed patient data collection form and medication adherence questionnaire were developed after assessing different standard forms by the team members with the help of guide for recording the patient case details .The protocol along with the study materials were submitted to institutional ethics committee for approval and ethical clearance were obtained from our instititution and Krishnagiri Government District Head Quarters Hospitalprior to initiation of the study. Data collection was done prospectively from the secondary data available from the leprosy centers in Krishnagiri and Dharmapuridistricts and through personal interviews. Full details of the case including patient demographics, past medical and medication history, clinical features, lab investigation details, treatment pattern, adverse drug reactions and other details were brought into self designed data collectionform.Disability grade of the patient was assessed with the help of EHF(eye, hand, feet) score. Patients were categorized into grade 0, grade 1 and grade 2 disabilities. Medication adherence questionnaire was used to evaluate patient's adherence to multidrug therapy. The data was entered in Microsoft excel for easy reference and analysis of results later. The entire data collected were analyzed using different statistical method in consultation with the statistician. The sample size for the study was set as 104. Z test was used for comparison of proportion and Chi square test for testing the

goodness of fitness ofratio.

STATISTICS

The sample size for the study was set as 104 by taking the P value as 88.7 % with a confidence of 95% and an error of estimate of 6.1 %. Simple random sampling technique was adopted for drawing patients to the study. Chi square test for testing the goodness of fitness of ratio.

RESULTS

AGE WISE DISTRIBUTION OFRESPONDENTS

A total of 104 patients were included in the study. Significantly highernumber of patients belongs to the age group 31-50years (χ^2=36.385, DF=3, p<0.001). Mean ± SD of age=42.13 ± 18.61 years, followed by 16-30 and 51-99 years. Least common age group was found to be 0-15.

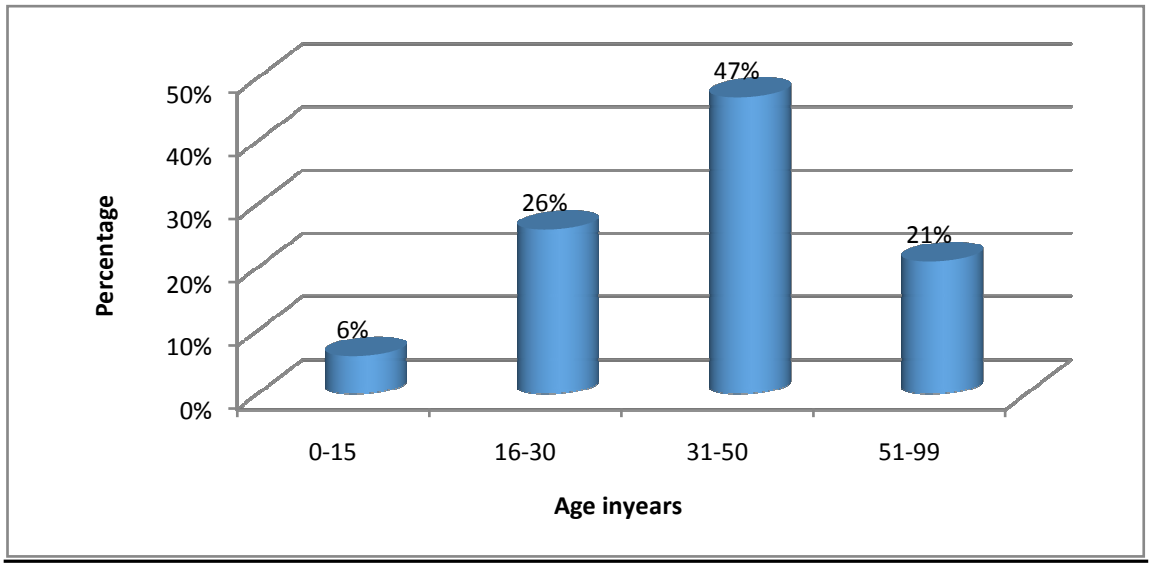

Fig:-1

GENDER WISE DISTRIBUTION OFRESPONDENTS

The gender wise distribution showed that the issue of leprosy was pronounced in males than females (χ^2 = 18.615, do = 1,p<0.001).

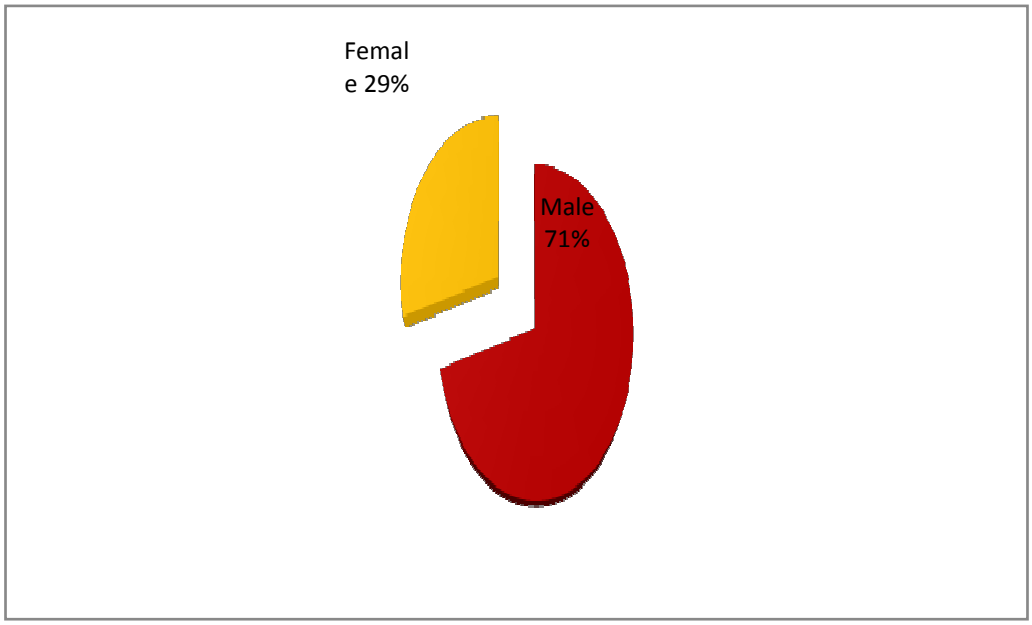

Fig:-2

RESIDENTIAL STATUS OFRESPONDENTS:-

The residential status of the responders show that no significant difference could be detected between the number of patients from rural and urban sector (χ^2 = 0.962, DF = 1, p>0.05)

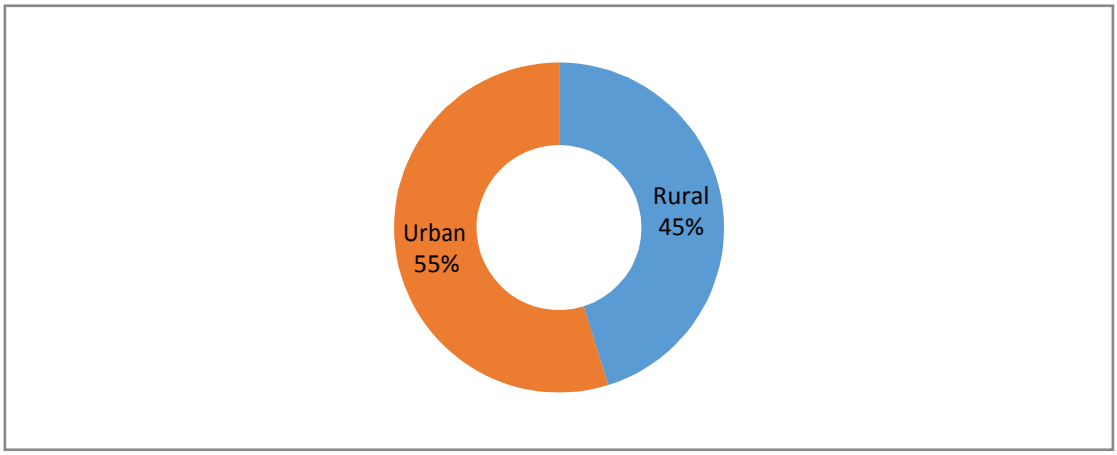

Fig:-3

EDUCATIONAL STATUS OFRESPONDENTS

Educational status of the responders were classifies as illiterate, primary secondary and tertiary. Significantly higher number of patients had secondary education (χ^2 = 25.730, DF= 3, p<0.001)

