A STUDY ON REACTION STATES IN LEPROSY

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(**BRANCH XII A**)

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CERTIFICATE

This is to certify that this dissertation entitled **'A STUDY ON REACTION STATES IN LEPROSY'** submitted by **Dr. S. Bharathi** to The Tamil Nadu Dr.M.G.R. Medical University, Chennai is in partial fulfillment of the requirement for the award of M.D., [DERMATO VENEREO LEPROLOGY] and is a bonafide research work carried out by her under direct supervision and guidance.

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DECLARATION

I, **Dr. S. Bharathi** solemnly declare that I carried out this work on ' **A STUDY ON REACTION STATES IN LEPROSY'** at Department Of Dermatology, Government Rajaji Hospital during the period of Oct 2009 – Sep 2011.

I also declared this bonafide work or a part of this work was not submitted by me or any other for any award, degree and diploma to any university, board either in India or abroad.

This is submitted to The Tamil Nadu Dr. M.G.R Medical University, Chennai in partial fulfillment of the rules and regulation for M.D.,[D.V.L] Degree examination.

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LIST OF ABBREVATIONS USED

MB	-	Multibacillary
PB	-	Paucibacillary
RR	-	Reversal reaction
EN	-	Erythema nodosum
ENL	-	Erythema nodosum Leprosum
BI	-	Bacteriological index
CMI	-	Cell mediated immunity
IL	-	Interleukin
IFN γ	-	Interferon gamma
TNF α	-	Tissue necrosis factor alpha
NF κB	-	Nuclear factor kappa B
BT	-	Borderline Tuberculoid
TT	-	Tuberculoid tuberculoid
BB	-	Borderline borderline
BL	-	Borderline lepromatous
LL	-	Lepromatous lepromatous
LLs	-	Subpolar lepromatous
TTs	-	Secondary tuberculoid
HIV	-	Human Immunodeficiency Virus
PMNL	-	Polymorphonuclear leucocyte
ESR	-	Erythrocyte sedimentation rate
Hb	-	Haemoglobin

LFT	-	Liver Function Test
RFT	-	Renal Function Test
SSS	-	Split Skin Smear
M. leprae	-	Mycobacterium leprae
ALD	-	Anti leprosy drugs
MDT	-	Multi Drug Therapy
RFT	-	Relief from treatment.
RA	-	Rheumatoid Factor
ANA	-	Antinuclear antibodies
Ig	-	Immunoglobulin
C	-	Complement
CRP	-	C-reactive protein
SGPT	-	Serum Glutamic Pyruvic Transaminase
DIF	-	Direct immunefluorescence
BP	-	Blood pressure
TB	-	Tuberculosis
CTD	-	Connective tissue disorder
HT	-	Hypertension
DM	-	Diabetes milletus
NSAID	-	Non Steroidal Anti-inflammatory Drugs
ILEP	-	International Federation of Antileprosy Association
HAART	-	Highly Active Anti Retroviral Therapy

CONTENTS

INTRODUCTION

Leprosy or **Hansen's disease** is a chronic actively progressive granulomatous disease caused by *Mycobacterium leprae*, infectious in some cases and affecting the peripheral nerves , the skin and certain other tissues including reticulo-endothelial system, bones and joints, mucous membranes, eyes, testes, muscles, adrenals, etc. Named after the Norway physician Gerhard Henrik Armauer Hansen, who discovered the bacilli first in 1873, *Mycobacterium leprae* is the first bacterium to be identified as a human pathogen and it is the only species of mycobacteria to infect peripheral nerves and specifically Schwann cells.

Leprosy is an ancient disease, which has existed in our community for a longtime. Leprosy today is not the `Leprosy' of yesterday – a far off, little understood disease, during its long course, there may occur acute bouts of exacerbation, generally called as 'Reactions'.

Reactions are defined as `acute episodes occurring in an otherwise chronic course of infection'. It does not apply to the general progression or increase in the manifestations of disease. Remissions and relapse are the hallmark of reactions and these may last for a few weeks to few months.

Leprosy reactions are immunological phenomenon that occurs before, during or after the completion of multi-drug therapy (MDT). They contribute immensely to the burden of leprosy and need to be diagnosed and treated early to prevent nerve function impairment and permanent disability.

Reactions in leprosy are classified into Type-1 reaction, Type-2 reaction and Lucio phenomenon or Type-3 reaction .This study has been undertaken to determine the incidence and to study the clinical and histopathological features of lepra reactions in detail.

AIM OF THE STUDY

1. To study the incidence of different types of lepra reactions in various spectrum of leprosy.

2. To study the clinical & histopathological features of lepra reactions in detail.

REVIEW OF LITERATURE

HISTORICAL ASPECTS OF LEPRA REACTION

The word '**Lepra'** was first used by Hippocrates (460-377BC) for a scaly skin condition The hebrew originals of the old testament books used 'Tsaraath' for number of scaly skin diseases [e.g summer prurigo and psoriasis] and the Greek equivalent 'Lepra' was later offered in new testament work, thus the word 'Lepra' was applied. It could be said that the synonyms of modern leprosy may be 'Lepra arabum' and 'Elephantiasis graecorum'.[1]

Danielsson and Boeck (1848) and Hansen and Looft (1898) described a peculiar eruption in lepromatous leprosy, which resembled Erythema nodosum (EN) in its clinical appearance.[2] A Japan leprologist Murata (1912), proposed the term 'Erythema Nodosum Leprosum' (ENL) based on the clear cut clinical and histopathological features. In 1939 Desouza Lima and Maurano had written that EN was the most frequent cutaneous symptom of lepra reactions. Desouza Lima and Desouza recorded the exacerbation of leprosy reactions in patients on sulphone therapy, which were described as pseudoexacerbation for lack of better caption.[2] In 1942 Pecarno made particular attempt to delineate the difference between ENL and EN.

Pogge and Ross (1946) stated in an article that " leprosy is a chronic disease in which there are atleast at times acute manifestation, the local lesion of which may be

those of erythema nodosum or less often erysipeloid reaction of the skin, painful neuritis or painful lymphadenopathy'.

In 1955 Wade H. W first used the term ' Reversal reaction' to describe the appearance of skin lesion resembling those of tuberculoid morphology.[3] Tajiri (1955) reported a similar reaction as 'acute lepromatous infiltration'. He also attempted to distinguish upgrading and downgrading reaction later.[4] In 1959 W.H. Jopling introduced the terms Type I and Type II reaction and differentiated them.[5] The term ENL has been in use for long time, since numerous symptoms occur in addition to ENL W.H.Joppling prefer the term Type 2 reaction.[6]

A real breakthrough however was enacted by Ridley who based his observation on pathognomic histological abnormalities. He was the first to use the term upgrading reaction in 1969.[2] Wolcott R. R (1977) observed that the incidence of lepra reaction rose from 7% in the presulphone period to 93% in the post sulphone period. He emphasized the need for difference between simple progression of the disease and reaction.[2] Davidson A.R pointed out that higher the original bacteriological index, the more likely it was that ENL would develop. He concluded that ENL had a bad prognostic significance.[7]

Type III lepra reaction was first described by Lucio and Alvarado in 1852. The eponoymic designation 'Lucio phenomenon' was first proposed by Latapi in 1948. It was Latapi and Zamora who brought the paper to the notice of the medical world.[8]

LEPRA REACTION

DEFINITION

Lepra reactions are episodes of acute hypersensitivity to antigen of *Mycobacterium leprae* brought about by a disturbance in the preexisting immunological balance in leprosy patients. Clinically described by the appearance of symptoms and signs of acute inflammation in lesions of patients with leprosy.[1]

Ridley defined 'reactions' as an apparent clinical and histological expression of an allergic inflammatory process, which essentially may not be part of infective process, either in its spread or resolution, though it may be associated with these phases.[2] Ridley, Debi and Mohanty and Seghal et al defined ' reactions' as acute episodes occurring in an otherwise chronic course of infection.[2]

CLASSIFICATION

Reactions in leprosy are incomprehensive both in concept and nomenclature. Various authors gave various classification at different times with different terminologies.

Cochrane and Dharmendra classification [9]

1. Reactions in tuberculoid leprosy and reactional tuberculoid.
2. Reactions in dimorphous leprosy.

3. Reactions in lepromatous leprosy.

    - Erythema nodosum leprosum
    - Progressive lepra reaction
    - Lucio phenomenon or necrotic lepra reaction

Hastings classification [1]

1. Type 1 reaction associated with cell mediated hypersensitivity.
2. Type 2 reaction associated with immune complexes.
3. Lucio phenomenon associated with necrosis of arterioles whose endothelium is massively invaded by Mycobacterium leprae.

Jopling W. H Classification [10]

This classification was accepted at present.

1. Type I Lepra reaction:- Upgrading or reversal reaction
   Downgrading reaction
2. Type II Lepra reaction
3. Type III Lepra reaction

World health organization [WHO] has been using the term Reversal reaction (RR) for Type 1 reaction and Erythema nodosum leprosum for Type 2 reaction.

TYPE I REACTION

SYNONYMS - [Borderline reaction, Tuberculoid reaction**,** Reversal reaction**,** Jopling type 1**,** Coombs and Gell Type IV reaction**,** Non lepromatous lepra reaction]

INCIDENCE

In review of reaction, in the post multi drug treatment [MDT] era, Type I reaction was encountered in 11- 39 % of borderline tuberculoid [BT], 75- 100% of borderline borderline [BB], 15-44% of borderline lepromatous [BL], 2.4- 6.5% of lepromatous leprosy subpolar [LLs] and 3.8% of tuberculoid [TT].[11] Overall development of reaction at any time vary from 3.5% among pauci leprosy [PB] and 47.5% among multibacillary [MB] cases.[12]

AGE

Type I reaction occur commonly in age group of 20 – 40 yrs. In children type I reaction are rare despite the high prevalence of leprosy in the form of Indeterminate or tuberculoid type.[13]

SEX

Type I reaction occur in both sexes with equal frequency. Nerve damage is much more common in male patients with BT leprosy.[11]

TIME OF ONSET

80% of Type I reaction develop within 6 months of MDT. It can also occur even after 12 months to 2 years. Kumar et al reported that RR occurs most frequently during 6-12months after starting MDT. Recurrent episodes of RR occurred within 3 months of stopping the course of prednisolone administered for the previous reaction.[14]

TYPE I LEPRA REACTION ACROSS SPECTRUM OF LEPROSY

Type I reaction are commonly seen in borderline spectrum of leprosy because of their immunological instability [i.e - BT, BB, BL]. Borderline patient may upgrade to TT to form secondary tuberculoid [TTs] or it may downgrade to subpolar LL [LLs].[6, 15]

PRECIPITATING FACTORS

Upgrading reaction may be precipitated by [15, 16]

1. Antileprosy treatment especially dapsone
2. Pregnancy
3. Postpartum state
4. Lepromin testing
5. Immunotherapy

In BT, reversal reaction may occur spontaneously even before in taking the treatment.

Downgrading reaction may be precipitated by [15, 16]

1. Psychological stress
2. Intercurrent infection – streptococcal, malaria, filarial, parasitic infestation
3. Vaccination – Typhoid, TT, BCG.
4. Malnutrition
5. Pregnancy
6. Other rare precipitating factors include hyperthyroidism,[17] OC pills,[18] hormonal factors in puberty.[19]

RISK FACTORS [11]

A recent study delineated the following risk factors

1. Facial patch
2. Enlarged ulnar nerve
3. Positive Bacteriological Index [BI]
4. Disease involving more than 2 body parts.
5. Presence of antiphenolic glycolipid antibody in PB leprosy.

CLINICAL FEATURES

CUTANEOUS MANIFESTATIONS

The most prominent sign is a rapidly developing change in the appearance of one or all the skin lesions, the existing lesions become erythematous, edematous, raised with distinct edge, more prominent, warm to touch, tender and resembling erysipelas. Similar

new lesions can occur in crops but unusual. Lesions resolve with desquamation and scaliness and flattened later to form wrinkled surface. Sometimes they may ulcerate and heal with scarring. Another manifestation is edema of the involved site. It can occur over hands, feet or face either independently or together. Tenderness of palms and soles are sometimes present.[20]

Dogra et al [2004] reported a case of BL Hansen disease in Type I reaction presented as phimosis.[20] Gupta et al reported a case of erythematous infiltrated plaque over scrotal skin in a 4yr old child diagnosed as BL in Type I reaction.[21] A case report of lepra reaction presenting as acute polyarthritis in the setting of Type I downgrading reaction has been reported by a rheumatologist.[22]

NEURITIS

It is the most important component of Type I reaction. It may occur independently or together with skin changes. Most common in males with BT Hansen. Clinically manifest as neural pain at the site of predilection and the pain may refer to the region of skin it supplies. Nerves are thickened and tender on palpation. There may be acute loss of function resulting in both sensory or motor paralysis. Anesthesia or extent of anesthesia develops rapidly in the region of distribution of the affected nerve. Sudden paralysis of the muscles of hand, foot or face occurs as claw hand, wrist drop, foot drop and facial palsy including lagopthalmus. Rarely nerve abscess forms producing fluctuant tender swelling. Nerves at risk for paralysis are ulnar nerve, lateral popliteal nerve and facial nerve. Nerve abscess are commonly seen in ulnar nerve, greater auricular nerve and

lateral popliteal nerve. Sometimes, nerve function may get affected without any pain or tenderness of the nerve or inflammation of skin lesions. Van Brakel and Khawas proposed the term "Silent neuropathy (SN) /Quiet nerve paralysis'' to describe this phenomenon of nerve function impairment occurring in the absence of symptoms.[23]

Systemic disturbances such as fever, malaise, are unusual, seen only in severe reaction. Tenosynovitis of extensor tendon over back of wrist may develop during Type I reaction.

GRADING OF TYPE I REACTION [11]

There are three grades to access the severity of Type I lepra reaction.

MILD – erythema, swelling and tenderness of existing lesion / a few lesions may appear.

MODERATE – erythematous patches/ plaques with effusion of joints / edema of limbs.

SEVERE – numerous inflamed lesions that may ulcerate with painful neuritis causing paralysis.

COMPLICATIONS

1. Sudden onset of paralysis resulting in claw hand, foot drop, wrist drop or facial paralysis.
2. Ulceration of skin lesion

HISTOPATHOLOGY [1,6]

In acute stages, there is profound dermal edema which causes disorganization and dispersal of the granuloma. In upgrading reaction, there is increased number of defensive cells such as lymphocytes, formation of giant cells and small cluster of epitheloid cell and decrease in number of bacilli. In downgrading reaction, defensive cells are replaced by macrophages and there is increase in number of bacilli. In severe reactions, necrosis may occur in small foci or sometimes causing liquefaction of the entire granuloma, there may be fibrinoid necrosis and finally fibrosis.

IMMUNOLOGY AND PATHOGENESIS

Type I reaction is a delayed hypersensitivity reaction [Gell and Coombs type IV hypersensitivity] in which cell mediated immunity plays the major role. It occurs as a result of interaction of T lymphocytes with antigens liberated from M. leprae. On break down of microorganism two portions of antigen are released. The protein fraction elicits the cell mediated immunity and polysaccharide portion elicit a humoral immunity.[6] These antigens react with T lymphocytes and on T cell activation Th1 mediated cytokines IL-2, IFN-γ and TNF-α are released.

