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Original Research Article

Study of Various Laboratory Parameters in Leprosy and Lepra Reaction Cases at A Tertiary Care Centre

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Abstract:

Introduction: Leprosy is a chronic mycobacterial disease caused by Mycobacterium leprae with more than 2,00,000 new cases reported every year from more than 120 countries.[3] Leprosy is endemic in tropical countries, and more prevalent in developing countries. In year 2020 in Gujarat total new cases detected was 4081, ANCDR was 5.77 and prevalence rate was 0.36 with percentage MB cases were 57%. Early detection and treatment are key for prevention of leprosy associated disabilities and deformities and also prevention of leprosy in community.

Materials and Methods: This prospective study was carried out at tertiary care hospital.

- **Study design** – Cross sectional analytical study.
- **Study duration-** July 2021 to October 2022

Results: In present study all clinically diagnosed cases of leprosy and lepra reactions during July 2021 to October 2022 that presented to our OPD and satisfied the inclusion and exclusion criteria were enrolled. Considering leprosy prevalence of 0.57 / 10,000 in year 2019-20 calculated sample size was 54 but we enrolled total 64 patients in present study.

Conclusion: Total 64 patients were included in the study, out of which 17 (26.5%) were patients withreaction. Mean age in this study were 33.73 years. Majority of the patients were male. Male to female ratio was 3.26. Most of the patients belonged to 20 to 40 years age group.

Keywords: Leprosy, Reaction, Tertiary center.

Introduction

Leprosy is a chronic mycobacterial disease caused by Mycobacterium leprae with morethan 2,00,000 new cases reported every year from more than 120 countries.[3] Leprosy is endemic in tropical countries, and more prevalent in developing countries. In year 2020 in Gujarat total new cases detected was 4081, ANCDR was 5.77 and prevalence rate was 0.36 with percentage MB cases were 57%. Early detection and treatment are key for prevention of leprosy associated disabilities and deformities and also prevention of leprosy in community. The etiologic agent, Mycobacterium leprae, was identified by Norwegian physician Gerhard Armauer Hansen in 1873, therefore, it is also called Hansen's bacillus.[4] Leprosy manifests with varied clinical presentations ranging from no visible inflammatory signs (e.g., hypopigmented lesions) to marked inflammatory signs (e.g., erythematous and infiltrated lesions) across the spectrum of leprosy and lepra reactions. M. leprae infects mainly Schwann cells and macrophages. Host immune response against M. leprae decides the outcome of disease. In endemic area people with adequate immuneresponse against M. leprae did not develop the disease, while people with inadequate immuneresponse developed the disease. People who develop leprosy have variable humoral and cell mediate immune response against M. leprae and predominant immune response decide the clinical manifestation of leprosy. Based on clinical, immunological, and histopathological criteria,[5] Ridley & Jopling (1962,1966) classified leprosy into Tuberculoid (TT) form, the lepromatous (LL) form as polar group and borderline form. Borderline leprosy further divided into borderline-tuberculoid (BT), borderline-lepromatous (BL), according to the greater proximity to one of the poles, and borderline-borderline (BB).[6] Cell mediated response is higher side towards tuberculoid pole and humoral response towards lepromatous pole, while variable and

fluctuating immune response in borderline leprosy. Lepra reactions are immunological inflammatory response seen in leprosy and are associated with significant morbidity resulting from neural damage and deformities.

Leprosy reactions can be classified as type 1 & type 2 lepra reaction. Type 1 reaction is caused by rise of cellular immunity against M. leprae antigens with exacerbation of local inflammatory signs with minimal or no systemic symptoms. Type 2 reaction and/or Erythema nodosum leprosum (ENL) is an immune mediated systemic inflammatory response seen mostly in lepromatous leprosy (LL) & borderline lepromatous (BL) leprosy with higher bacterial index.[7] Immune response against M. Leprae usually trigger rise of cytokines, magnitude of which is different with spectrum of leprosy and reaction status. In tuberculoid leprosy, Th1 mediated immune response and related cytokines (IFN-gamma, IL-2) rise. Th1 response pattern through production of inducible nitric oxide synthase and activation of macrophages through TNF alpha destroys bacillus by free radicals, while in lepromatous leprosy, Th2 response with related cytokines (IL-4, IL-5. IL-10, TGF beta) and anti-bodies rise that leads tosurvival of the bacillus. [8]