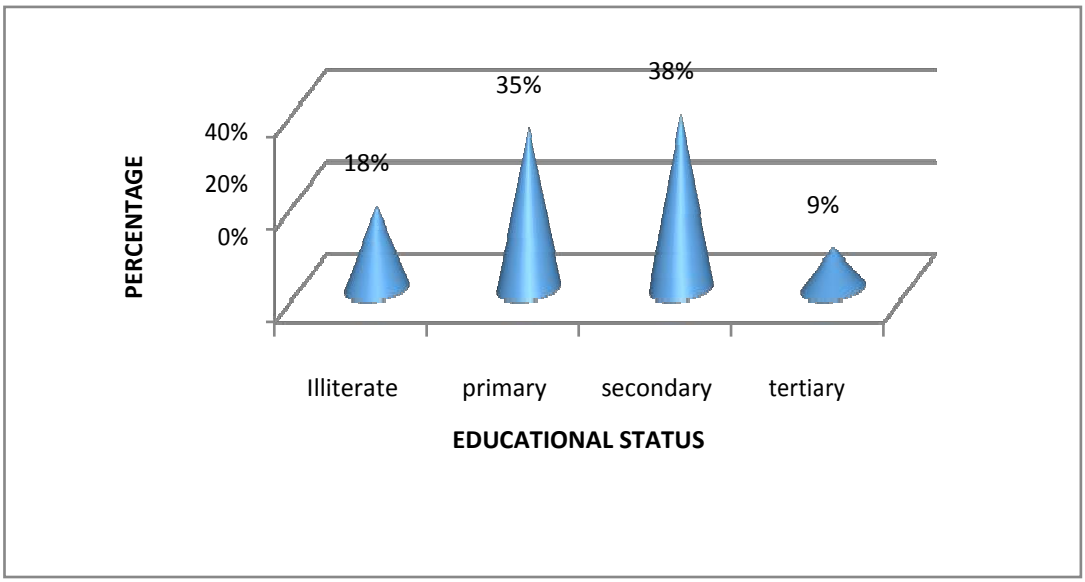

Fig:-4

TYPE OF LEPROSY

The most prevalent type of leprosy was found to be Multibacillary (MB) [χ^2 = 22.231, DF = 1, p<0.001] with 86 cases while paucibacillary (PB) type accounted for only 18 cases. This indicates that most of the respondents suffered from multibacillary types of leprosy.

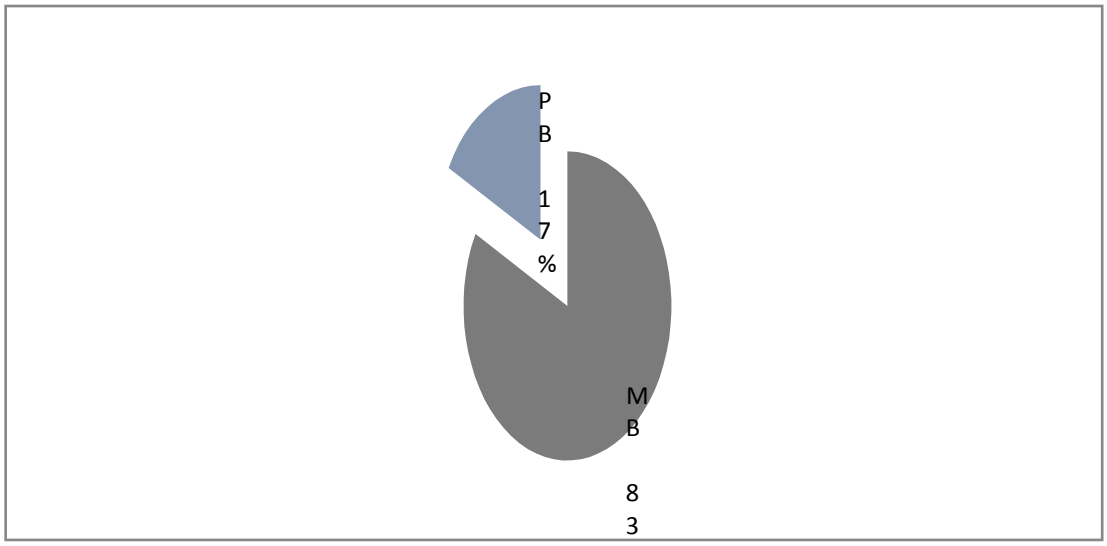

Fig:-5

CLINICAL FORM OFLEPROSY

Clinical form of leprosy were Borderline borderline, Borderline tuberculoid, borderline lepromatous, Lepromatous leprosy...Among these Borderline tuberculoid(BT) form of leprosy (69 cases) was found to be significantly higher in the sample (χ^2 = 127.391 , df = 3, p < 0.001) followed by lepromatous leprosy with 16 cases.

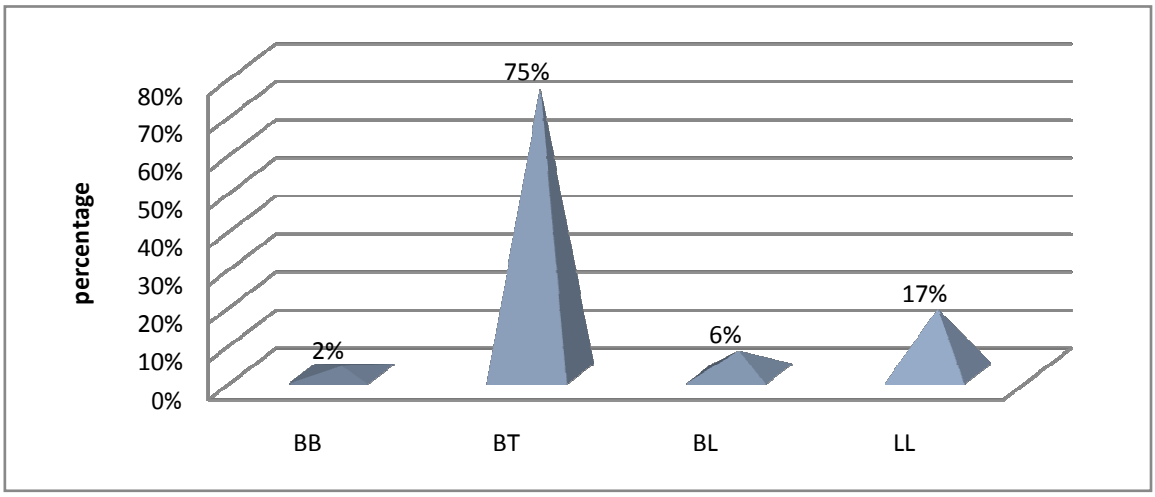

Fig:-6

CLINICAL FEATURES OFLEPROSY

88 (84.61%)Patients showed hypopigmented patches, Loss of sensation were showed by 41 (39.42%) patients followed by numbness 33 (31.73%), deformities19(18.27%),slippageofchappals 18(17.30%) ,icthyosis 11(10.58%), madarosis 7(6.73%) and epistaxis 4(3.84%) are shown in the above figure.{ χ^2 = 191.300 , df = 7 ,p<0.001}

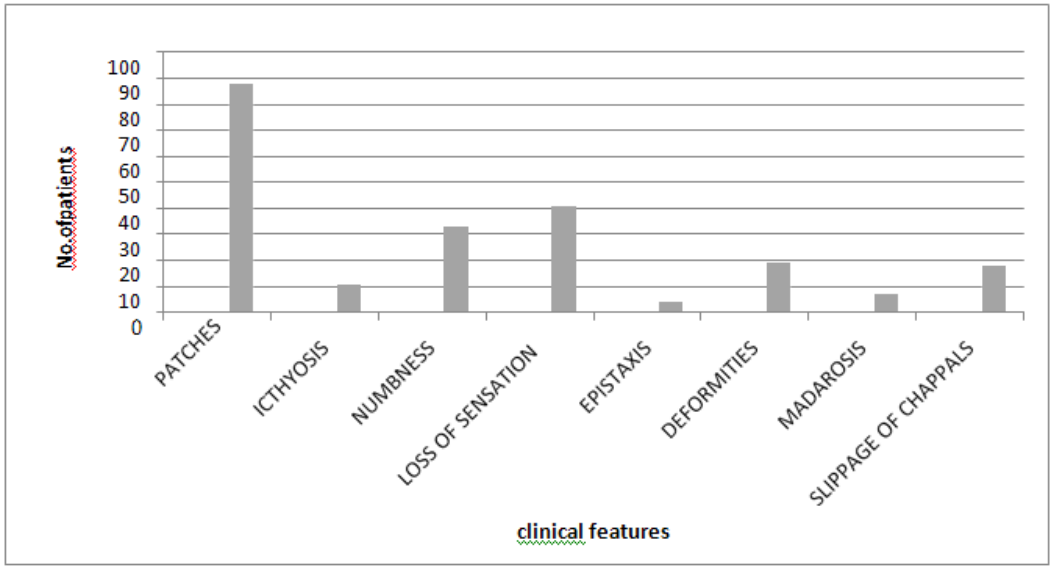

Fig:-7

DURATION OF SIGNS ANDSYMPTOMS

Duration of Signs and symptoms were found to be significantly higher in patientswith 1-10 years duration compared to the other two groups (χ^2 = 41.857,df = 2,p<0.001)