These inflammatory cytokines are thought to be responsible for nerve damage.[24] Pro-inflammatory cytokines IL-6, IL-10, IL-13 are also released and have number of effects within the granuloma including promotion of protective cellular response, maintenance of granuloma formation and initiation of nerve damage.[25,26,27] The presence of both pro and anti-inflammatory cytokines highlight the multiplicity of cytokine

expression within the granuloma and suggest Th1 cell mediated immune response plays a role in reactional pathology.[25]

Normally during leprosy a delicate balance exists between the antigen available for immune reaction and host response. Any alteration of the balance induces a reactional state. Any change in the immunological status brings about a shift in the clinical spectrum of leprosy. The various shift across the leprosy spectrum are LL -> BL -> BB -> BT -> TTs.[2] Lepromatous leprosy polar [LLp] and tuberculoid polar [TTp], the polar forms are immunologically stable. The reverse occur in downgrading reaction BT -> BB -> BL -> LLs.[6]

In reversal reaction there is a progressive increase in CMI and destruction of bacilli. RR can occur either spontaneously or during and after completion of treatment. Sometimes it may occur long after the treatment or cessation of lesions. The longest period reported so far is 16 years after release from treatment [RFT].[28] They are called as late reversal reaction. Late reactions is known to occur mostly within first 3 to 4 years after RFT. This was explained by the possible mechanism that persisters in inaccessible area escape from organic defence and drugs, often go for multiplication when conditions are favourable due to intercurrent illness or immunological changes.[29]

Shetty et al who studied 25 patients of BT leprosy, some of who presented with late RR occurring 1-13 years after MDT.[30] Patients with low bacilli count resolved

completely as the body defense are able to deal with them. And those with high number of bacilli new reactions, nerve damage and disability are common.

The activation of T cells in case of RR is evidenced by 10 fold increase of IFN-γ in lesions of RR. In another study 4 fold increase of human gene serine factor [huHF] a marker of cytotoxic cells was observed. Also observed are increased levels of neopterine at the onset of RR and its decline after steroid therapy.[31] There is also increased conversion of lymphocytes to lymphoblast and increase in Langerhans cells in the skin.[11] This immunological upgrade can be evidenced by a previously negative lepromin test becoming positive.

In downgrading reactions there is decrease in CMI and increase in the number of bacilli. This occurs when the patient is not on treatment. The continuous multiplication of the bacilli leads to overwhelming of antigen resulting in immune paralyses and cause downgrading reactions. This is evidenced by previously positive lepromin test becoming negative.

DIAGNOSIS

The diagnosis is mainly clinical. In Type I reaction it may sometimes difficult to differentiate RR and downgrading reactions. The following investigation may be helpful in differentiating them.

1. Lepromin test
2. Skin biopsy

3. Lymphocyte transformation test

4. Lymphocyte stimulation test

DIFFERNCE BETWEEN REVERSAL AND DOWNGRADING RAECTION

	REVERSAL REACTION	**DOWN GRADING REACTION**
RELATION TO TREATMENT	Occur while on taking treatment.	Occur without treatment / on irregular / default treatment.
CHANGE IN EXISTING SKIN LESION	Well defined and more prominent / no change in all lesion.	No marginal definition / appear less prominent / changes in all lesion.
NEW LESION	No new lesion	More new lesion
NEURITIS	No new nerve damage/ already involved may be inflamed.	New nerve involvement occurs.
BACTERIOLOGICAL INDEX	Decreases	Increases
LEPROMIN TEST	Negative reverts to positive.	Positive become weakly positive or negative.
HISTOPATHOLOGICAL FEATURES	Defensive cells such as lymphocytes, epitheloid cells / increased giant cells / fibrosis present / bacilli decreased.	Defensive cells are replaced by macrophages / no fibrosis / bacilli increased.
COURSE AND PROGNOSIS	Subsides in few weeks / relapse uncommon.	Prolonged course / recurrence more common.

DIFFERENTIAL DIAGNOSIS

1. Erysipelas
2. Urticaria
3. Relapse of Hansen

DIFFERENCE BETWEEN REVERSAL REACTION AND RELAPSE

	REVERSAL REACTION	RELAPSE
Occurrence	Occur in BT, BB, BL, LLs type of leprosy.	Occur in all types and subtypes of leprosy.
Onset	Sudden. Within 6months – 2yrs of termination of treatment.	Insidious. After 1-5yrs of termination of treatment.
Clinical features	Erythema and edema of existing lesions appear. Similar new lesions occur. Edema of hands and feet present.	Old lesion show slow extension in areas with increase signs of activity. New lesions appear . Edema not prominent.
Nerves	Previously involved nerve tender and detoriate with sensory or motor defecit. Nerve abscess occur	Fresh nerve involvement. Sudden paralysis not seen. Nerve abscess not seen.
SSS	Usually Negative.	Positive in BL, LL relapse. Negative in TT relapse.
Response to steroid	Respond well within 2 months.	Disease progressive.

COURSE AND PROGNOSIS [9]

Upgrading reaction is usually a temporary condition and subsides in a few weeks. Relapse are uncommon, the acute exacerbation often influence the prognosis favorably. If the reaction is severe, it may result in permanent nerve damage with consequent deformity. Downgrading reaction run a prolonged course and recurrence are more common.

TYPE II REACTION

SYNONYMS :- [Roseolar leprosy**,** Jopling type II, Erythema nodosum leprosum**,** ENL syndrome, **[6]** Lepromatous lepra reaction**,** Coombs and Gell type III **,** Lepra Fever**,** Acute exanthem of leprosy. **[32]]**

INCIDENCE

Overall incidence of ENL reported to occur in 50% of LL and 25% of BL in the pre MDT era. In post MDT era it has fallen to 12% in LL and 2.1% in BL.**[14]** Occur in about 35% of patient with LL**33** and 3.1% of pediatric patient with LL.**[34]**

AGE

Type II reaction occurs mainly in age group 20 – 40 years. The highest incidence of ENL reactions has been noted between 11- 40 years, corresponding to the highest age incidence of leprosy in South India.**[35]**

SEX

Type II reaction occurs in both sexes with almost equal frequency showing some predominance in males. A study of ENL cases in South India had attributed the male predominance to the high proportion of male patients attending the hospital.[35] Browne had reported high incidence among males.[36] Guinto reported high incidence in female.[37]

TIME OF ONSET

50% of ENL reactions occurred in the 2nd or 3rd year after starting MDT. Reaction continued to occur up to 8 years after RFT. Kumar et al reported that ENL occur mostly during 2nd or 3rd year after starting MB MDT.[14]

ENL may present as denovo at first visit. A publication from Los Angeles reported a series of 32 adults presenting with reaction for first time and 69% had ENL.[38] In a study reported from India 40% of LL patients presented with ENL at the first visit.[39]

The overall incidence of recurrent ENL was 64.3% and manifest 5 or more episodes over a period of 2 years. Transaction of 16th International Leprosy Congress labeled 'chronic ENL' if the patient needs continued antireaction treatment for a period of more than 6 months.[14]

TYPE II REACTION ACROSS SPECTRUM OF LEPROSY

Type II reaction occurs only in lepromatous form of leprosy [ie BL, LLs, LLp]. 50% of LL and 25% of BL can suffer from Type II reactions.[14] Previously Histoid Hansen was thought not go in for ENL. But more recently ENL has been reported in Histoid Hansen.[39, 40]

PRECIPITATING FACTORS [6, 14]

1. Psychological stress
2. Physical stress and injury
3. Surgery
4. Physiological stress – menstruation, pregnancy, parturition, puberty
5. Intercurrent infection – malaria, filarial, chicken pox, typhoid
6. Drugs – dapsone, sulphonamide, thioacetazone, rifampicin, iodides, bromides
7. Seasonal variation – Murata reported ENL more common during summer or autumn.
8. Others - ingestion of alcohol/ hot foods/ mantoux testing/ vaccination.

RISK FACTORS [14, 41]

1. Female gender
2. Higher BI > 3
3. HIV
4. Pregnancy and lactation

CLASSIFICATION OF TYPE II REACTION[42]

Based on mode of onset of reaction ENL are classified as

1. Rheumatic type - start with fever and joint pain and later develop skin lesion.
2. Exanthematous type – start with fever and skin lesion simultaneously.
3. Mixed type - start with fever, joint pain and skin lesion simultaneously.

CLINICAL FEATURES [9]

CUTANEOUS MANIFESTATIONS

ENL lesions are most characteristic cutaneous lesion of Type II. They occur as crops of erythematous, evanescent [lasting only for 2- 3days], painful, slightly raised, dome shaped nodules; ill-defined in margin measuring few mm to cm, blanches on light finger pressure. They tend to appear more in the evening [at time when endogenous corticosteroid production is at its lowest]. They occur more commonly on face, arms and distributed bilaterally and symmetrically, not superimposed on old leprosy lesion. They resolve with desquamation and scaling leaving behind a bluish stain in the skin. Recurrences occur at the same site.

The classical lesions are papules, nodules and plaques. Apart from classical ENL Type II reaction can also manifest as vesicular, bullous, hemorrhagic, pustular, ulcerated and EMF like lesions.[43] Bullous type of ENL cases have been reported from Mexico, South India and Nepal.[44]

Pustular and haemorrhagic ENL carry poor prognosis.[42] Pustules contain sterile pus with polymorphonuclear leukocytes and degenerated bacilli. Erythema necroticum ulcerans has been reported in adults and rarely in children barring one case report by Pandhi et al.[34]Pretibial ulceration also reported in Type II reaction.[42]

NEURITIS

Neuritis are less common and less dramatic in Type II reaction when compared to Type I reaction. Only in severe reaction nerve become enlarged, tender and lose function rapidly.

CONSTITUTIONAL SYMPTOMS

ENL is usually accompanied by generalized systemic illness which manifest in the form of fever, malaise, headache, anorexia, insomnia and depression. The fever is usually intermittent, high grade, high in the evening and associated with chills and rigor. Edema of hands, feet, face and painful dactylitis are other general manifestations of Type II reaction.

SYSTEMIC MANIFESTATION

EYE

Ocular manifestation includes iritis, episcleritis, iridocyclitis, conjunctivitis, keratitis, lagophthalmos and secondary glaucoma. Most dreaded among them is

iridocyclitis. It manifests as redness, diminished vision, photophobia, epiphora and ocular pain. Any delay in treatment of iridocyclitis, may result in irreversible blindness.

A case of Orbital apex syndrome describing the orbital involvement due to ENL has been reported. Dhaliwal et al described the involvement of left maxillary and ethmoid sinus along with destruction of medial orbital wall associated with vasculitis.[45]

ENT

ENL lesions can involve the mucus membrane of nose, mouth, pharynx and larynx. It may result in rhinitis, epistaxis, nasal blockage, difficulty in breathing, erosion, ulceration and perforation of nasal septum.

MUSCULOSKELETAL

Myositis and arthritis are common manifestations in Type II reaction. ENL lesions extending to the fascia and muscle produce tender, woody hard lesion on the muscle particularly seen in brachioradialis. Multiple ENL nodule with inflammatory edema along with arthritis of interphalangeal joint constitute a condition known as 'The Reaction Hand'.

Arthritis in Type II reaction are of rheumatic type and commonly affects knee, metacarpophalangeal joint, inter phalangeal joint, wrist and ankle. It manifest as painful warm joint swelling with limitation of movements. The joint manifestations are inversely proportional to the skin lesion.

Dactylitis is an another feature in Type II reaction manifesing as painful spindle shaped swelling of the phalanges. Periostitis and osteoporosis are other manifestations of Type II reaction affecting mainly the long bones, tibia and phalanges. The radiological findings include soft tissue swelling, osteoporosis, subarticular collapse, pseudo cyst [as punched out area of rarefaction], ankylosis and disorganization.

LYMPHADENITIS

Half of Type II reaction cases shows lymphadenitis. Preauricular lymphadenitis precedes the onset of lepra reaction and it is a premonitory sign in Type II. Other groups involved are cervical, axillary, intercostal and inquinal nodes. Initially they are discrete, later become matted and sometimes go for necrosis or suppuration.

EPIDIDYMO-ORCHITIS

Its one of the important manifestations of Type II reaction. It may be unilateral or bilateral. May be acute with painful swollen testis that atrophies quickly. Gyanecomastia usually follows testicular atrophy. Acute mastitis can occur in females as a result of Type II reaction.

OTHER SYSTEMS

Pleuritis can occur as respiratory system manifestation. Hepatitis which is reversible may occur and sometimes it may lead to persistent hepatomegaly, ascites and hepatic amyloidosis. Renal involvement may manifest as glomerulonephritis causing haematuria, oliguria and sometimes lead to renal amyloidosis. Cardiovascular changes

with low BP and pericardial friction rub has been reported. The occurrence of leprous vasculitis and leprous meningiovasculitis has been reported in lepra reaction.

GRADING OF TYPE II LEPRA REACTION [42]

MILD – Temperature up to 100^{o} F and a few skin lesion on one or more extremities.

MODERATE - Temperature up to 102^{o} F, skin lesion are more numerous in all four limbs and few on the trunk and face with occasional vesicle and pustule. Extra cutaneous signs present.

SEVERE – Temperature above 102^{o}F, vesiculation and pustulation present. Visceral involvement present.

COMPLICATIONS

1. Paralysis of involved nerves
2. Ulceration of skin lesions
3. Blindness
4. Infertility
5. Perforation of nasal septum and hard palate
6. Secondary amyloidosis
7. Debility and exhaustion

HISTOPATHOLOGY [1,6]

In skin, pathology is seen in deep dermis or subcutis. At the onset it is characterized by edema of papillary dermis, sharp influx of neutrophils and lymphocytes. Mixed dermal inflammatory infiltrate composed of neutrophils and lymphocytes superimposed on collection of foamy macrophages containing fragmented bacilli. Neutrophilic leucocytoclastic vasculitis affecting the arterioles or venules is a significant feature with endothelial swelling and intense infiltration of polymorphonuclear leucocytes around blood vessel. Scanty fragmented and granular bacilli are seen around the vessels. Extravasated erythrocytes are often seen. The subcutis shows mixed lobular and septal panniculitis. DIF reveals deposition of Ig G and C3 in the walls of dermal vessels.

In erythema necroticans, involvement of superficial dermis and epidermis with ulceration, in addition to vasculitis and necrosis are seen. In bullous ENL intraepidermal cleft with diffuse polymorphonuclear infiltrate and few foamy histiocytes along with few AFB.[44] In addition to skin, the reacting granuloma may be found in nerves, lymphnodes, liver, muscle and synovium.

IMMUNOLOGY AND PATHOGENESIS

Type II reaction is an immune complex mediated syndrome [Coombs and Gell type III hypersensitivity reaction] where the humoral immunity plays the major role. Large amount of M. leprae antigens are available both intracellularly and extracellularly after release from the macrophages. The pathogenesis of release of antigen is not fully understood but suggested as an immunological process. The polysaccharide portion of M. leprae is responsible for elicitation of humoral immune response. These antibodies cross react with cardiolipin and antigen of many different organs. The released mycobacterial antigens combined with antibodies get deposited as immune complex along vulnerable capillaries of skin, synovial membrane and glomeruli. Complement is activated by immune complexes and attracts neutrophils which release lysozomal enzymes resulting in tissue damage.

It has been recently observed that these antibodies are of mainly Ig G3 subclass and it react with distinct motifs R.G.D [arginine, lysine, aspartic acid] which bind to fibronectin receptors of macrophages.[11] Wenambu et al found that Ig and C are present only in early ENL lesions and in ENL lesions examined after 24 hours, they found no such deposits in their lab animal experiment.[46]

Patnaik et al reported that immune complex mediated mechanism is responsible for the exudative lesion seen in hepatic morphology during ENL. The eyes, renal and joint manifestation of ENL are attributed to immune complex mediated mechanism.[47]

ENL is associated with a strong Th2 response with high expression of IL- 4, IL-5, and IL-10. TNF - α concentration in blood also rises to very high levels leading to systemic manifestation like fever. It has also been noted that there is increase CMI to M. leprae antigen in ENL reaction with increase in number of T cell and increase in CD4 / CD8 ratio up to two fold. It was observed that there is decrease in CD8 T cells and cytotoxic T cells in ENL lesion. This decrease in CD8 T cells may induce a change in amount and affinity of antibodies which favour the formation and deposition of immune complex.