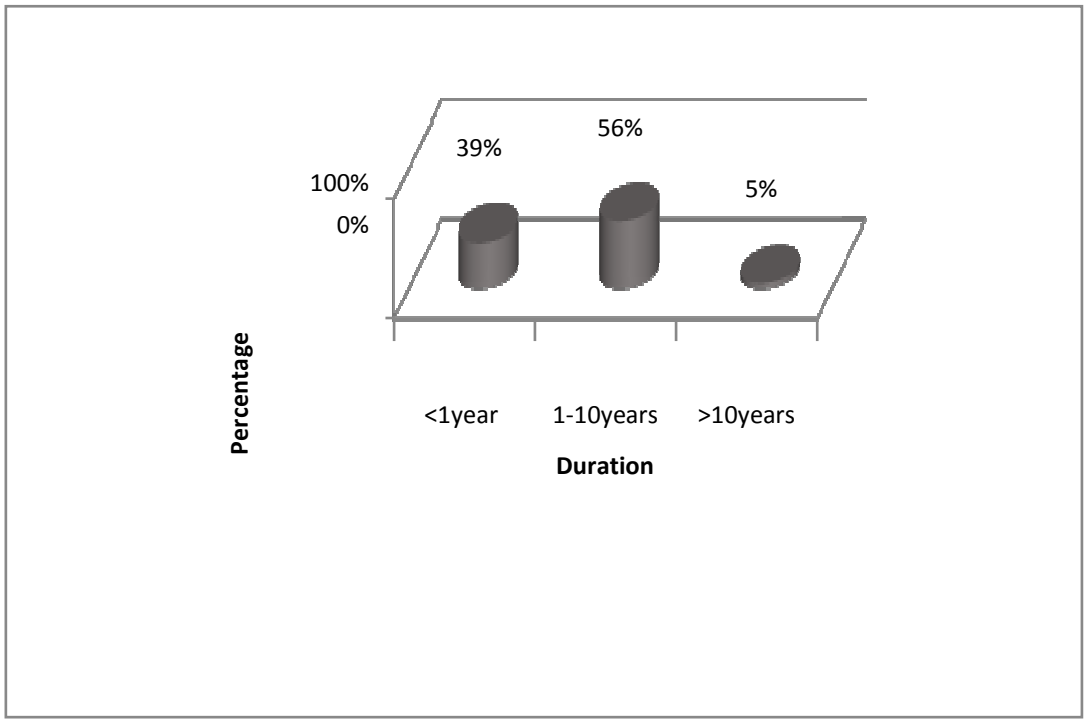

Fig:-8

TYPES OF LEPROSYPATIENTS

The patients came for the treatment were categorized as new cases(Newly reported),Retreat and Relapse .Among these New cases (84%) was found to be significantly higher than retreatment (6%) and relapse cases(10%) is shown in the above graph.[χ^2 = 122.143 , df = 2 , p <0.001]

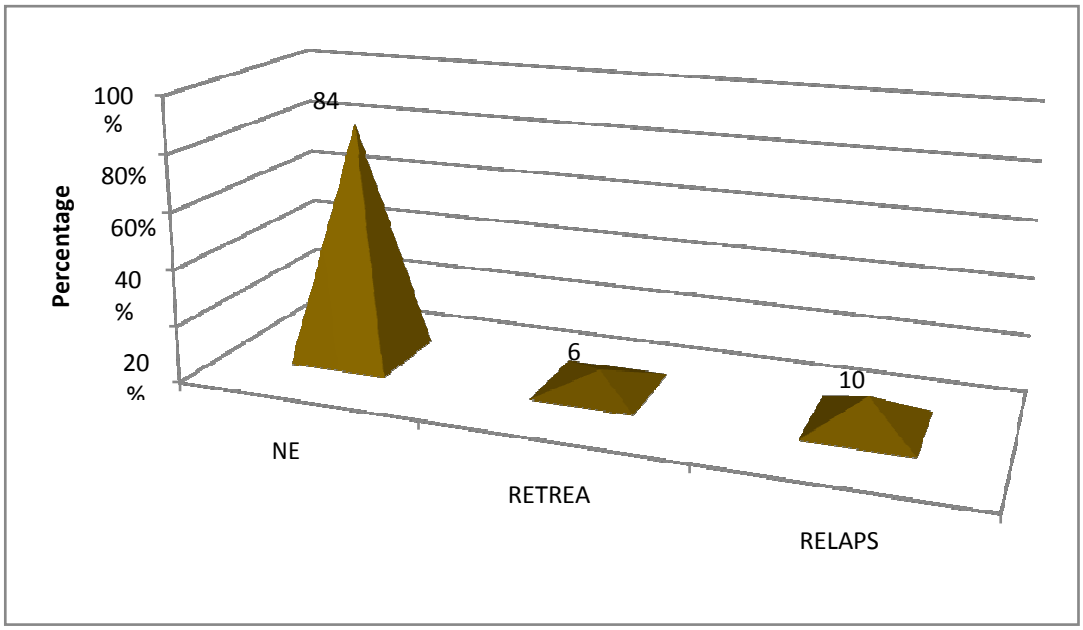

Fig: 9

TYPE OF LEPROSY VERSUSGENDER

Multibacillary type of leprosy was significantly associated with male gender than the female gender (χ^2 = 21.511, DF = 1, p<0.001)

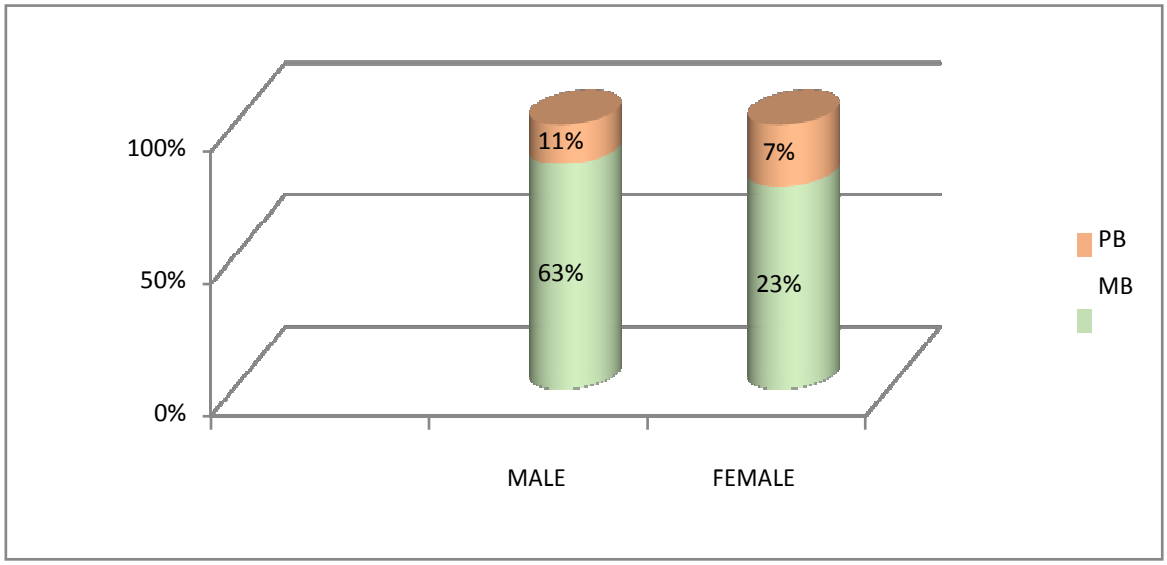

Fig: 10

NERVE INVOLVEMENT INLEPROSY

Among104patients,46%showedulnarnerveinvolvement, 26%showedcommonperoneal nerve involvement, followed by radiocutaneous nerve 15%, radial nerve 5% .(χ^2= 57.423, p <0.001)

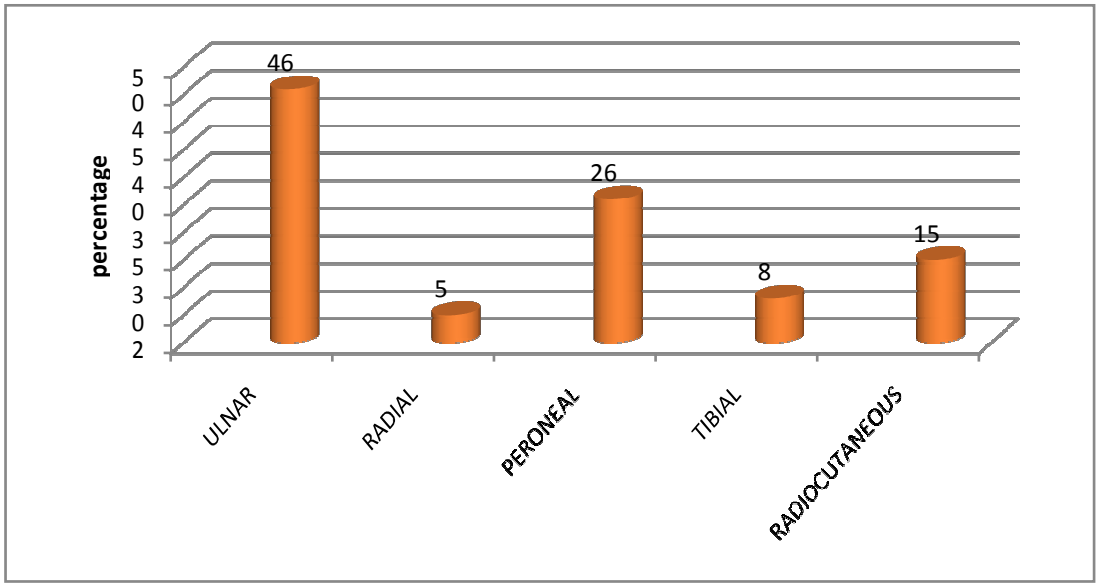

Fig:-11

LEPRAREACTIONS

Type 1 reaction was found to be significantly higher than type2 reaction(χ^2 =7.258, DF = 1, P<0.01)