Mshana et al pointed out the failure to excite arthus reaction on intradermal injection of M. leprae antigen into a LL patient.[48] Another phenomenon observed in ENL lesion is a significant increase in apoptosis observed at 6 months of treatment.[49] Oliveria and colleagues found apoptosis to be greatly accelerated in circulating neutrophils in patients experiencing ENL.[50]

The other serological abnormalities observed during Type II reaction includes positive for autoantibody such as RA factor / ANA. IgG, IgM, C2, C3 and CRP are also increased during the acute phase.

DIAGNOSIS

1. Mainly clinical.
2. Abnormalities in other laboratory investigations includes

Hematological

1. Leukocytosis
2. Thrombocytosis
3. Raised ESR
4. Normocytic normochromic anemia
5. Profound fall in Hb% and erythrocytes count [severe reaction].

Biochemical

1. Abnormal LFT showing increase in SGPT. Increase in Serum bilirubin occurs during hemolytic crisis in severe reaction.
2. Alteration of albumin to globulin ratio is another biochemical change reported mainly by increase in α-globulin.

Skin biopsy and histopathology

DIF – shows deposits of Ig G and C3 in the vessel wall.

DIFFERENTIAL DIAGNOSIS [DD]

DD for Classic ENL

1. EN lesions due to other causes like TB, CTD should be excluded.
2. Panniculitis secondary to infection, malignancy, vasculitis, Weber Christian disease.

DIFFERENCES BETWEEN ENL AND EN

	ENL	**EN**
Numbers	Numerous	Less in number
Site	All over the body including face.	Limited to legs.
Nature of lesion	Evanescent, may ulcerate.	No evanescence, never ulcerate.
Diurnal variation	Appears usually in evening.	No diurnal variation.
Histopathology	Septal panniculitis with foamy macrophages containing degenerated AFB in the dermis.	Septal panniculitis with dermis showing perivascular lymphocytic inflammatory infiltrate in early lesion and lipid laden macrophages in late lesion with no AFB.

DD for bullous and pustular ENL

1. Erythema multiforme
2. Varicella
3. Pemphigus vulgaris
4. Bullous pemphigoid
5. Pustular psoriasis

TYPE III LEPRA REACTION

SYNONYMS: - [Lucio phenomenon**,** Lepra manchada **]**

This type of reaction is confined to the diffuse non nodular form of LL chiefly encountered in Mexicans. This was first described by Lucio and Alvarado in Mexico [1852]. The unique feature is that it is seen only in untreated patients.

CLINICAL FEATURES

Painful and tender red patches appear on the skin, particularly on the extremities. They become purpuric, the centre of the purpuric lesions becomes necrotic and ulcerated and finally develops a brown or black crust [eschar] which falls off after a few days leaving a superficial atrophic scars. Lesions most commonly occur on the legs and less commonly on thighs, forearm and buttocks. Trunk and face are usually spared. Few lesions appear as bulla and burst to leave deep ulcers with jagged edges which heal slowly. Rea and Leavan in their study found that Type III reaction patients were afebrile throughout the course of reaction.[51]

COMPLICATION

1. Secondary pyoderma and cellulitis.
2. Secondary amyloidosis.

HISTOPATHOLOGY

Type III lepra reactions are histopathologically characterized by

1. Ischaemic epidermal necrosis.
2. Necrotizing vasculitis of small blood vessels in the upper dermis.
3. Severe focal endothelial proliferation of mid dermal vessels.
4. Presence of large number of bacilli in the endothelial cells.

IMMUNOLOGY AND PATHOGENESIS

The immunology of Lucio phenomenon is believed to be based on Sanarelli Schwartzman reaction [non allergic but hypersensitivity phenomenon] where the basic pathology is due to unhindered multiplication of M. lepra in the vascular endothelium.[52] The exposure of the bacterial antigen to the circulating antibodies results in vasculitis, infarction and necrosis.

If the patient with Lucio phenomenon are given a lepromin test, they usually develops extensive local reaction [the Medina – Ramirez reaction] occurring within 4 -6 hrs and is a reproduction of the lesion in Lucio phenomenon.[19] Other immunological abnormalities seen in Lucio phenomenon are hypergammaglobulinemia, mixed cryoglobulinemia and positive VDRL test for syphilis.

LABORATORY INVESTIGATION

The usual laboratory findings are leukocytosis or absolute neutrophils, anemia, high ESR, hypergammaglobulinemia and positive cardiolipin antigen test for syphilis.

DD for ulcerative skin lesion

1. Ecthyma
2. Pyoderma
3. Ischemic ulcers
4. Intra vascular coagulopathy
5. Deep mycosis
6. Lymphocytoma cutis

DD for purpuric lesions

1. Henoch Schoenlein Purpura
2. Pityriasis lichenoides et varioliformis acuta [PLEVA]
3. Cutaneous allergic vasculitis

MANAGEMENT OF LEPRA REACTIONS

Four principles that need to be considered in management of reactions are [53]

1. Control neuritis in order to prevent anesthesia paralysis and contracture.
2. Halt damage to eye preventing blindness.
3. Control the patients pain.
4. Kill bacilli and stop disease progression.

Depending on these principles four aspects of treatment are given as follows

1. Anti-inflammatory therapy primarily to reverse nerve damage.
2. Analgesia to control the patients' pain.
3. Physical measures to prevent or reverse contracture.
4. Antibacterial therapy of disease itself should be continued.

GENERAL MEASURES COMMON TO TYPE I AND TYPE II REACTION

1. Mild cases may be treated as ambulatory cases but severe cases must be hospitalized and complete bed rest should be reserved for those with impending motor palsies.
2. To relieve anxiety and mental stress a tranquilizer or sedative may be prescribed and antibiotics are added if intercurrent infection present as precipitating factors.
3. To alleviate the pain NSAID, aspirin [200 – 600 mg 4 to 6 times daily], ibuprofen [200 -400mg tds] or indomethacin [25 – 50mg bd / tds] can be given.

4. Reassurance and counseling are particularly important because patient thought that he is not responding to treatment instead getting worse. This may make them to discontinue the anti-leprosy drugs. They can be assured that they are recovering the lost immunity and the disease is getting eliminated.

MANAGEMENT OF TYPE I REACTION

Anti-Leprosy Treatment should be continued. If the patient is on dapsone at time of reaction it is continued at its full dose and if he is not on dapsone at the time of reaction it can be started after the reaction is brought under control.

CORTICOSTEROIDS

This is the mainstay of reaction management. In 1950, Chaussinand first mentioned about the use of cortisol / ACTH in the treatment of Type I reaction. Thereafter it was brought into use for both Type I and II reactions.

Mechanism of action

1. Suppresses both early and late phase of inflammation.
2. Normalizes disturbed T4 : T8 ratio.
3. Causes suppression of T cell driven inflammatory response to M. leprae antigen.

WHO steroid regimen for Type I reaction. Tablet prednisolone should be taken once daily in the morning as follows, [54]

40 mg - 2weeks
30 mg - 2weeks
20 mg - 2weeks
15 mg - 2weeks
10 mg - 2weeks
5 mg - 2weeks

Treatment proposal by Ben Naafs is as follows,[55]

Paucibacillary	Multibacillary
40 mg – 2 weeks	30 mg – I month
30 mg – 2 weeks	25 mg – 2 months
25 mg – 1 month	20 mg – 3 months
20 mg – 2 months	15 mg – 2 months
15 mg – 1 month	10 mg – 2 weeks
10 mg – 2 weeks	5 mg – 2 weeks
5 mg – 2 weeks	
Total – 6 months	Total – 9 months

Generally most BT patients require prednisolone for 4 – 9 months, BB patient for 6 – 9 months and BL patients for 6 – 18 months or even for 24 months.[1,6] Side effects of steroids includes HT, DM, osteoporosis, peptic ulceration, Cushing syndrome, cataract, glaucoma, reactivation of latent infection [such as TB], drug dependence, muscle wasting, etc.

So monitoring is considered very important by taking into account the following parameters

1. Monitor BP and weight at each visit.
2. Urine analysis and blood sugar estimation.
3. Gastric protection with H2 blockers or proton pump inhibitors.
4. Osteoporosis prevention.

CLOFAZIMINE [LAMPRENE]

Less useful in Type I reactions especially in RR. This red immunophenazine dye was first discovered by Dr. Vincent Mary and it was Dr. Stanely Browne who first used it clinically in leprosy. It is useful in reaction because of its anti-inflammatory property.

Mode of action [5,6]

1. Decreases neutrophilic chemotaxis to the inflamed area.
2. Decreases antibody formation.
3. Increases synthesis of lysozomal enzymes and enhance phagocytic ability of macrophage resulting in complete digestion or degradation of antigens to less antigenic form.

Clofazimine acts very slowly and take weeks for its full effect. So it has limited role in neuritis.

Dose: - Initial -> 300 – 400 mg/day then gradually tapered and maintained in dose of 100 mg/day.

Side effects include reddish brown pigmentation of the skin, conjunctiva, body secretion, faeces, cornea and retina, icthyosis, pruritus, photosensitivity and eosinophilic enteritis.

MANAGEMENT OF NEURITIS

Various treatment modalities for neuritis includes

1. NSAIDS.
2. Anti reactional drug – corticosteroids helps in dispersion of intra neuronal edema.
3. Supportive therapy in form of padded splint.
4. Sessions of graduated passive and active exercises to prevent joint stiffness and to aid muscle recovery.
5. Intra neural injection – a combination of 1 ml of 2% lignocaine, 1 ml of hydrocortisone and 1500 units of hyaluronidase are injected into swollen nerve or around the nerve using 14 size needle.
6. Surgical treatment – Nerve decompression [neurolysis], decompression with transposition or with epicondilectomy.

MANAGEMENT OF TYPE II REACTION

WHO expert committee discussed the management of Type I reaction and ENL together, advising a 12 week steroid regimen and proposed severe ENL can be treated with prednisolone a 12 weeks course with the maximum dose not exceeding 1mg / kg body wt.[54]

ILEP technical bulletin recommends treating severe ENL with corticosteroid at a starting dose of 30 – 60 mg and reducing every week by 5 – 10 mg. It also states that a maintenance dose of 5-10 mg may be needed for several weeks to prevent recurrence.[57]

Various other drugs used in ENL are as follows

1. **Anti-inflammatory drugs**, aspirin [400mg 6 hourly] and indomethacin [50mg 8 hourly] can be used in mild cases of ENL.
2. **Chloroquine** - It is used in mild & moderate ENL cases due to its anti-inflammatory property. It is given in the dose of 250 mg tds for 1 week, 250 mg bd for 2nd week and 250 mg once daily thereafter. Side effects like visual disturbance limit its use.
3. **THALIDOMIDE**

It is highly effective in acute severe and recurrent ENL. In 1965 Sheskin reported the effectiveness of thalidomide in the management of ENL. It is a racemic glutamic acid analogue composed of 2 enantoimers R- and S- Thalidomide. These 2

enantoimers have different properties; one is a potent suppressor of TNF release while the other is sedative.

Mode of action

- Inhibits the release of TNF, IFN- α, IL-10, IL-12 and NF κB.
- Decreases the effect of complement derived chemotactic factors resulting in reduction and non-recruitment of PMNL into the lesional site.

Side effects include teratogenicity, drowsiness, sedation, irreversible peripheral neuropathy, constipation, etc. WHO committee advises that it should be given only to men or post-menopausal women who are dependent on corticosteroid.[54]

4. **Clofazimine** is indicated in Type II reaction in the following situation
   - In patients who cannot be weaned off from steroids.
   - In patients who are troubled by continuous ENL.
   - Where thalidomide is not available or cannot be used

In severe recurrent chronic ENL pulsed i.v corticosteroid monthly once along with azathioprine 50mg daily can be tried as suggested by Mahajan et al.[58]

MANAGEMENT OF TYPE III REACTION

Mild cases - self-limiting.

Moderate and severe cases - Steroids are moderately effective. Thalidomide, clofazimine and other immunosuppressant are ineffective. Plasmapheresis is reported to be effective.

OTHER DRUGS IN LEPRA REACTION [56]

ANTIMONIALS - Potassium antimony tartrate and Stibophen were used in Type II reaction and mild Type I reaction. Since they are less effective and more toxic, less frequently used nowadays.

COLCHICINE- It has been found to be useful in recurrent severe ENL in dose of 1.5 – 2mg daily in divided doses. It is used in ENL for its ability to inhibit neutrophilic chemotaxis.

NON STEROIDAL IMMUNOSUPPRESSANTS

Azathioprine – it acts by decreasing the synthesis of TNF-α. It is effective in severe or refractory ENL in recommended dosage of 50mg / day.[59]

Mycophenolate mofetil – useful as steroid sparing agent and in patients in whom systemic steroids are contra indicated. It acts by inhibiting type II Inosine Monophosphate Dehydrogenase expressed in activated T and B lymphocytes resulting in induction of apoptosis of activated T cells and elimination of clones of cells.[60]

Methotrexate – useful in severe and refractory ENL.

Cyclosporine A – It is potent immunosuppressant shown to suppress activation of T helper cells, reduce IL-2 receptors and inhibit IL-2 production. Its role in ENL thought to be promising but relevant data are lacking.

PENTOXYPHYLLINE - used in Type II reaction because of its immunomodulator effect.[61]

LEVAMISOLE - It is considered in reaction for its ability to restore T cell numbers to normal.

ZINC - It is recommended in treatment of necrotic ENL and chronic leg ulcer in dosage of 220mg tds. It did its role by inhibiting neutrophilic chemotaxis and complement mediated reaction. This is still under extensive trial.[62]

PLASMAPHERESIS - Replacement of patients plasma with sterile albumin solution cause removal of immunostimulatory factors and cause dilution of cytokines, free antigen and antibodies.

ZAFIRLUKAST- This leukotriene antagonist has been tried in ENL with outcome measures not well defined.[63]

INFLIXIMAB – This chimeric monoclonal antibody suppresses TNF and has been reported in a single case of recurrent ENL.[64]

TREPTERYGIUMWILFERDIN HOOK – A CHINESE HERB –this has been reported to be effective in both Type I and Type II with efficacy of 96.6% and 98% respectively.[56]

TREATMENT OF COMPLICATIONS IN REACTIONS

Iritis / iridocyclitis – requires rest, dilation of pupil with mydriatics like atrophine and suppression of inflammation with local steroid eyedrops or ointment.

Epididymo orchitis – bed rest, NSAID and scrotal suspensory bandage gives symptomatic relief and steroids help in relieving the inflammation.

Arthritis / periostitis – Thalidomide and steroids control it rapidly. Temporary immobilization, analgesic and anti-inflammatory drugs may be additionally required.

Glomerulonephritis and amyloidosis – no drugs can reverse the renal pathology secondary to immune complex deposition but early and specific treatment can arrest the progression. Bed rest, adequate fluid intake, steroids and continuation of anti-leprosy drugs are all helpful.

LEPRA REACTIONS AND HIV [65, 66]

The relationship between leprosy and HIV infection is not yet fully understood. Earlier literature is replete with reports of increase frequency of Type I reaction, severe neuritis, poor therapeutic outcome and relapse among HIV infected leprosy patients.[67]

HIV infected patients responding to HAART developed reaction especially type I [RR] as a form of immune reconstitution inflammatory syndrome [IRIS] with a possibility of atypical presentation. It is usually seen in first 6months of starting HAART

and it result from an increase in CMI. In earlier literature HIV infection was thought to decrease the risk of ENL. But recent studies Nanda Lal Sharma et al and Geber et al recorded a definite higher risk of ENL reaction. [66, 67] Like other intercurrent infection HIV acted as a trigger for ENL reaction and appears to produce severe, recurrent necrotic lesions associated with neuritis. HIV is neurotrophic and may cause necrotizing vasculitis of the nerve.[68] The interaction of neurotropicity of M. leprae and HIV may result in neuropathy that is severe and unresponsive to steroid therapy. Similarly HIV induced vasculopathy may aggravate immune complex mediated vasculitis / panniculitis of ENL that responds poorly to steroid therapy.[69]

In case of ENL with HIV, thalidomide [100 – 400mg / day] is the currently recommended drug in moderate to severe reaction. Recently it has also been reported to produce antiretroviral effect possibly through inhibition of TNF production and by blocking TNF stimulated HIV replication.[66]

PREGNANCY AND LEPRA REACTION [6]

In pregnancy, there is increased incidence of lepra reactions.