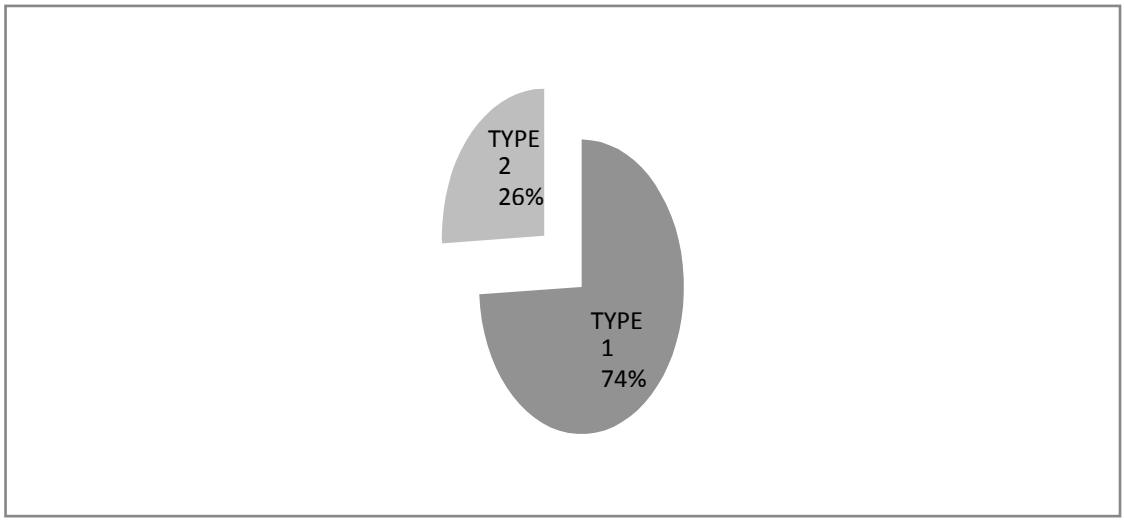

Fig:-12

TYPE OFDISABILITY

Types of disability were evaluated among 104 patients. 62% had ulcer, 33.33% had claw hands followed by foot drop 14.28% and lagophthalmus 9.52% (χ^2 = 11.96, DF =3, p<0.01)

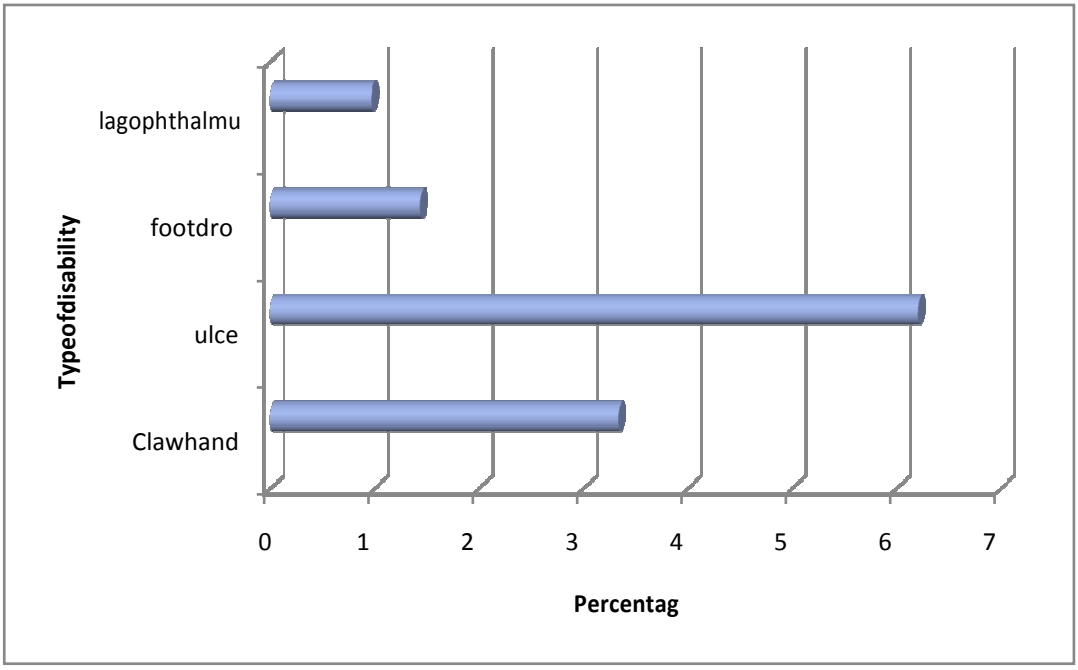

Fig:-13

GRADE OFDISABILITY

Grade of disability was evaluated among the leprosy patients.49% had no deformity, 31% were having Grade-1 deformity and 20% were having Grade -2 deformity. Number of patients in Grade-0 was found to be significantly higher than in Grade-1 and 2.

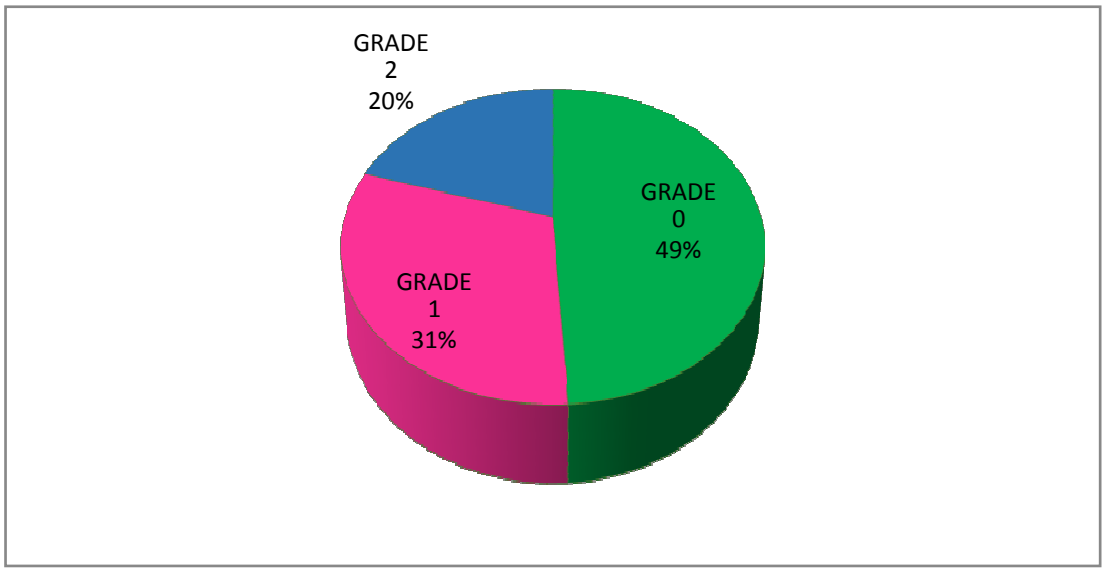

Fig: 14

DURATION OF SIGNS AND SYMPTOMS VERSUS DISABILITY GRADE

A) Less than 1year-Grade-1 disability was found to be significantly higher than grade-2 (χ^2= 4.263, DF = 1, p< 0.05)

B) 1-10 years:-No significant difference between Grade-1 and grade-2(χ^2 = 2.133,p>0.05)

C) Greater than 10 years-Patients with grade2 disability was found to be significantly higher than Grade1 (χ^2 = 4.000, DF = 1,p<0.05)