Type 1 reaction – During pregnancy, downgrading reaction may occur in borderline leprosy especially in 3rd trimester due to decrease in CMI. During puerperium, reversal reaction is most likely to occur when there is a rapid regaining of CMI.

Type 2 reaction – In LL, Type 2 reaction is most likely to occur in the 3rd trimester and the puerperium. In the puerperium, reaction is associated with physical stress of parturition and reversal of increased plasma ACTH and cortisol to normal level.

MATERIALS AND METHODS

This study on lepra reaction was conducted among the patients attending skin outpatient department, in Department of Dermatology, Govt Rajaji hospital, Madurai medical college, Madurai, during the period from Oct 2009 to Sep 2011. Permission from ethical committee of the hospital was obtained for this study. The patients were recruited for study with fulfillment of following criteria.

Inclusion criteria

1. Patients with clinical features suggestive of lepra reaction of any age and sex including both, leprosy patients presenting with lepra reaction for the first time and already diagnosed cases of lepra reaction presenting with recurrent episodes.

Exclusion criteria

1. Patients not willing for the study.
2. Treated cases of lepra reaction presenting with no active lesions at the time of examination.

METHODOLOGY

HISTORY

A detailed history was taken which includes exacerbation of existing skin lesions, appearance of new skin lesions with duration, constitutional symptoms, systemic complaints, recurrence , neural pain , sudden onset of sensory loss or motor paralysis, onset of symptoms in relation to initiation of antileprosy drugs, and precipitating factors if any.

CLINICAL EXAMINATION

A detailed general examination and systemic examination was done. Detailed dermatological examination was done which included number, morphology, distribution, symmetry, tenderness and sensation of skin lesions. Nerve involvement with thickening and tenderness, sudden sensory impairment and motor paralysis were noted. The clinical type of leprosy was assessed.

INVESTIGATION

Routine lab investigation like urine routine, complete blood count, LFT, RFT were done. Diagnosis of type of leprosy was confirmed by SSS. Skin biopsy for histopathology study done for all patient.

DIAGNOSIS

Type 1 reaction was diagnosed by erythema and edema of existing skin lesions or appearance of new similar lesions with or without nerve tenderness or sudden impairement of sensory or motor function. Type 2 reaction was diagnosed by appearance of crops of erythematous tender nodules with any one of the following, fever, arthritis, neuritis, edema of hands and feet, dactylitis, iritis, epistaxis, epididymo orchitis, lymphadenitis. Neuritis was diagnosed by neural pain, nerve thickening and nerve tenderness. Both Type 1 and Type 2 reaction were graded according to their severity.

TREATMENT AND FOLLOW UP

MDT started for the new cases according to the type of leprosy and continued for those who already on MDT. Both Type 1 and Type 2 reactions were treated with standard WHO regimen of 12 weeks of steroid therapy. Tablet Predinisolone 40 mg was started with tapering once in 2 weeks. Analgesics were added to neuritic patients along with prolonged course of steroid. Antibiotics were added to patients with intercurrent infections.

Clofazimine 300mg was given to patients who had exacerbation and recurrence on and off and those who could not be weaned from steroids. Thalidomide was given to patient who was recalcitrant to both steroids and clofazimine. All patients were followed up for a minimum period of 6months to a maximum period of 12 months.

TYPE 1 REACTION IN BORDERLINE SPECTRUM

BT Hansen in Type 1

BB Hansen in Type 1

BL Hansen in Type 1

Facial patch [BT] in Type 1

TYPE 2 REACTION IN LEPROMATOUS SPECTRUM

LL Hansen in Type 2

LL Hansen with ENL lesions

BL Hansen with resolving ENL lesions

Histoid papules and ENL lesions in Histoid Hansen

MOTOR DEFORMITIES IN TYPE 1 REACTION

Left facial palsy in BT Hansen

Left foot drop in BT Hansen

Left claw hand in BT Hansen

CUTANEOUS LESIONS IN TYPE 2 REACTION

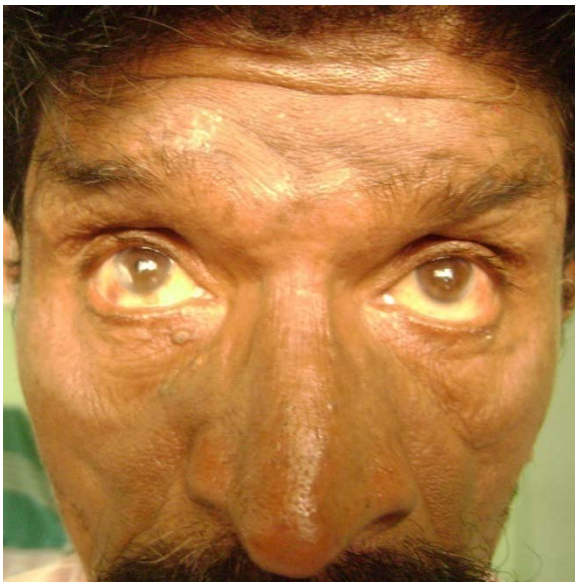
Ulcerative ENL in LL

Pustular ENL in LL

Necrotic ENL in LL

ENL plaque and nodule in LL

EXTRA CUTANEOUS FEATURES IN TYPE 2 REACTION



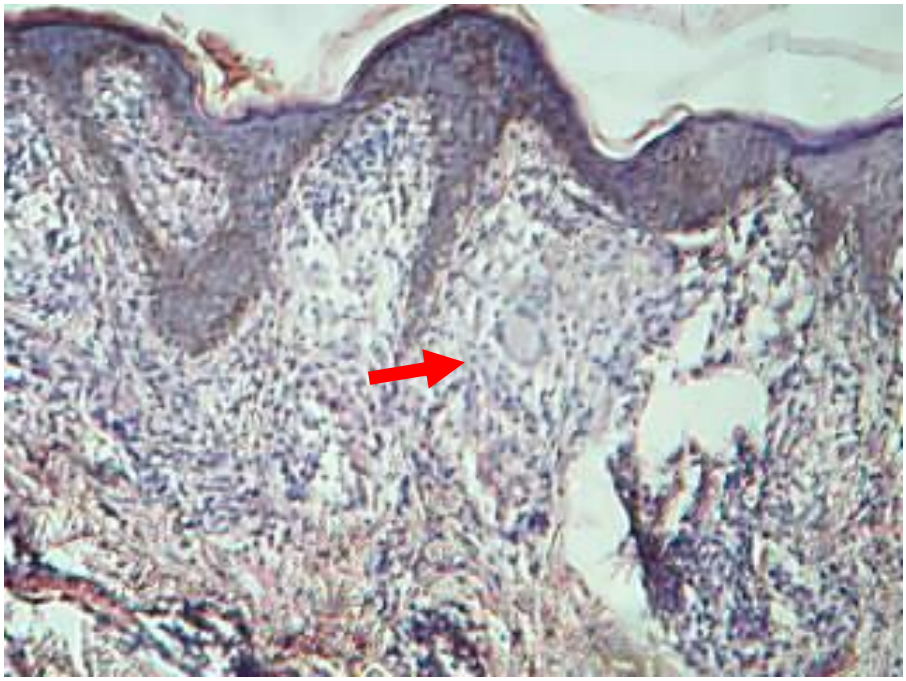
Bilateral iritis in LL

Dactylitis in LL

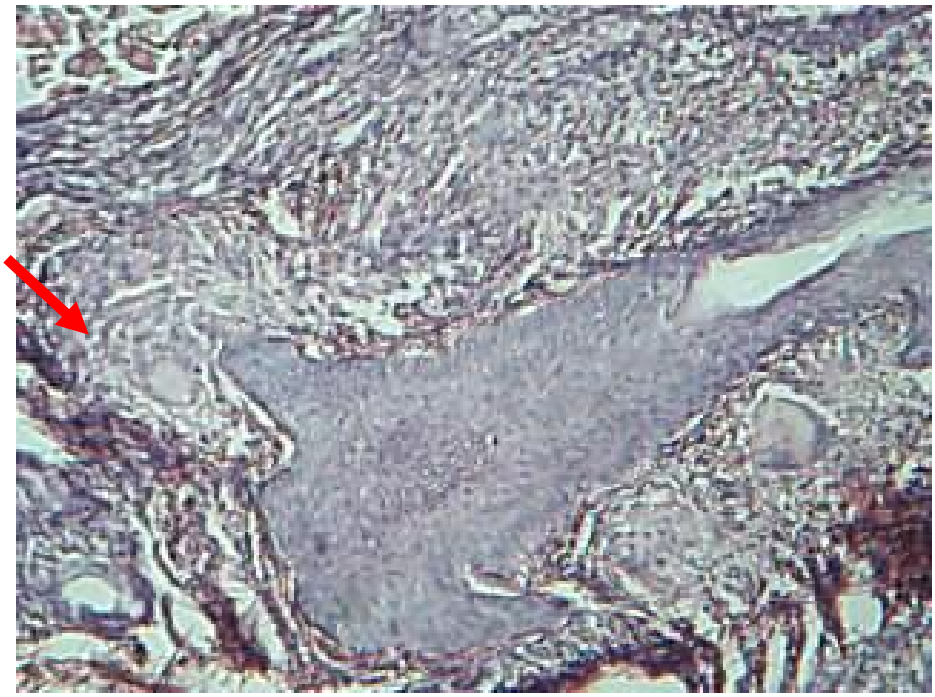
Inguinal lymphadenitis in LL

Edema of hands & feet in LL

HISTOPATHOLOGY OF TYPE 1 REACTION
[Biopsy from reactional patch in BT Hansen with Type 1 reaction]

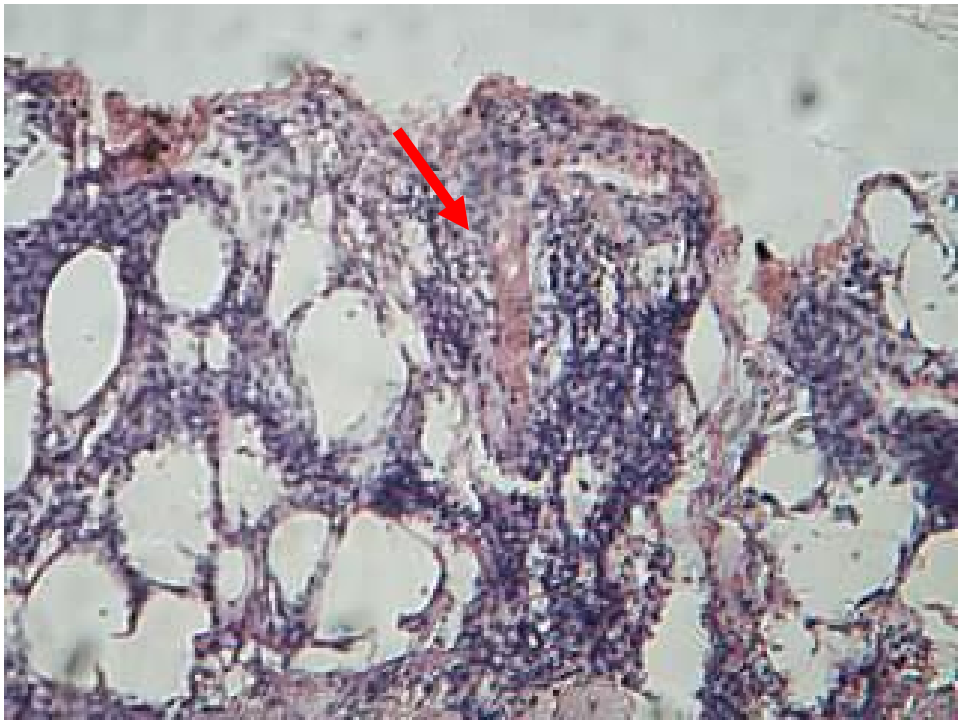


Epitheloid granuloma with giant cells dispersed by dermal edema

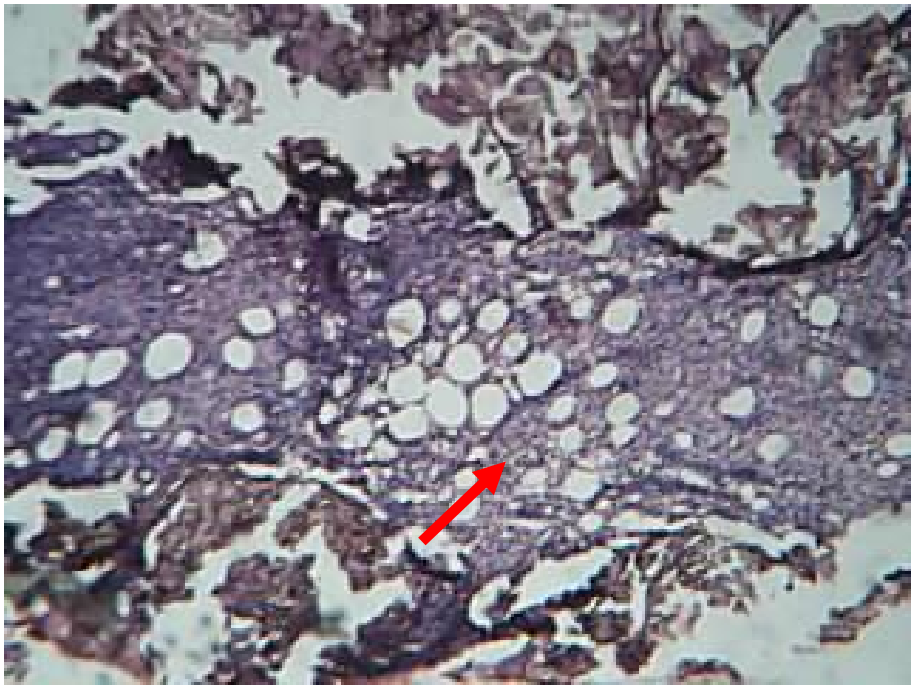


Periappendageal epitheloid granuloma with giant cells dispersed by dermal edema

HISTOPATHOLOGY OF TYPE 2 REACTION
[Biopsy of ENL nodule in LL Hansen with Type 2 reaction]

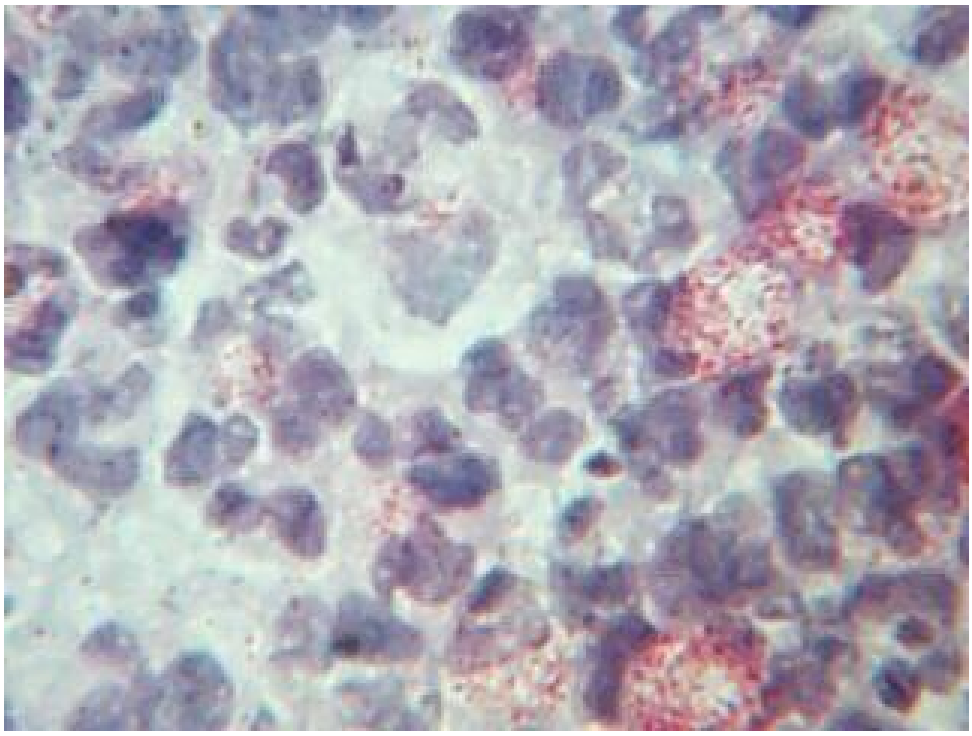


Septal panniculitis with neutrophilic vasculitis

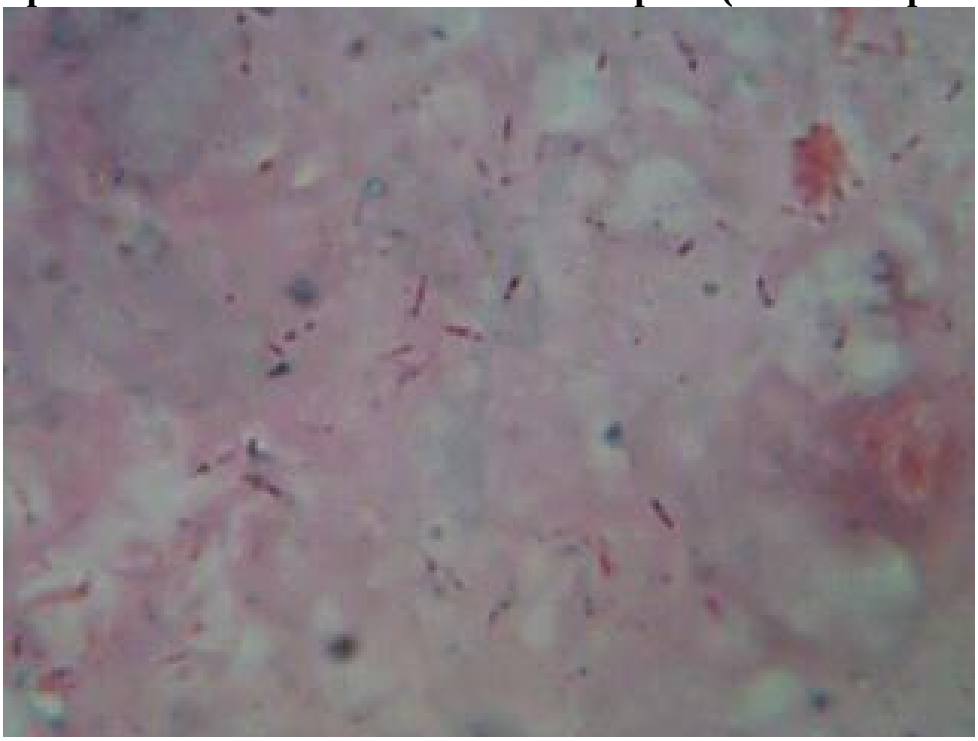


Septal panniculitis with neutrophilic infiltrate

AFB BACILLI IN SPLIT SKIN SMEAR

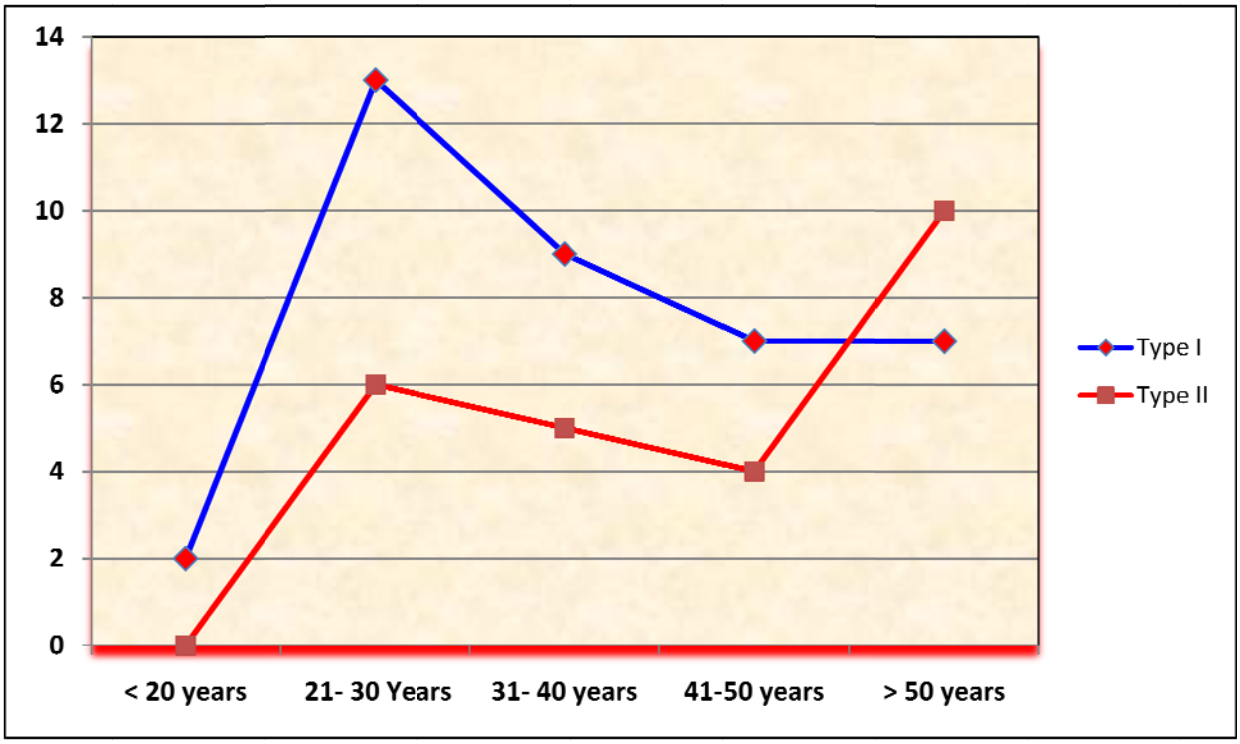


Clumps of AFB bacilli admixed with neutrophils (from ENL pustule)



Fragmented AFB Bacilli (from ENL nodule)

AGE DISTRIBUTION



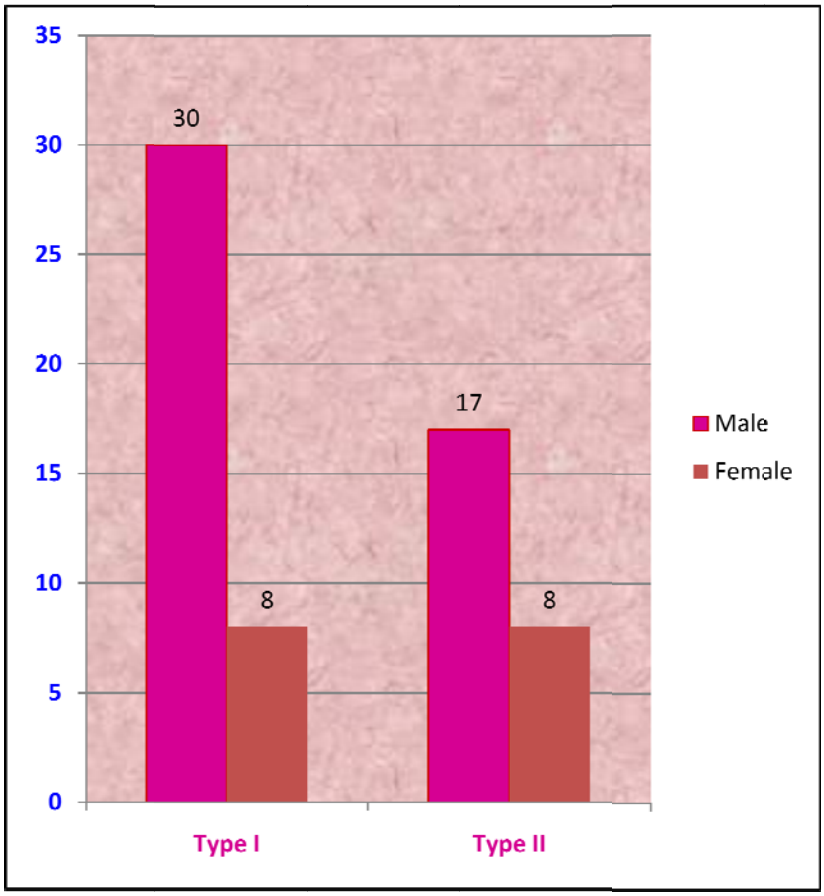
OBSERVATION AND RESULTS

Total no of cases attended the skin department (both inpatient and outpatient) in this 2 year study was 1,03,536. Out of which 63 patients were diagnosed to be having lepra reaction and were included in the study based on inclusion criteria. The overall incidence of lepra reaction was found to be 0.06%. Out of 63patients, 38 were Type I and 25 were Type II reaction. No case of type III reaction was reported

Table 1 : Age distribution

Age group	**Type 1 Reaction**		**Type 2 Reaction**	
	No	**%**	**No**	**%**
< 20 years	2	5.2	-	-
21- 30 Years	13	34.2	6	24
31- 40 years	9	23.7	5	20
41-50 years	7	18.4	4	16
> 50 years	7	18.4	10	40
Total	38	100	25	100
Range	15-63 years		22-61 years	
Mean	37.8 years		43.8 years	

SEX DISTRIBUTION



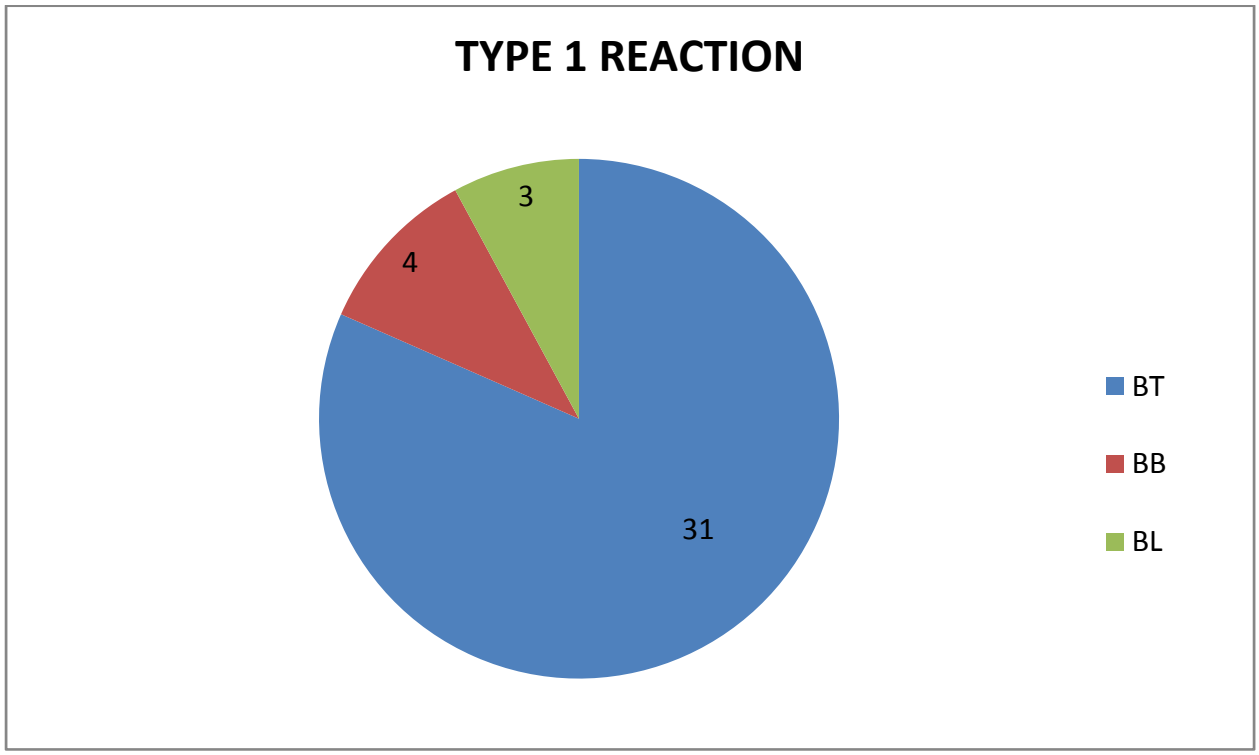
The Type 1 reaction cases had an mean age of 37.8 years and the Type 2 reaction cases had an mean age of 43.8 years. In our study, Type 1 reaction was common in 21 - 30yrs of age group [34.2%] and Type 2 was commonly seen above 50yrs of age [40%]. The youngest patient in the study group was 15 years of age and the oldest studied was 68 years of age. Both of them were male patients.

Table 2 : Sex distribution

Sex	Type 1 Reaction		Type 2 Reaction	
	No	**%**	**No**	**%**
Male	30	78.9	17	68
Female	8	21.1	8	32
Total	38	100	25	100

There were total of 47 males and 16 females presented with lepra reaction with the sex ratio of 2.9 : 1. The sex ratio of Type 1 and Type 2 reaction were 3.8 : 1 and 2.1 : 1 respectively.