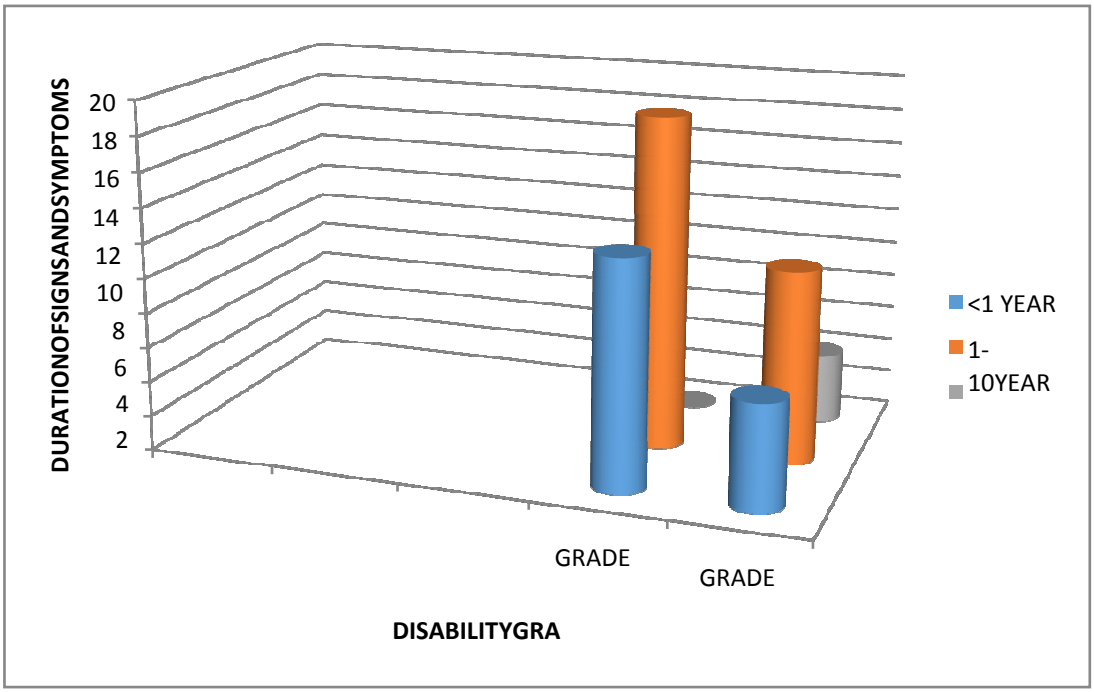

Fig:-15

TREATMENT PATTERN OFLEPROSY

Treatment regimens used for managing the patient condition was determined .The treatment of multibacillary leprosy was through the use of combination of Dapsone,Rifampicin,andClofazimine.(74%).Paucibacillary leprosy was treated with the combination of Dapsoneand Rifampicin (16%),(χ^2 = 209.404 , df =4 ,p<0.001)

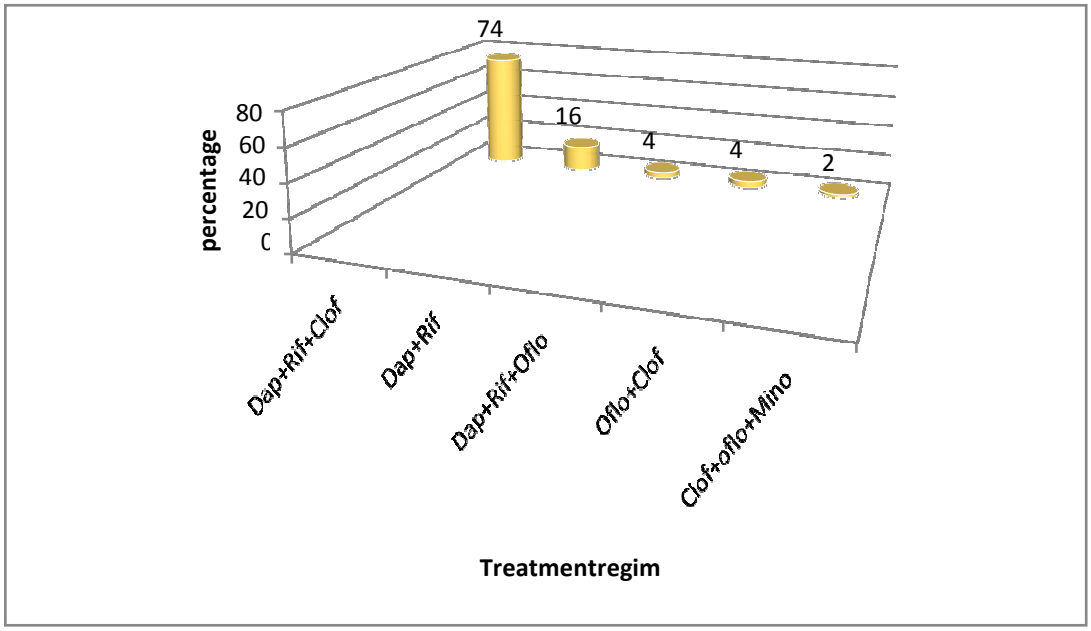

Fig:-16

MANAGEMENT OF LEPRAREACTIONS

Among patients with typr-1 reaction, significantly higher number of patients are treated with prednisolone compared to others (χ^2 = 22.201, DF = 2, p<0.001).Type-2 reaction was managed by using prednisolone and thalidomide (χ^2 = 10.506, DF =2,p<0.01)

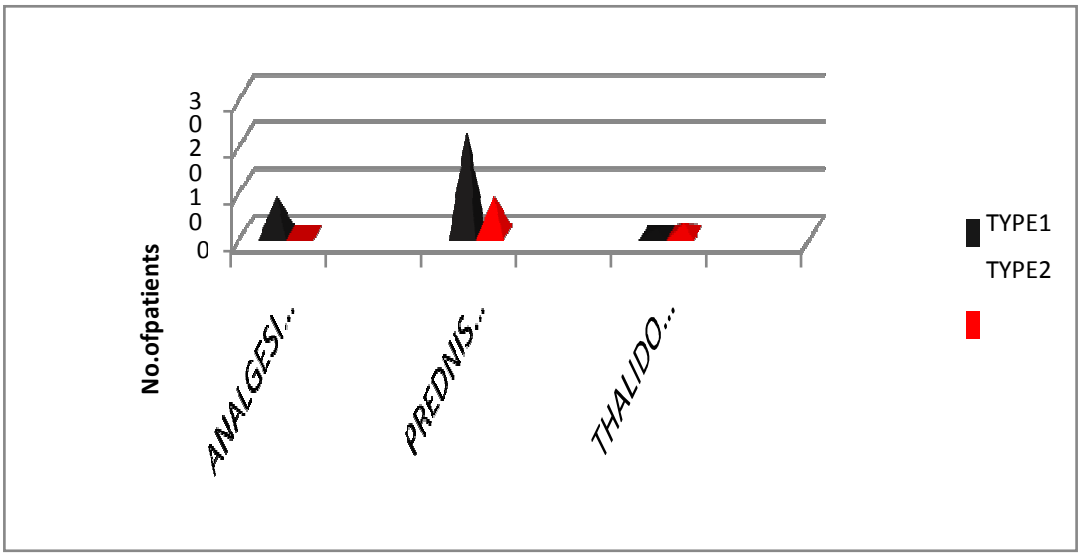

Fig:-17

ADVERSE DRUGREACTIONS

The most common ADR that was commonly seen at the time of study duration were anaemia, GI problems, hepatic abnormality, Flu-like illness, dapsone syndrome, pedal odeamaetc.The most prevalent ADR in the patient population was found to be anaemia(33%) followed by hepatic abnormalities(22%).{ χ^2 = 29.692 , df = 6 ,p<0.01}

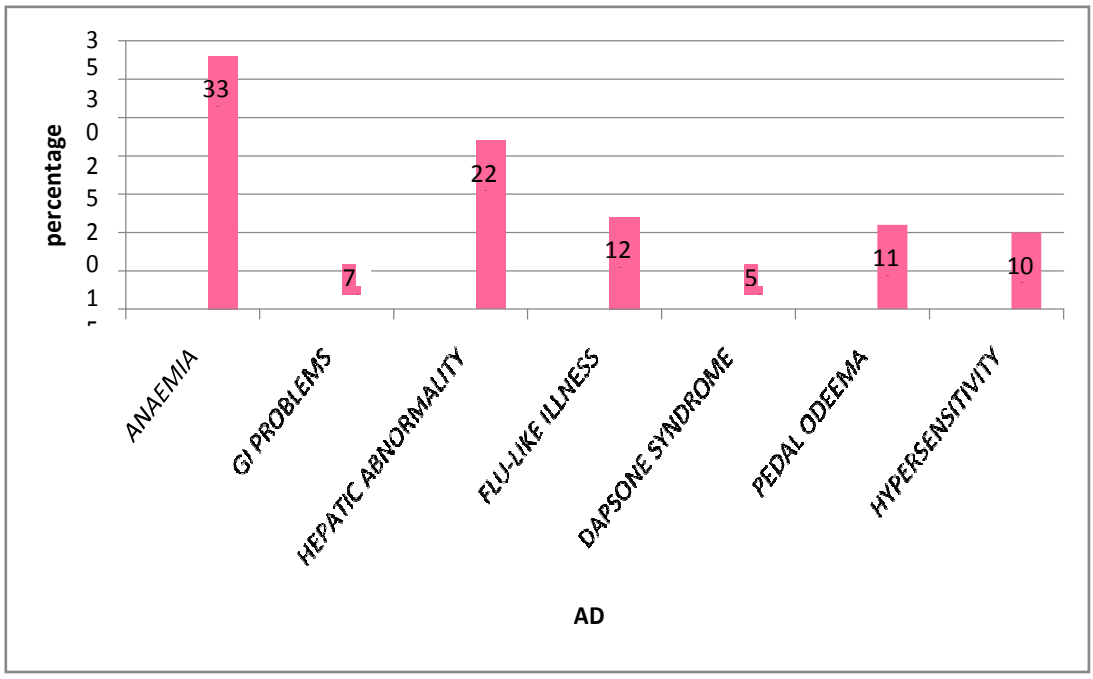

Fig:18

SUPPORTIVE THERAPY

Iron supplements were given for the management of anemia in 26% of patients. Antibiotics were being prescribed for 24% of patients in case of exacerbations.

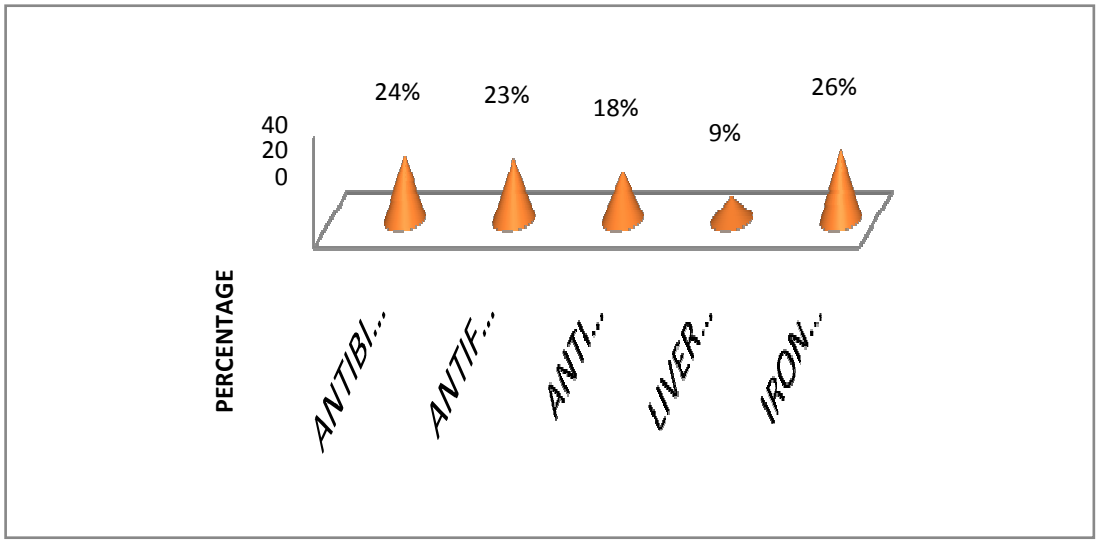

Fig:-19

MEDICATION ADHERENCE

The subjects were categorized into 3 categories namely highly adherent, moderately adherent, and non-adherent based on their level of medication adherence .Majority of the patients was found to be moderately adherent.(χ^2 = 14.657 , df = 2 ,p<0.01).18% of patients werenon-adherent.

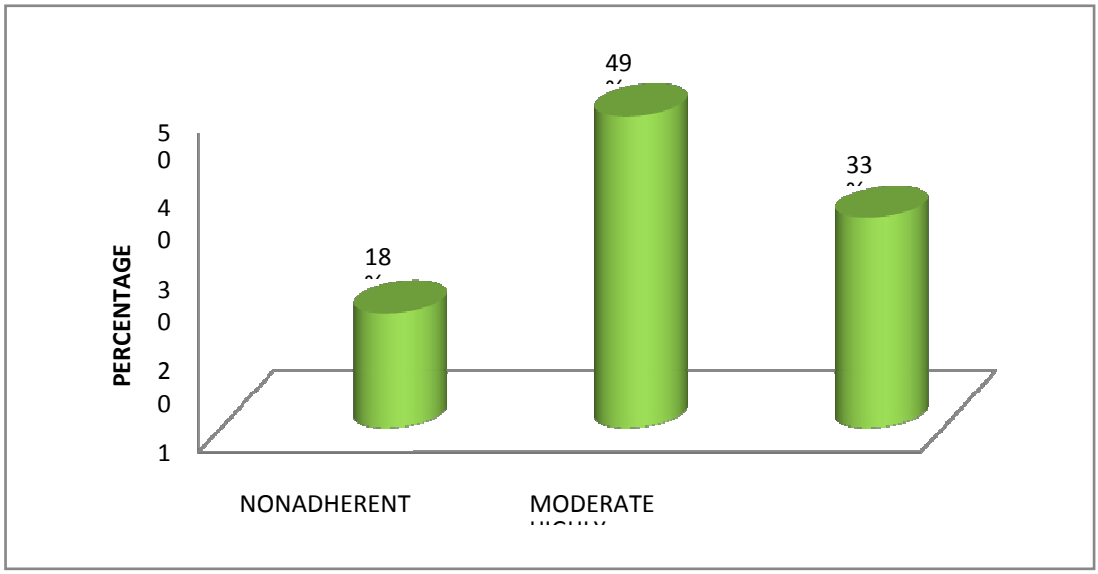

Fig:-20

TREATMENT OUTCOME

Among the 104 patients, significantly higher number of patients in the sample are continuing the treatment(69%).21% of patients got complete relief from the disease and 11% of patients were found to be defaulters(χ^2 = 14.657, df = 2 , p<0.01)

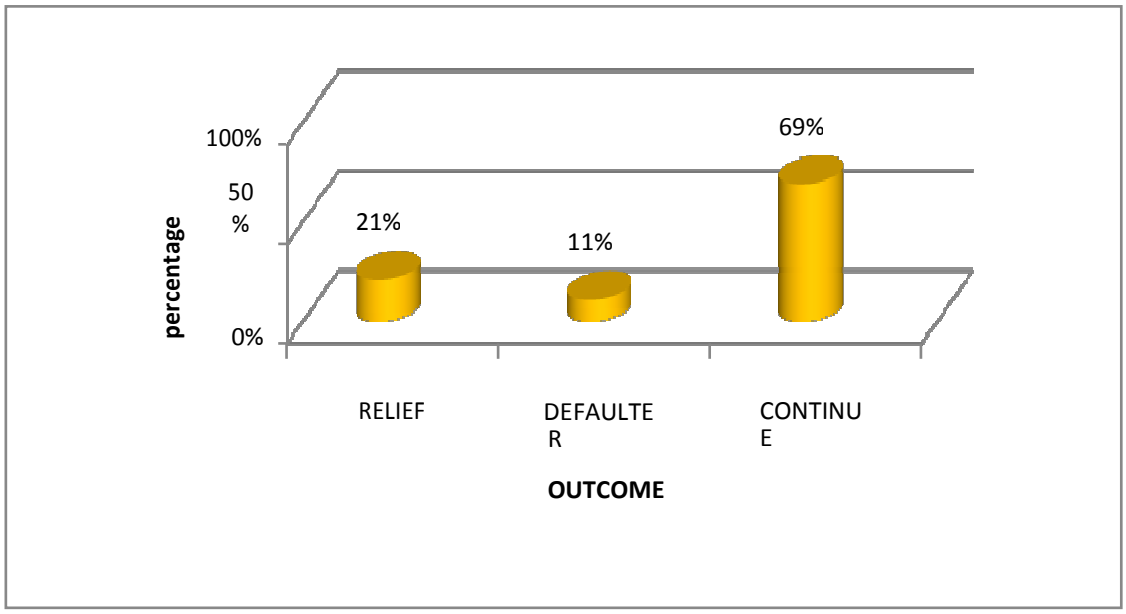

Fig: 21

DISCUSSION

A prospective observational study was carried out for six months among the leprosy patients in two districts in Tamilnadu (Krishnagiri and Dharmapuri).The study was carried out to determine the prevalence, treatment pattern and drug related problems among the leprosy patients. During our study period 40 cases were reported from Dharmapuri district and 64 from Krishnagiri. So the prevalence of leprosy in Dharmapuri and Krishnagiri district was found to be 0.001 and 0.002 respectively.

In the current study among among a total of 104 patients included, 49 (47%) were in the age group of 31-50 years. The mean age was 42.13±18.61 years. Nearly 6% of the patients were aged less than 15 showing the transmission is still going on the community. This high prevalence in younger age group calls for more vigorous means of case detection like active search for cases especially in communities known to be leprosy endemic.104 patients were enrolled in the study, of them 74(71%) were males and 30(29%) were females, demonstrating male predominance over female population. This result is similar to study conducted by B.L Ajibadeet-al **(2)** in which 79.7% was males.

No significant association could be found out between the residential status of patient and disease. Leprosy, an ancient disease, was thought to be confined to rural and underdeveloped geographical areas. But, on the contrary, our study found no such association, as we found an equal prevalence or incidence of the disease in urban and rural regions.