REACTIONS IN VARIOUS SPECTRUM OFLEPROSY



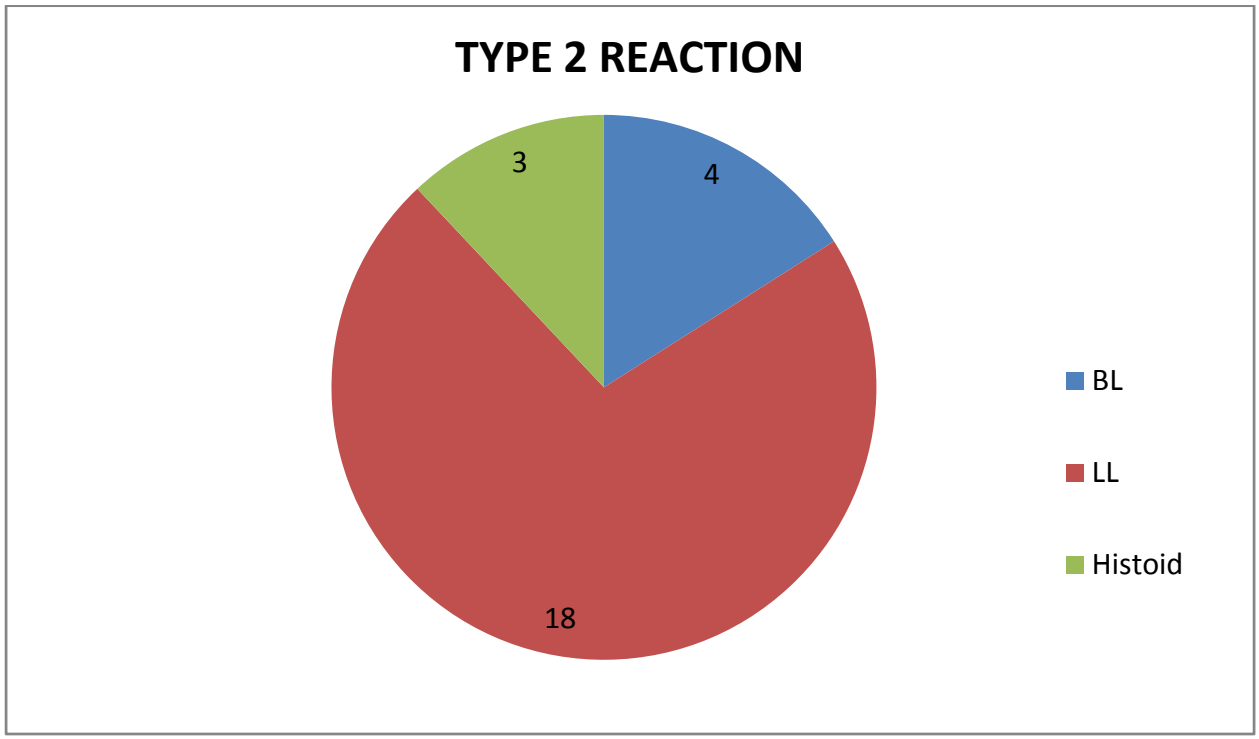


Table 3: Type of reaction in various spectrum of leprosy

Type of leprosy	Type 1 Reaction		Type 2 Reaction	
	No	%	No	%
BT	31	81.5	-	-
BB	4	10.5	-	-
BL	3	7.9	4	16
LL	-	-	18	72
Histoid	-	-	3	12
Total	38	100	25	100

BT type of leprosy was predominant (81.5%) in Type 1 reaction cases and LL in Type 2 reaction cases (72%). Among 38 patients of Type 1 reactions, 31 [81.5%] cases were BT, 4 [10.5%] cases were BB and 3 [7.9%] cases were BL. Among Type 1 reaction all cases were upgrading except for one case which downgraded from BT to BL. Out of 25 cases of Type 2 reaction, 4 [16%] cases of BL, 18 [72%] cases of LL and 3 [12%] cases of Histoid Hansen were reported.

Table 4: Occurence of reaction in relation to Anti Leprosy drugs

Anti-Leprosy drugs	Type 1 Reaction		Type 2 Reaction	
	No	%	No	%
Drugs taken	20	52.6	18	72
Drugs not taken [de novo]	18	47.4	7	28
Total	38	100	25	100

Out of 38 cases of Type 1 reaction, 18 cases occurred de novo without any relation to the anti-leprosy drug, 20cases [52.6%] developed reactions after the intake of antileprosy drugs. Out of 25 cases of Type 2 reaction, 7cases [28%] developed reaction de novo, 18 cases developed after intake of drugs.

Table 5: Onset of reaction in relation to the initiation of antileprosy drugs

Duration from the initiation of drug	Type 1 Reaction		Type 2 Reaction	
	No	%	No	%
≤ 3 months	5	25	2	11.1
4-6 months	1	5	2	11.1
7-12 months	5	25	4	22.2
1-2 years	3	15	6	33.3
3-5 years	3	15	1	5.6
> 5 years	3	15	3	16.7

It was observed that 25% of Type 1 reaction developed within 3months of taking the drug and another 25% developed Type 1 reaction after 7 – 12 months of taking the drug. In Type 2 reaction 33% of cases and 22% of cases developed the reaction after 1-2 years and 7- 12 months of taking the drugs respectively. Five cases of reaction [2- Type 1 and 3- Type 2] had dapsone monotherapy form of anti-leprosy treatment and all others had MDT regimen.

Table 6 : Total cases presented with precipitating [ppt] factors

Precipitating factors	**Type 1 reaction**		**Type 2 reaction**	
Single ppt. factor	23	60.5	18	72
Multiple ppt. factors	7	18.4	7	28
Nil factors	8	21	-	-
Total	38	100	25	100

Among 38 cases of Type 1 reaction, 30 patients had precipitating factors. Single precipitating factors was present in 23 cases [60.5%] and multiple ppt factors was seen in 7 cases [18.4%]of Type 1. Without any precipitation, 8 cases [21%] developed Type 1 reaction. Precipitating factors in form of single and multiple factors were present in all patients of Type 2 reaction.

Table 7 : Various precipitating factors

Precipitating factors	Type 1 Reaction		Type 2 Reaction	
	No	%	No	%
Antileprosy drugs	20	52.6	18	72
Physical stress	9	26.5	4	16
Mental stress	-	-	2	8
Inter current infection	3	8.8	3	12
Surgery	2	5.9	3	12
Postpartum	-	-	1	4
Trauma	2	5.9	1	4

The main precipitating factor in the study was intake of antileprosy drugs which was present in 20 patients of Type 1 and 18 patients of Type 2 reaction. Among the precipitating factors other than ALD, physical stress constituted 26.5% and intercurrent infection [viral hepatitis, typhoid, chicken pox] constituted 8.8% in Type 1 reaction. In Type 2 reaction 4 cases were precipitated by physical stress, 3 cases were precipitated by surgery [cataract surgery, hernioraphy, orthopedic surgery] and inter current infection each.

Table 8 : Constitutional symptoms

Constitutional symptoms	Type 1 Reaction		Type 2 Reaction	
	No	%	No	%
Present	14	36.8	24	96
Absent	24	63.1	1	4
Total	38	100	25	100

Constitutional symptoms were present in only 36.8% of Type 1 cases. But 96% of Type 2 cases had them. The constitutional symptoms taken into account both in Type 1 and Type 2 were fever, arthralgia and malaise.

Table 9 : Cutaneous features

Cutaneous features	Type 1 Reaction		Type 2 Reaction	
	No	%	No	%
Erythema & edema of old lesion	29	79.3	-	-
New similar lesion	6	15.8	-	-
Nodule	-	-	25	100
Plaque [subcutaneous]	-	-	8	32
Pustule	-	-	1	4
Ulcer	-	-	5	20

Erythema and edema of old lesions were present in 79.3% of Type 1 cases and 15.8% showed new similar lesion. Nodules were present in 100 % of Type 2 cases. Ulcer was seen in 5cases of Type 2. One case of pustular ENL was observed.

Table 10: Extracutaneous features

Extracutaneous features	Type 1 Reaction		Type 2 Reaction	
	No	%	No	%
Edema of hands	10	26.3	11	44
Edema of feet	5	13.2	13	52
Dactylitis	2	5.3	5	20
Iritis	-	-	1	4
Epistaxis	-	-	2	8
Epididymo orchitis	-	-	3	12
Lymphadenitis	-	-	4	16

Edema of hands and feet were noted in both Type 1 and Type 2 reaction. In Type 2 reaction, 11 cases [44%] and 13cases [52%] manifested with edema of hands and feet respectively. Dactylitis was present in 2 cases and 5 cases of Type 1 and Type 2 reaction. Among 25 cases of Type 2 reaction, 1 case of Iritis, 2 cases of epistaxis, 3 cases of Epididymo-orchitis and 4 cases of Lymphadenitis were observed.

NEURITIS IN REACTIONS

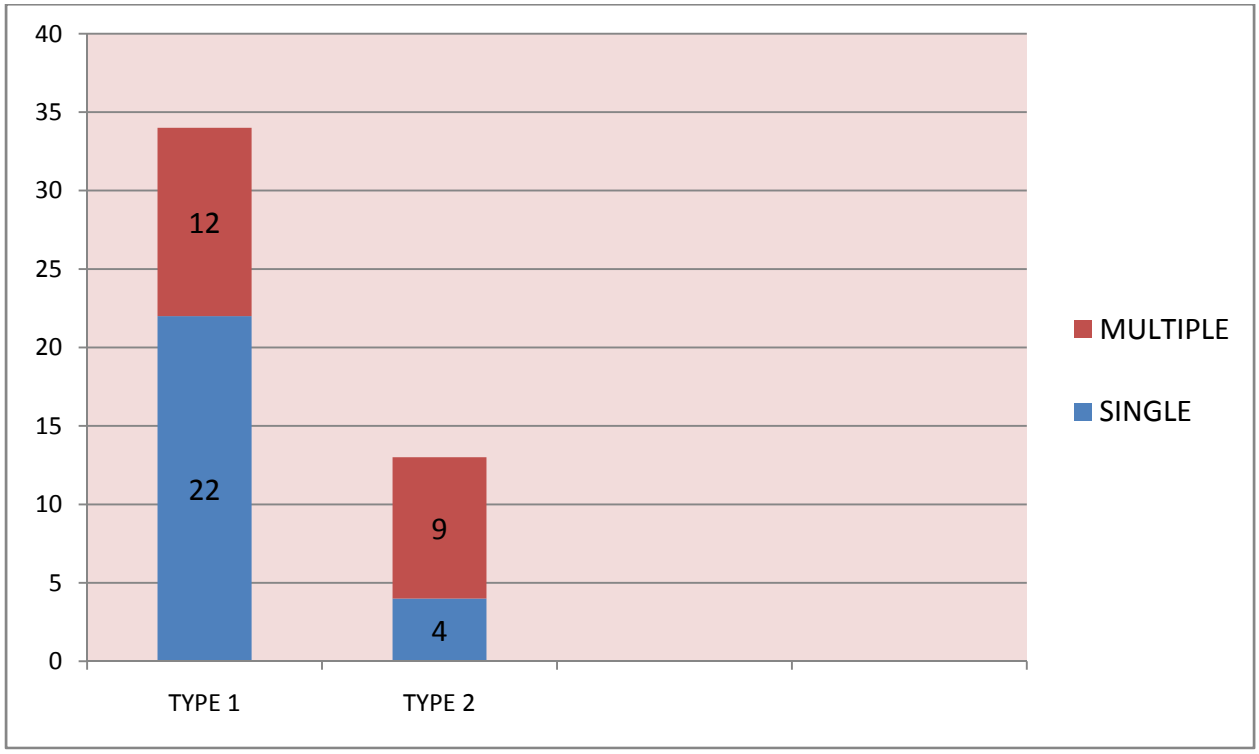


Table 11 : Neuritis

Neuritis	Type 1 Reaction		Type 2 Reaction	
	No	%	No	%
Single nerve	22	57.9	4	16
Multiple nerves	12	31.5	9	36
No neuritis	4	10.5	12	48
Total	38	100	25	100

Neuritis was seen in most cases [89.4%] of Type I reaction as single neuritis in 57.9% and multiple neuritis in 31.5% whereas neuritis was seen only in 52% of Type 2 cases. Ulnar nerve and lateral popliteal nerve were the common nerves involved in neuritis.

Table 12 : Sensory impairment along the course of neuritis

Sensory impairment	Type 1 Reaction		Type 2 Reaction	
	No	%	No	%
Present	21	55.3	8	32
Absent	13	34.2	5	20

Sudden onset of sensory impairment in form of altered sensation, pain, extend of anesthesia in areas supplied by the affected nerve was present in 55.3% of Type 1 cases and 32% of Type 2 cases.

MOTOR PARALYSIS IN REACTIONS

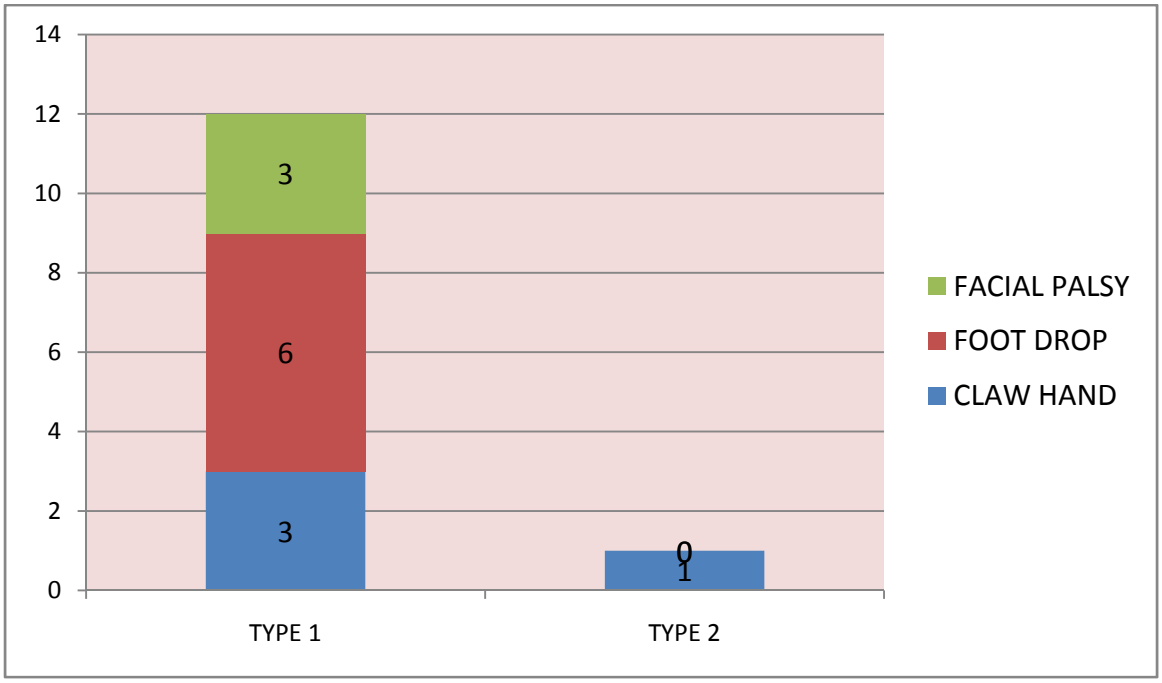


Table 13 : Motor paralysis

Motor palsy	Type 1 Reaction		Type 2 Reaction	
	No	%	No	%
Claw hand	3	7.9	1	4
Foot drop	6	15.8	-	-
Facial palsy	3	7.9	-	-
Nil	26	68.7	24	96
Total	38	100	25	100

Out of 38 cases of Type 1 reaction, 3cases developed claw hand, 6 cases developed foot drop and 3 cases developed facial palsy. There was only one motor palsy [claw hand] noticed in Type 2 reaction.

Table 14: Skin biopsy

Histopathological features	Type 1 Reaction		Type 2 Reaction	
	No	%	No	%
Dermal edema	26	68.4	-	-
Epitheloid granuloma	28	73.6	-	-
Dermal infiltration superimposed on foamy macrophages	2	5.2	22	88
Panniculitis	-	-	21	84
Neutrophilic vasculitis	-	-	14	56

Dermal edema and epitheloid granuloma dispersed by dermal edema were observed in 26 cases and 28 cases of Type 1 respectively. Lymphocytes infiltrate admixed with macrophage were observed in 2 cases of Type 1 in BL spectrum. Neutrophilic infiltrate super imposed on foamy macrophage granuloma noticed in 22 cases of Type 2 reaction. Panniculitis and neutrophilic vasculitis were seen in 21cases and 14 cases of Type 2 reaction respectively.

RESPONSE TO STEROID REGIMEN

Table 15: Response to WHO Steroid regimen

Response	Type 1 reaction		Type 2 reaction	
	No	%	No	%
Good	34	89.5	17	68
Exacerbation < 12 weeks	3	7.9	2	8
Exacerbation > 12 weeks	1	2.6	3	12
Recurrence & Recalcitrant	-	-	3	12
Total	38	100	25	100

Response to WHO steroid regimen was good in 89.5% of Type 1 reaction cases and 68% of Type 2 reactions. Exacerbation was noticed before 12 weeks in 3cases of Type 1 and 2 cases of Type 2 reaction. Exacerbation after 12 weeks was noticed in one case of type 1 and 3 cases of Type 2 reaction. Three cases of Type 2 reactions showed recurrent episodes and dependent on steroids. Even after addition of clofazimine, recurrence occurred in that 3 cases and became recalcitrant. Out of 3 one case responded well to thalidomide.

BACTERIOLOGICAL INDEX

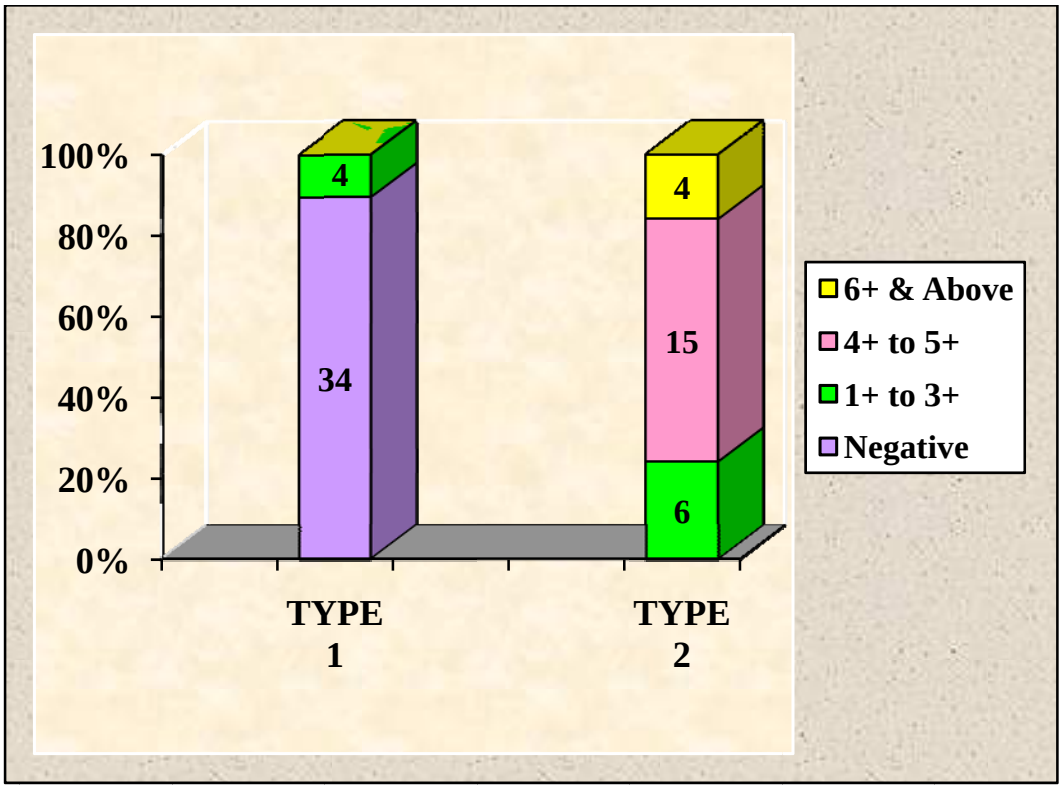


Table 16: Bacteriological Index [BI]

Bacteriological Index	Type 1 reaction		Type 2 reaction	
	No	%	No	%
Negative	34	89.5	-	-
1 + to 3 +	4	10.5	6	24
4+ to 5+	-	-	15	60
≥ 6+	-	-	4	16
Total	38	100	25	100

Bacteriological index was negative in 89.5% of Type 1 reaction cases and 4 cases showed BI of 1+ to 3+ in Type 1 reaction. In Type 2 reaction 60% showed bacteriological index of 4+ to 5+, 24% showed BI of 1+ to 3+ and 16% showed BI of ≥ 6+.

DISCUSSION

INCIDENCE

Out of 1, 03,536 patients attending the skin department, 63 patients were found to have lepra reaction. Out of which Type 1 reactions constituted 0.04% and Type 2 reaction constituted 0.02%. The overall incidence of lepra reaction observed in our study was 0.06%.

AGE

In our study, 34.2% of Type 1 reaction belonged to the age group of 21 -30 years followed by 23% in 31 – 40years. This age incidence is comparable with the study conducted by Scollard et al in which the highest age incidence for Type 1 reaction mentioned was 21 – 40 years.[70] In our study no patient of < 20 years was presented with Type 2 reaction. All were above 20 years of age. This is comparable with Scollard et al study in which 83% of Type 2 reaction belonged to the age group of 20 years and above. Mnandhar et al in his study observed patients older than 40years were at significantly decreased risk of ENL.[71] But in our study majority of ENL cases [56%] were above 40 years of age.

SEX

In our study lepra reactions both Type 1 and Type 2 were found in an incidence of 74 % among males and 25% among females. The incidence of male predominance is

comparable with the studies done at Belgian leprosy centre, Polambakkam, Madurantakam, South India and Job et al.[35,72] The female incidence clearly correlates with the 26% of female incidence observed in the Scollard et al study.[70]

INCIDENCE IN VARIOUS SPECTRUM OF LEPROSY

In our study, among the 38 patients who had Type 1 reaction, 31 patients were BT, 4 were BB and 3 were BL. Thus BT patients had higher incidence of Type 1 reaction. Out of 25 patients who had Type 2 reactions, 4 were of BL and 18 were of LL and 3 were of Histoid Hansen.

In the study of Desikan et al, out of 412 patients who presented with Type I reaction 313 patients had BT, 9 patients had BB, 85 patients had BL and 5 patients had LL. Among 95 patients who had Type II reaction 61 had LL and 34 had BL. [73]

In the study of Seghal et al, out of 22 patients who presented with reaction 11 were of Type I (BT-6, BB-1, BL-4) and 11 patients were of Type II reaction and all the patients belong to LL spectrum in Type 2. [74]

In Histoid leprosy, ENL reaction has been reported by some authors, Bhutani found ENL reaction in 3 of 20 Histoid patients.[75] Kaur et al observed ENL in 40% of Histoid patients. [39]

Thus the type of reaction and its relation to the clinical leprosy in our study is almost similar to the observations made in the above studies

ONSET OF REACTION IN RELATION TO ANTILEPROSY DRUGS

In our study, among 38 cases of Type 1 reaction, 18 patients [47.4%] developed reaction before initiation of MDT [de novo] and among 25 cases of Type 2 reaction, 7 patients [28%] developed it before initiation of MDT. This is comparable with the Kumar et al study in which he observed the time of onset of reaction as follows, 35.9 % presented with type 1 reaction at the time of first visit to the leprosy clinic and 19.75% presented with Type 2 reactions at the time of first visit. [14]

In our study, the patients after starting MDT, developed Type 1 reaction mostly [25%] during 6 -12 months of starting drugs and 33% of Type 2 reactions developed during 1 -2 years of starting MDT. This is well comparable with Kumar et al study who reported that the incidence of Type 1 was highest during 6 -12 months after starting MDT and also reported that ENL occurred mostly during 2^{nd} or 3^{rd} year following MDT.[14]

PRECIPITATING FACTORS

In our study, antileprosy drugs [60.3%] constituted the major risk factor for precipitating lepra reactions. Other factors like physical stress [20.6%], intercurrent infections [9.5%], surgery [7.9%] all constituted some risk in precipitating both type 1 and Type 2 reactions. The precipitating factors in our study correlate with those of Kumar et al. [14]

CLINICAL FEATURES OF TYPE 1 REACTION

The predominant clinical features of Type 1 reaction observed in our study were raised erythematous skin lesion [79.3%], neuritis [89.4%] and constitutional symptoms [36.8%]. Hastings mentioned that the erythema and swelling of the existing lesion and neuritis, the predominant features in cases of Type I reaction along with mild constitutional feature like fever. This has been mentioned by Jopling also. So the predominant features in our study are concurrent with those of Hastings' and Jopling's.

In the study of Lockwood et al, 31.8% had only neuritis and 22.7% had both skin lesions and neuritis. [76] In comparison with Lockwood study the incidence of neuritis was very much higher in our study. Single neuritis was commonly seen than multiple neuritis. Deformities like claw hand, foot drop and facial palsy were seen in 7.9%, 15.8% and 7.9% respectively. In our study, foot drop was seen in higher incidence in contrast to Richardus et al study who mentioned that the most commonly involved nerves of motor function deformity during reactions were the ulnar.[77] Both Richardus and Sharma reported that 7.9% of patients developed claw hand due to Type 1 reaction.[77, 78] This is concurrent with the incidence of claw hand in our study. Other features observed in our study were edema of hands, edema of feet and dactylitis seen in 26%, 13% and 5.3% respectively.

CLINICAL FEATURES OF TYPE 2 REACTIONS

In the present study, 100% of Type 2 reaction patients presented with crops of erythematous and tender nodules, subcutaneous plaque along with nodule was seen in 32% of patients. Ulcerative lesion was seen in 5cases and pustular lesion in one case. Constitutional symptoms [96%] (like fever, arthralgia and malaise), neuritis [52%], edema of feet [52%], edema of hands [44%] were the next common clinical features. Dactylitis [20%], lymphadenitis [16%], epididymo-orchitis [12%] epistaxis [8%] and iritis [4%] were the least features encountered.

Van Brakel et al study shows presence of following clinical signs is diagnostic of ENL i.e., multiple, tender nodules, with or without ulceration, neuritis (shooting or burning), fever, edema, involvement of other organs, e.g., Iritis, orchitis and arthritis.[79] The features are almost in concurrence with the present study.

HISTOPATHOLOGY

Biopsy taken from the erythematous tender plaque of Type 1 reaction cases showed epitheloid granuloma in almost all cases. But the characteristic features of Type 1 reaction such as edema in the dermis with hazy collagen fibers and epitheloid granuloma dispersed by dermal edema was seen in 68.4% and 73.6% respectively. Other features like increased lymphocytes, multi nucleated giant cells, foci of fibrinoid necrosis and destruction of the appendages were also observed. All this features are comparable with similar features mentioned in Ridley DS and Radia KB.[80] In 2 cases of Type 1 reaction

belonging to BL spectrum and downgrading type, lymphocytes admixed with macrophages were observed which is also concurrent with the findings of Ridley and Radia.

In Type 2 reaction of 25 cases, 88% patients had neutrophilic infiltration of the dermis overlying foci of foamy macrophages, and 84% showed panniculitis. Vinod Kumar Sharma in his study mentioned that polymorphonuclear invasion of the vessel wall is a characteristic finding in ENL. [81] In 56% of cases neutrophilic vasculitis was observed and this proved the characteristic finding of ENL in comparison with Vinod Kumar Sharma study.

RESPONSE TO STEROIDS

During the follow up of minimum 6 months to maximum 1year period, 34 patients [89%] of Type 1 reaction showed good response. Exacerbation was seen in 4 cases [10.5%] with 7.9% developed it < 12 weeks and 2.6 % developed it > 12 weeks. All that 4 cases treated with prolonged steroids. Rao et al in his study suggested longer duration of prednisolone treatment gave less poor outcomes than a short course of prednisolone.[82] Good response to short course regimen is thus correlated with the findings of Rao.

Out of 25 cases of Type 2 reaction, 68% responded well to steroid, 8 patients [32%] went for exacerbation in form of recurrent episodes. They were treated with prolonged steroids and few were added with high dose clofazimine. Out of that 8patients,

3cases [12%] developed multiple reccurences and became recalcitrant. This finding is correlated with the study of Shen et al who found that the standard 12 week regimen of prednisolone was effective only for mild Type 1 and Type 2 reaction cases but was not effective for severe cases of reactions especially Type 2 reactions.[83]

BACTERIOLOGICAL INDEX [BI] IN REACTIONS

BI was negative in 34 cases [89.5%] and positive in 4 cases [10.5%] of Type 1 reactions. All the positive cases showed BI < 3+. All cases of Type 2 reaction were positive for BI. Out of 25 cases, 6 cases [24%] showed BI < 3+, 15 cases [60%] showed BI 4+ to 5+ and 4 cases [16%] showed BI $\geq$ 6+. This is very much comparable with Nery et al study who mentioned that the RR rate was significantly higher among patients showing BI < 3, while ENL predominated among those patients with BI > 3.[84] Manandhar et al mentioned that there was a linear relationship in the risk of ENL with an increasing BI [bacterial index (BI) of > 4+].[71] Our study confirmed this finding by showing 76% of BI > 4+ in Type 2 reaction.

SUMMARY

- 63 patients with clinical features of lepra reaction were included in the study.
- 38 cases of Type 1, 25 cases of Type 2, no case of Type 3 reaction were observed.
- Overall incidence of lepra reaction was 0.06%.
- Mean age for Type 1 was 37.8yrs and mean age for Type 2 was 43.8yrs.
- Male preponderance was observed with sex ratio of 2.9:1.
- More number of BT patients had Type-I reaction and more number of LL patients had type II reaction.
- Anti-leprosy drugs were found to be the most common precipitating factor followed by physical stress and intercurrent infection.
- Erythema and swelling of the skin lesions, neuritis and edema of hands and feet were common features of Type I reaction.
- Neuritis was most commonly seen in Type 1 than inType 2 reaction.
- Sensory and motor deformities were seen in 46% and 20.6% of cases.
- Crops of tender evanescent nodules, fever, joint pain, neuritis and edema of hands and feet were common in Type 2 reaction.
- Pustular and ulcerative type of ENL lesions were present in signicant number.
- Classical histopathological features were present in three fourth of cases.
- Steroids are effective in 89% of Type 1 and 68% of Type 2 reaction.
- BI was <3+ in Type 1 and >4+ in Type 2 reaction.

CONCLUSION

TYPE 1 REACTION

Type 1 reaction was the most common type of reaction seen. The majority of the patients with Type 1 had BT hansen. Most of the patients developed it after 6-12 months of starting MDT and significant proportion of cases developed de novo. Antileprosy drugs were found to be the commonest precipitating factor followed by physical stress and intercurrent infection. Neuritis was the predominant clinical feature observed followed by erythema/swelling of the skin lesion and edema of hands /feet. Motor paralysis in form of foot drop, claw hand and facial palsy were significantly observed. Dermal edema with dispersed epitheloid granuloma were the predominant histopathological features observed. Exacerbation of Type 1 reaction was commonly observed during tapering of steroids [< 12 weeks]. Interesting observation of shift from BT to BL was observed in one case.

TYPE 2 REACTION

Type 2 reaction was observed predominantly in LL and rarely in BL. Most of the patients developed it after 1-2 years of antileprosy drugs. Seven cases presented with ENL at their first visit [de novo]. Erythematous tender nodules, fever, edema of hands / feet and neuritis were the predominant clinical features. Rare variants of pustular and ulcerative ENL were also observed. Iritis and epididymo-orchitis were seen in few cases. Neutrophilic infiltration of dermis with panniculitis and vasculitis were the predominant

histopathological features observed. Exacerbation and recurrence of Type 2 reaction were commonly observed after withdrawal of steroids [> 12 weeks], which insists the need for prolongation of steroids. There was a linear relationship in the risk of ENL with an increasing BI. An interesting observation in our study was, 3 patients primarily diagnosed as Histoid Hansen developed Type 2 reaction, which has also been observed in some recent studies.

Early diagnosis, adequate treatment and proper follow up are very essential to prevent the deformities and systemic complications associated with lepra reactions.