According to our study, the most prevalent type of leprosy was found to be multibacillary (MB) with 86 cases (83%) while paucibacillary (PB) type accounted

for only 18(17%) cases. Similar results were shown in studies conducted by B.L Ajibade et-al[2] and SileshiBaye[18] .The definition of PB leprosy has been evolving over the last two decades, with an increasing number of erstwhile PB patients being included in the MB group for the treatment purpose. This might be one of the important reasons for the progressive shrinking of the pool of PB cases in our study [21].Male gender (63%) showed significant association with multibacillary leprosy. Considering clinical form of leprosy Borderline tuberculoid (BT) form (75%) was found to be predominant over other forms. These results showed similarity with the study conducted by S.Karat et-al [7].

Hypo pigmented patches were the most common type of cutaneous lesions (84.61%) observed in leprosy patients taking multidrug therapy, followed by loss of sensation over the patches(39.42%) and numbness(31.73%). Madarosis were seen in 6.73% of patients. A nerve involvement affects sensory nerves earliest and most commonly, but it also affects the motor and autonomic function of peripheral nerves. In the present study the most commonly affected nerves are Ulnar (46%) followed by common peronealnerve(26%) , radiocutaneous nerve (15%) and tibial nerve (8%).This findings was similar to thestudyconducted by ShivlalRawlani et-al.[21]

Delay in diagnosis of patients augments the transmission of infection, and allows progression of disease and more severe disability [22].Among the study group 56% of patients had duration of signs and symptoms of leprosy within the range of 1-10 years. Delay in diagnosis greater than 10 years (5%) have been reported. Leprosy related disability is preventable if diagnosed early; but many

cases are diagnosed late with significant physical impairment [8].This study reveals that 51% of the leprosy patients studied had disability of grade-1 or grade-2. Among those with disability, 30.77% had Grade-1 and 20.19% had Grade-2 disabilities. Among grade-2 disability patients, ulcer (62%) was found to be more prominent followed by claw hands (33.33%), foot drop (14.28%). Lagophthalmous were reported in 9.52% of patients. On the other hand as per the study conducted by ShivlalRawlani et –al[21], disability in the form ofclaw hands(16.7%) was found to be more prominent.The major risk factors known for leprosy disability and physical deformity are delay in diagnosis, misdiagnosis and delay in provision of proper care for the disease.[8]In the present study we were able to establish a significant association between duration of signs and symptoms and grade of disability.Grase-2 disability was found to be significantly higher in patients who had delay in diagnosis of leprosy (>10 years).The longer the duration of symptoms the higher thelikelihood of developing nerve damage and sensory loss,both of which subsequently lead todisability. I f patient had chance of being diagnosed early, they could have been cured from the disease before any of the complications appeared.[8]

Among 104 leprosy patients, 31 patients developed lepra reactions. Out of this type1 reaction was found to be significantly higher than type2 reactions.The treatment pattern of leprosy where analysed in the present study. The treatment of leprosy is in the form of multi drug therapy (MDT) which is the combination of 2 or 3 of the following drugs. Cap.Rifampicin, Cap.Dapsone, Cap.clofazimine. Out of total 104 patients 74 cases were treated with combination of Dapsone, Rifampicin and clofazimine. (MDT-MB Regimen); Patients were treated with combination of

Dapsone and Rifampicin (MDT-PB Regimen). Rifampicin is the most important antileprosy drug and is included in regimens for both paucibacillary (PB) and multibacillary (MB) patients. Treatment of leprosy with only one antileprosy drug may result in development of resistance to that drug. Treatment with Dapsone or any other antileprosy drug as monotherapy should be considered unethically. In addition, it would be considerably more hazardous to use the compounds separately. These might be the reasons why the combinations wereprescribed**(9).**In **our** study few patients (4 %) were not willing to take clofazimine because of cosmeticconcern. Clofazimine can cause hypo pigmentation of skin and face. In these patients clofazimine was replaced with ofloxacin. 2 patients were found to be allergic to rifampicin, so the drug was stopped and an alternative regimen was started which is a combination of clofazimine, ofloxacin and minocycline. Other antibiotics (24 %) such as ciprofloxacin, azithromycin, metronidazole, amoxicillin – cloxacillin combinations were prescribed in exacerbative cases. A few patients developed fungal infections like onychomycosis, lichened lesions etc and were managed using antifungal drugs (clotrimazole, miconazole, fluconazole etc)

Lepra reactions were managed in our study by using analgesics, corticosteroids and thalidomide. In type-1 lepra reactions, mild reactions with no evidence of neuritis was managed with analgesics such as paracetamol and diclofenac.Type-1 Reactions with nerve involvement where treated with combinations of analgesics and corticosteroids such as oral prednisolone.The dose is then gradually reduced weakly and eventually stopped.Type-2lepra reactions (Erythema nodosumleprosum) were treated with analgesics and corticosteroids; or thalidomide.According to WHO the frequency of adverse reactions caused by MDT

is very low, and when such reactions occur, the standard regimen should simply be adjusted, so that treatment can be continued. During the study period a total of 73 adverse drug reactions Were identified. The most common adverse drug reaction was anaemia (33%) followed by hepatic abnormalities (22%), pedal oedema (11%).Dapsone Syndrome was reported in 5% of patients. On contrary, the study conducted by Harminder Singh et al [17]revealed thatflulike illness was found to be more prominent over other adverse drug reactions. Haemolyticanaemia was defined as reduction of haemoglobin from base line to the end of 30 – 90 days (< 12 .7 g/L for men and <11.5 g/L for women).Iron and folate supplements were given to patient (26 %) who had baseline low hemoglobin. Hepatic abnormalities were defined as any alterations at liver function tests with or without clinical evidence of jaundice, malaise and other symptoms. Liver protectants (9 %) such as silymarin 75 mg and UDCA 150 mg were given to patients who had altered LFTs. Flu-like illness include fever, runny nose,sore throat, cough, muscle/joint aches, and malaise. Gastrointestinal manifestations were managed using

H2receptorantagonists(ranitidine)orprotonpumpinhibitors(pantoprazole, omeprazole)Management of hypersensitivity reactions were done through the use of anti- histaminics (cetrizine and chlorpheniramine maleate) in 18 % of patients. Adhering to a treatment schedule and successfully completing it are crucial to the control of any disease. In our study majority of patients (49 %) were found to be moderately adherent to multi –drug therapy.33 % of patients showed high adherence. Non – adherence were reported in 18 % of patients. Significantly higher numbers of patients in the sample are continuing the treatment (69%).21% of patients successfully completed the treatment and 11% of patients were found to be

defaulter. On the other hand, the study conducted by PSSRao [19] revealed significantly higher number of defaulters.

The reasons for defaulting or non – adherence may bePersonal factors- stigma and other social, psychological reasons and economic reasons such as travel costs, loss of wages,etc.

(a) Medical problems such as worsening of the disease, non - disappearance of patch or other symptoms, or even a feeling that they have been cured as their symptomsdisappeared.

(b) Health service related factors. - includes complaints about health staff behaviour, lack of proper instructions or guidance, drug shortage,etc.

CONCLUSION

Leprosy is a chronic disease caused by bacteria Mycobacterium leprae that causes damage to skin and peripheral nervous system. The disease develops slowly and results in skin lesion and deformities, most often affecting the cooler places on the body.

A prospective observational study was carried for a period for 6 months among the leprosy patients in two districts in Tamilnadu .The total number of cases collected for the study purpose was 104 and the findings of the study reveals that most of the patients were in the age group of 31-50 years and the male patients were predominant over the female population. The most prevalent type of leprosy was found to be multi - bacillary (MB) and among these MB cases, borderline tuberculoid was most commonly reported. Hypo pigmented patches were the most common type of cutaneous lesions observed in leprosy patients taking multidrug therapy. The finding of the study also illustrates that delay in diagnosis of patients augments the transmission of infection, and allows progression of disease and more severe disability.74% of the Multi - bacillary patients were treated with MDT-MB regimen with Dapsone, Rifampicin and Clofazimine and 16% of the paucibacillary patients were treated with MDT-PB regimen with Dapsone and Rifampicin. The most common ADR found by using the MDT regimen was anemia and it was managed by using iron supplements. Adverse effects attributed to MDT are comparable to previous studies and we found that ADR due to Dapsone was very high. If patients are properly informed about the common ADR and are advised to report to their health care provider if and when ADRs occur, and are appropriately motivated about the benefits of MDT, most can be managed by MDT only with

supportive treatment, without replacing the suspected drug, except in few cases with serious, complicated or life threatening ADR. The continuing occurrence of new cases means that the first priority is the need for these cases to be detected early and treated effectively to cure leprosy and prevent disability. If we fail to do this then the prevalence of leprosy will start to increase and all that has been achieved will belost.

MDT introduction came with additional benefits such as an intense monitoring of patients, coverage of affected populations, and improvement of the closeness between leprosy patients and medical care, and that leprosy changed into a curable disease.

There are three important principles for leprosy work in the future. It includes;Sustainability (new cases of leprosy are continuing and many of the consequences are lifelong so our approaches need to be sustainable) , the leprosy workers cannot do everything themselves(they need to work in alliances at all levels with other agencies, other health care workers, social services, communities, patients themselves and their families),Anti-leprosy services need to be integrated with general health and social services(this includes training, primary health care, hospital care, and community based rehabilitation)

Finally we would like to emphasize the importance of a proper health education, daily ulcer care and shoe adjustments as systemic therapy and also to prevent the development of new ulcers.

LIMITATIONS OF STUDY

- The study was a cross-sectional study and thus the follow-up of patients was not possible.
- Due to fear of stigma and discrimination some patients were not willing to cooperate with thestudy.
- Immigrant patients were been excluded because of the difficulty in obtaining the relevantinformation.
- The questionnaires were filled with the help of Assistant Leprosy Officers of the respective hospitals, because patients visited the leprosy center one time per month. So it was difficult for us to fill up thequestionnaires

There is a chance of reportingbias.

REFERENCES

1) Training Manual for Medical Officers. National Leprosy Eradication Programme, page no.6-30

2) B.L. Ajibade, Okunlade, J.O, Olawale Femi, O.P. Adisa, M.O.A Adeyemo. Prevalence, Management and Percieved Psychological Impacts of Leprosy Disease in National Tuberculosis and Leprosy Training Centre, Saye Village, Zaria .The International Journal of Social Sciences and Humanities Invention Volume 2 issue 05 2015 pageno.1298-1312

3) JyotsnaA.Saonere. Leprosy: An overview .Journal of Infectious Diseases and Immunity Vol. 3(14), pp. 233-243, 29 November,2011

4) S. J. Yawalkar .Leprosy - for medical practitioners and paramedical workersEighth revised edition,2009

5) Fathima et al. Multi-drug regimens for treatment of leprosy UJAHM 2015, 03 (03): Page no.20-28

6) Prof. Cairn Smith, Leprosy past, present and future, International seminar, University of Aberdeen,

7) S. Karat, P. S. S. Rao and A. B. A. Karat .Prevalence of Deformities and Disabilities Among Leprosy Patients in an Endemic Area Internaional journal of leprosy Volume 40, Number 3.page no.265-270

8) TigistShumet, MeazaDemissie, YonasBekele. Prevalence of Disability and Associated Factors among Registered Leprosy Patients in All Africa Tb and Leprosy Rehabilitation and Training Centre (ALERT), Addis Ababa, Ethiopia .Ethiop J Health Sci. Vol. 25, No. 4 October 2015 page no. 313 –320

9) Patrica D. Adverse effects from Multi-drug therapy in leprosy: a Brazilian study Lepr Rev (2007) 78,216–222.

10) Textbook of preventive and social medicine, contact diseases .page no.228-240.

11) WHO Model prescribing information – Drugs used in leprosy (1998) .page no.1 –26.

12) K. D Tripathi, Essentials of Medical Pharmacology, seventh edition page no; 751 –756.

13) H.L Sharma & K.K Sharma, Chemotherapy of microbial diseases, Principles of pharmacology page no.785-787.

14) Diana L. Williams & Thomas P .Gillis, Drug-resistant leprosy: Monitoring and current Status , Lepr Rev (2012) 83,269–281.

15) PadmajaUdaykumar, Chemotherapy of tuberculosis and leprosy, Medical pharmacology. fourth edition pageno.452-454.

16) Returnofanoldcurse;Keralaisnolongerimmunetoleprosy,Indianexpress,7th December 2015.

17) Harmindersingh,Bithikanel, Vivekdey, Pawantiwari and Naveen dulhan.Adverse effects of Multi-drug therapy in leprosy, a two years' experience (2006–2008) in tertiary health care centre in the tribal region of Chhattisgarh state (Bastar, Jagdalpur) Lepr Rev (2011) 82,17–24.

18) SileshiBaye .Leprosy in Ethiopia: Epidemiological trends from 2000 to 2011 Advances in life sciences and health Volume 2, Number 1, February 2015 pageno.31-49.

19) PSS Rao. A Study on Non-adherence to MDT among Leprosy Patients. Indian J Lepr 2008, 80:149-154.

20) Huan-Ying Li, Lu-Fang Hu, Pei-Wei Wu, Jiu-Si Luo, and Xue-Ming Liu2. Fixed- Duration Multidrug Therapy in Multi -bacillary Leprosy. International journal of leprosy 1996 Volume 65, Number 2 page no. 230-237. (ISSN0148-916X).

21) ShivlalRawlani et al. Current scenario of leprosy patients taking multidrug therapy Journal of Pakistan Association of Dermatologists 2012;22:130-135.

22) Henry et al. Factors Contributing to the Delay in Diagnosis and Continued Transmission ofLeprosy in Brazil – An Explorative, Quantitative, Questionnaire Based Study.PLOS Neglected Tropical Diseases | DOI:10.1371/journal.pntd.0004542 March 15, 2016 page no. 1-12

23) Wim H. van Brakel Disability and Leprosy: The Way Forward-Special Editorial. Annals Academy of Medicine. January 2007, Vol. 36 No. 1 page n0.86-87.

24) NitinJ.Nadkarni,AntonioGrugni,andManjunathS.Kini[2] Fixed-Duration MDT in paucibacillaryLeprosy.International journal of leprosy 1993 volume 61,Number 2 page no.25-28.

25) LuzivanderS.Soares,Rodrigo de O.Moreira, VanessaV. Vilela, MarcioJ.M. Alves, AnaFlaviaM.Pimentel,Ana Paula Ferreira,HenriqueC.Teixeira. Artigo article. Cad.saudepublica, Rio-de janerio, Volume 16(2) Page no: 343-350, abr-jun,2000.

26) A.K.Das, J.C.Das, A.Roy, B.De.Effect of Multi Drug Therapy on leprosy: Analysis Based on a study in West Tripura District, Tripura, India.Indian journal of Hospital pharmacy 45(2008) page no:70-71.

ANNEXURES

DEPARTMENT OF PHARMACYPRACTICE

PADMAVATHYCOLLEGE OF PHARMACY

A STUDY ON THE TREATMENT PATTERN OF LEPROSY INCLUDING

PREVALENCE OF THE DISEASE, ADR MONITORING AND

ASSESSMENT OF ADHERENCE TO DRUG THERAPY

DATA COLLECTION FORM

Case No: Date:

PATIENT DEMOGRAPHIC DETAILS:-

Age: Sex: DOA:- Marital Status:

SOCIAL HISTORY:-

a. Residential status :village/town/city/tribal area

b. Educational status:

c. Occupational status:

d. Alcoholic: ☐ Yes ☐ No

e. Smoking: ☐ Yes ☐ No

f. Other abusive habits:

REASON FOR CONSULTATION (CLINICAL FEATURES):-

DURATION OF SIGNS AND SYMPTOMS:-

MODE OF DETECTION: - Voluntary / by contact / referred by other TYPE OF CASE:-New case / immigrant / Relapse / Restart or referral PAST MEDICAL AND

MEDICATION HISTORY

DM ☐ Renal Disease ☐

HTN ☐ Liver disease ☐

Others, if any :

DIAGNOSIS

REACTION OR NEURITIS (IF PRESENT):-

ASSESSEMENT OF DISABILITY AND NERVE FUNCTION:-

TREATMENT PATTERN

ADVERSE DRUG REACTIONS; IF ANY

RELEVANT LAB PARAMETERS:-

END STATUS

A STUDY ON THE TREATMENT PATTERN OF LEPROSY INCLUDING PREVALENCE OF THE DISEASE, ADR MONITORING AND ASSESSMENT OF ADHERENCE TO DRUG THERAPY

DEPARTMENT OF PHARMACY PRACTICE

PADMAVATHY COLLEGE OF PHARMACY

PATIENT DEMOGRAPHICS

Patient name:- Age:-

Gender:-

MEDICATION ADHERENCE QUESTIONNAIRE:-

1) Do you ever forget to take your medication? Yes ☐ No ☐

2) Are you careless at time taking the medication? Yes ☐ No ☐

3) When you feel better, do you sometimes Yes ☐ No ☐
Stop taking your medication?

4) Sometimes if you feel worse (ADR) Yes ☐ No ☐
When you take medication, do you stop taking it?

5) I take medications of my own free choice? Yes ☐ No ☐

6) If you happen to miss a single dose, Will you be Yes ☐ No ☐
Taking a double dose the next time?

7) My thoughts are clearer on medication? Yes ☐ No ☐

8) Medications make me feel tired and sluggish? Yes ☐ No ☐

9) I am on a lot of medication, and it's hard form to Yes ☐ No ☐
Sometimes to keep track of themall?

10) Medication makes me feel more relaxed? Yes ☐ No ☐

11) Do you collect your medicines(leprosyonly) Yes ☐ No ☐

On a regular basis everymonth?

12) Do you receive adequate information Yes ☐ No ☐

Regarding your medication?