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PROFORMA

NAME:

AGE / SEX:

ADDRESS:

OCCUPATION / INCOME:

SOCIOECONOMIC STATUS:

HANSEN IN FAMILY MEMBERS:

DATE OF DETECTION :

DURATION OF DISEASE:

DATE OF REPORTED :

TYPE OF HANSEN : TT /BT /BB /BL /LL /Neural /Histoid

NATURE OF TREATMENT : PB MDT /MB MDT

DATE OF Rx STARTED :

DURATION OF TREATMENT:

RELEIVED FROM TREATMENT:

CHIEF COMPLAINTS ; [with duration]

Skin lesion :

Systemic complaints:

HOPI

Onset – sudden / insidious

Progression – slow / rapid

Skin lesion – old lesion

- new lesion

Site -

Distribution -

Sensation – Loss of sensation / painful

No/ of recurrences

Duration between recurrences

Rx at recurrences

Constitutional symptoms – Fever / arthralgia / malaise / fatigue / headache

Neuritis – Neural pain / tingling and numbness

Extent of anaesthesia

Sudden motor palsy / weakness

Systemic involvement –

Eye – redness / blurring of vision / pain / photophobia

Edema of hands & feet

Swollen & tender testis

Muscle pain & bone pain

Joint pain & swelling

Rhinitis / epistaxis / acute resp. obstruction

PAST H/O

DM / HT / other systemic disease

Hansen in the past – yes / no

If yes – when

- Type of Hansen

[from record / no/- of patch / no/- of nerve]

Any ppt factors – [surgery / vaccination / IC infection / pregnancy / drugs / lactation / menstruation / Physical stress / mental stress / trauma / others]

TREATMENT H/O

ALT taken in the past –

Regimen taken Dapsone monotherapy / ROM

PB MDT / MB MDT

Date of Rx Started on -

Date of completion -

RFT -

Default / regular / dropout -

PERSONAL H/O

Single / married Smoking

Children Alcohol

Family Planning Betelnut chewer

GENERAL EXAMINATION

Febrile

Anemic

Jaundice

Pedal edema

Gen LN

Reg LN

VITALS – P.R / B.P

SYSTEMS – CVS / RS / ABD / CNS

DERMATOLOGICAL EXAMINATION

New lesion ; Type – Nodule

Plaque

Vesicle / bulla

Ulcer / necrosis

Old lesion; Type – Patch

Plaque

Margin – Well / ill defined

Extent of margin

Surface – Warm

Shiny / edematous

Scaly / exfoliation

Dry & wrinkled / scar

Color – Erythematous / Skin color

Hypopigmented / Hyperpigmented

Infiltration

Tenderness

Site

Distribution – Symmetrical / Asymmetrical / U/L / B/L

Sensation – Hypoaesthetic / Hyperaesthetic / Anesthetic

Other skin lesion – Madrosis

Nasal depression

Ear lobe infiltration

Leonine facies

Edema /exfoliation in hands & feet

Gyanecomastia

NERVE EXAMINATION

CRANIAL NERVE; 5th nerve - Corneal sensation

- Sensation on face

7th nerve – Facial expression

- Wrinkling of forehead

- Blinking of eye

- Deviation of mouth

- Lid lag

PERIPHERAL NERVES	RIGHT	LEFT	firm/soft/tender
Supraorbital nerve			
Infraorbital nerve			
Facial nerve			
Greater auricular nerve			
Supraclavicular nerve			
Radial nerve			
Ulnar nerve			
Median nerve			
Radial cutaneous nerve			
Ulnar cutaneous nerve			
Lat popliteal nerve			
Post tibial nerve			
Sural nerve			
Sup peroneal nerve			
Any feeding nerve - thickened / tender			

SENSORY SYSTEM

Anaesthesia along nerve course - partial / complete loss

Extent of anaesthesia / Distribution of sensory impairment

Glove & stocking anaesthesia

MOTOR SYSTEM

Acute palsy – Claw hand - partial / total

Wrist drop

Foot drop

Facial palsy

VMT – Ulnar nerve - Little finger abduction

Card test

Froment's sign

Radial nerve – wrist extension

Median nerve – pen test

Lateral popliteal nerve – dorsiflexion of foot

Posterior tibial nerve – eversion of foot

OTHER SYSTEMS

Eye – iritis / Conjunctivitis / iridocyclitis / scleritis

Dactylitis - Edema / Tenderness

Lymphadenitis – firm / Tender

Site –

Epididymo orchitis – swelling / Tenderness

Myositis – muscle tenderness

Arthritis – jt swelling / tenderness

INVESTIGATION

Urine - Alb - [proteinuria]

RBC – [hematuria]

Blood – TC

DC

ESR

Hb /-

Other findings

RFT –

LFT

USG ABD - renal

SSS – BI / MI

BIOPSY - Site

Report with biopsy no/

FINAL DIAGNOSIS;

REACTION GRADING -

TREATMENT; Steroids started

Tapered

Response

Other drugs-

FOLLOW UP: Date Clinical progress Rx tapering

MASTER CHART

						Onset of reaction in relation to ALD			CUTANEOUS						
S.no	Name	Age	Sex	Type Of Reaction	Leprosy. Type	Intake	Duration [months]	Other PPT	Const.Symp.	Erythema & edema of old lesion	New similar lesion	Nodule	Plaque	Pustule	Ulcer
1	Ramu	50	M	2	4	1	11	PS	1			1	0	0	1
2	Malaisami	58	M	2	4	1	7		1			1	0	0	0
3	Mohammed Yusuf	15	M	1	1	1	3		1	1	1				
4	Amose	52	M	2	5	1	18	PS	1			1	0	0	0
5	Kannammal	50	F	1	1	0			0	1	0				
6	Selvam	50	M	1	1	0			0	1	0				
7	Seethalakshmi	37	F	2	5	1	11		1			1	1	0	0
8	Vasu	31	M	1	1	1	1	PS	0	0	0				
9	Tharamani	40	F	1	1	1	12		0	1	0				
10	Janaki	30	F	2	4	1	24		1			1	0	0	0
11	Velusamy	38	M	1	2	1	9		0	1	1				
12	Papathi	21	F	1	1	0		IC	0	1	0				
13	Pattamuthu	54	M	1	2	1	60		0	1	1				
14	Sathish kumar	15	M	1	1	1	2		1	1	0				
15	Raj konar	53	M	2	4	0		PS	1			1	0	0	0
16	Andichi	30	F	1	1	1	11		1	1	0				
17	Arumugam	63	M	1	1	1	12		0	1	0				
18	Kottaisamy	61	M	2	4	1	120	IC	1			1	0	0	0
19	Gopi	24	M	2	4	1	2		1			1	0	0	1
20	Fathima	50	F	1	1	0			0	0	0				
21	Balakrishnan	58	M	1	1	1	6		0	1	0				
22	Nagaraj	21	M	1	1	1	24		0	1	1				
23	Hariharan	33	M	1	2	0		S	0	1	0				
24	Selvi	31	F	2	4	0		L	1			1	1	0	0
25	Pandiammal	40	F	2	3	0		S	1			1	1	0	0
26	Bose	53	M	2	5	1	6	IC	1			1	0	0	0
27	Panju	50	F	1	1	0		PS	1	1	0				
28	Sayeed	57	M	1	2	0			0	1	0				
29	Papu	32	F	1	1	1	120		1	1	0				
30	Selvi	30	F	2	4	1	4		1			1	0	0	0

MASTER CHART

						Onset of reaction in relation to ALD			CUTANEOUS						
S.no	Name	Age	Sex	Type Of Reaction	Leprosy. Type	Intake	Duration [months]	Other PPT	Const.Symp.	Erythema & edema of old lesion	New similar lesion	Nodule	Plaque	Pustule	Ulcer
31	Syed Ahmed	40	M	2	4	1	120		1			1	0	0	0
32	Ebinezar	40	M	1	1	0			0	1	0				
33	Balasubramanian	61	M	1	1	1	10	T	0	1	1				
34	Mookan	43	M	1	3	0		PS	1	1	0				
35	Abdul majid	41	M	2	4	1	24		1			1	1	0	0
36	Vasanthi	50	F	2	4	1	1		1			1	0	0	1
37	Shankar	68	M	2	4	1	240		1			1	0	0	0
38	Balakrishnan	42	M	1	3	1	240		1	1	0				
39	Marimuthu	22	M	1	1	0		IC	1	1	0				
40	Chetty	60	M	1	1	0			0	0	0				
41	Jeyamani	37	M	1	1	0			1	1	0				
42	Karuthammal	50	F	2	3	0		MS	1			1	1	0	0
43	Parvathi	55	F	2	3	0		MS	1			1	0	1	0
44	Palanisami	60	M	2	4	0		S	1			1	0	0	1
45	Sundar	29	M	1	1	1	72	PS	0	1	0				
46	Ponraj	37	M	1	1	0		T	0	0	0				
47	Kumar	30	M	1	1	0		PS	0	0	0				
48	Murugesan	48	M	1	1	1	2	PS	0	1	1				
49	Muthupandi	30	M	1	3	1	2	PS	1	1	0				
50	Velu	27	M	1	1	0		IC	1	1	0				
51	Sivakumar	21	M	1	1	0			1	1	0				
52	Saviriraj	60	M	2	4	0		S	1			1	1	0	1
53	Ganesan	51	M	2	4	1	36	IC	1			1	0	0	0
54	Sivaraj	26	M	2	4	1	18	PS	1			1	1	0	0
55	Stalin	22	M	2	3	1	18		1			1	1	0	0
56	Chinnasamy	37	M	2	4	1	11	T	1			1	0	0	0
57	Manimaran	30	M	2	4	1	24		0			1	0	0	0
58	Moorthi	23	M	1	1	1	24		1	0	0				
59	Kumar	28	M	1	1	0			0	0	0				
60	Muthu	56	M	1	1	0		S	0	1	0				
61	Malliga	39	F	1	1	1	24		1	0	0				
62	Madurai veeran	25	M	1	1	1	36	PS	0	1	0				
63	Chella pandi	30	M	1	1	1	36	PS	0	0	0				

MASTER CHART (continued)

		SYSTEMIC MANIFESTATION									MOTOR PALSY			SKIN BIOPSY						
S.no	Name	Edema of Hands	Edema of feet	Dactylitis	Iritis	Epistaxis	Epididymo-orchitis	Lymphadenitis	Neuritis	Sensory impairement	Claw hand	Foot drop	Facial palsy	Dermal edema	Epitheloid granuloma	Dermal Infiltrate & Foamy Macrophage	Panniculitis	Neutrophilic vasculitis	Response to trt.	Bact. Index
1	Ramu	1	0	1	0	0	0	0	M	P	1					1	1	1	good	6+
2	Malaisami	0	0	0	0	0	0	0	M	P						1	1		Exa. > 12 wks	2+
3	Mohammed Yusuf	0	0						S	P				1	1				good	- ve
4	Amose	0	0	0	0	0	0	0	0	A						1	1		recurrence	4+
5	Kannammal	0	0						S	A				1	1				good	- ve
6	Selvam	0	0						M	P		1		1	1				good	- ve
7	Seethalakshmi	0	1	0	0	0	0	0	M	P						1	1	1	good	6+
8	Vasu	0	0						M	A			1						good	- ve
9	Thavamani	0	0						S	A				1	1				good	- ve
10	Janaki	1	0	0	0	0	0	0	0	A						1	1		good	4+
11	Velusamy	0	0						S	P	1			1	1				good	- ve
12	Papathi	0	0						M	A				1	1				good	- ve
13	Pattamuthu	0	0						S	P				1	1				good	- ve
14	Sathish kumar	0	0						M	A			1	1	1				good	- ve
15	Raj konar	1	1	1	0	0	0	0	0	A						1	1	1	recurrence	3+
16	Andichi	0	0						S	A			1	1	1				good	- ve
17	Arumugam	0	0						S	A				1	1				Exa. > 12 wks	- ve
18	Kottaisamy	0	0	0	0	0	0	0	0	A						1	1		recurrence	4+
19	Gopi	0	0	0	0	0	0	1	S	P						1		1	Exa. > 12 wks	4+
20	Fathima	1	0						M	A									good	- ve
21	Balakrishnan	0	0						S	P	1			1	1				good	- ve
22	Nagaraj	0	0						0	A				1	1				good	- ve
23	Hariharan	1	0						M	P				1	1				good	4+
24	Selvi	0	0	0	0	0	0	0	0	A						1	1		good	3+
25	Pandiammal	0	1	0	0	0	0	0	M	A						1	1	1	good	4+
26	Bose	0	0	1	0	0	0	0	0	A						1	1	1	good	2+
27	Panju	0	0						S	A				1	1				Exa. <12 wks	- ve
28	Sayeed	1	0						M	P				1	1				Exa. <12 wks	- ve
29	Papu	0	1						M	A				1	1				good	- ve
30	Selvi	0	0	0	0	0	0	0	0	A						1	1	1	good	4+

MASTER CHART (continued)

		SYSTEMIC MANIFESTATION									MOTOR PALSY			SKIN BIOPSY						
S.no	Name	Edema of Hands	Edema of feet	Dactylitis	Iritis	Epistaxis	Epididymo-orchitis	Lymphadenitis	Neuritis	Sensory impairement	Claw hand	Foot drop	Facial palsy	Dermal edema	Epitheloid granuloma	Dermal Infiltrate & Foamy Macrophage	Panniculitis	Neutrophilic vasculitis	Response to trt.	Bact. Index
31	Syed Ahmed	0	1	0	0	0	0	0	M	P						1	1	1	good	5+
32	Ebinezar	0	0						S	P				1	1				good	1+
33	Balasubramanian	1	0						S	P					1	1			good	- ve
34	Mookan	1	0	1					S	P				1	1				good	1+
35	Abdul majid	1	0	0	0	0	0	0		A						1	1	1	Exa. > 12 wks	6+
36	Vasanthi	1	1	0	0	0	0	0	M	P						1	1	1	good	6+
37	Shankar	1	0	0	1	0	1	1		A						1		1	good	4+
38	Balakrishnan	0	0	1					S	P					1	1			good	- ve
39	Marimuthu	1	0							A				1	1				good	- ve
40	Chetty	1	0						M	P									good	- ve
41	Jeyamani	1	1						S	A				1	1				good	- ve
42	Karuthammal	1	1	0	0	0	0	0	0	A						1			good	4+
43	Parvathi	1	1	1	0	0	0	0	S	A									good	1+
44	Palanisami	0	1	0	0	0	0	0	0	A						1	1	1	Exa. <12 wks	4+
45	Sundar	0	1						M	P				1	1				good	- ve
46	Ponraj	1	0						M	P		1							good	- ve
47	Kumar	0	1						M	P	1	1							Exa. <12 wks	- ve
48	Murugesan	1	0						S	A				1	1				good	- ve
49	Muthupandi	0	1						0	A				1	1				good	2+
50	Velu	0	0						0	A				1	1				good	- ve
51	Sivakumar	0	0						S	P									good	- ve
52	Saviriraj	0	1	0	0	0	0	1	0	A						1	1	1	good	3+
53	Ganesan	1	1	1	0	1	1	1	M	P							1	1	Exa. <12 wks	2+
54	Sivaraj	1	1	0	0	0	0	0	S	A							1		good	4+
55	Stalin	0	1	0	0	1	1	0	S	A						1	1		good	4+
56	Chinnasamy	1	0	0	0	0	0	0	M	P						1	1		good	4+
57	Manimaran	0	1	0	0	0	0	0	M	A						1	1		good	4+
58	Moorthi	0	0						S	P		1							good	- ve
59	Kumar	0	0						S	P		1							good	- ve
60	Muthu	0	0						S	A				1	1				good	- ve
61	Malliga	0	0						S	P									good	- ve
62	Madurai veeran	0	0						S	P				1	1				good	- ve
63	Chella pandi	0	0						S	P		1							good	- ve

CODE FOR MASTER CHART

TYPE OF REACTION

1 – Type 1 reaction

2 – Type 2 reaction

TYPE OF LEPROSY

1 - BT

2 – BB

3 – BL

4 – LL

5 – Histoid Hansen

Ppt – Precipitating factors

Const. – Constitutional symptoms

NEURITIS

S – Single nerve involvement

M – Multiple nerve involvement

SENSORY IMPAIREMENT

P – Present

A – Absent

IN ALL OTHER COULMNS

1 – Present

0 – Absent

Exa – Exacerbation

Trt - Treatment

Bact. Index – Bacteriological index