Borderline leprosy is characterised by variable Th1 & Th2 cell response. In lepra reaction variety of inflammatory cytokines and immune cells play role in pathogenesis and there is boosting of Th1 cellular response during T1R, while ENL (erythema nodosum leprosum) / T2R (type 2 lepra reaction) is thought to be immune complex mediated reaction [9]. The rises of cytokines have autocrine, paracrine and endocrine effects and influencethe function of other organ system e.g., hemopoietic, renal and liver etc.

Materials and Methods

This prospective study was carried out at tertiary care hospital.

Study Design: Cross sectional analytical study.
Study Duration: July 2021 to October 2022
Study Approval: The study protocol was approved by the local Institutional Ethics Committee. (Approval letter Reference no. IEC/No 45; Date: 04-08-21)
Sample Size: It was calculated considering prevalence (for year 2019-2020) of leprosy-0.57/10,000 from National Health Portal of India.
p = 0.0057.
e = Allowable error = 2 %
Z = Level of confidence = 95 %

$$n = \frac{Z^2 p(1-p)}{e^2}$$

Using this, Sample size turned out to be 54'

Sampling technique- Purposive sampling

Selection of cases

After approval by IEC, all newly diagnosed leprosy cases and those already on treatment and presented with lepra reactions, coming to dermatology OPD/IPDfulfilling inclusion criteria and willing to participate in study were included in the study.

Inclusion criteria:

1. Patients with any one of the cardinal signs of leprosy and/or clinical features suggestive of lepra reactions.
2. All age group patients.
3. Both male and female sex.

Exclusion criteria:

1. Refusal for participation in the study
2. Severely ill patients diagnosed with serious systemic illness and on treatment forthe same.

Results

In present study all clinically diagnosed cases of leprosy and lepra reactions during July 2021 to October 2022 that presented to our OPD and satisfied the inclusion and exclusion criteria were enrolled. Considering leprosy prevalence of 0.57 / 10,000 in year 2019-20 calculated sample size was 54 but we enrolled total 64 patients in present study.

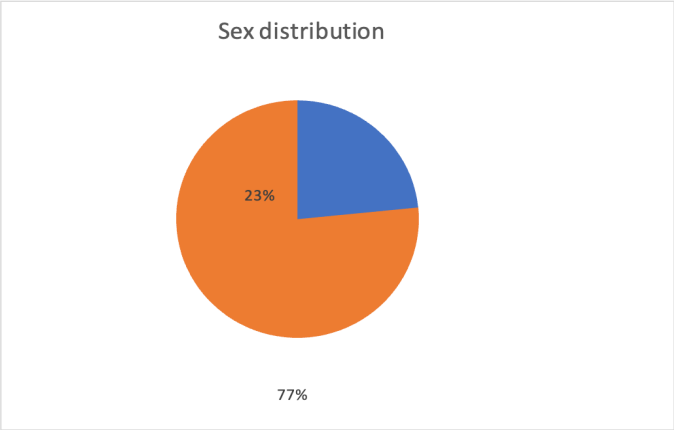
There were total 17 reaction patients with seven type 1 reaction patients and ten type 2 reaction patients. Single recurrent episode was present in one type 1 reaction patient and three type 2 reaction patients.2 recurrent episodes were present in two type 2 reaction patients. All observations were included in the study. The clinical and laboratory findings were entered in Microsoft excel sheet and analysed. For comparison of laboratory parameters, 64 age (± 2 years) and sex-matched healthy individual's (student, employee, pilgrim coming for fitness purpose) laboratory data were collected.

There was no statistically significant difference among the case and the comparison group regarding age. (p= 0.463).

Table 1: Gender Distribution in Total Patients of Leprosy (N=64)

Sex	No. of Patients	Percentage (N=64)
Male	49	76.5%
Female	15	23.4%

Out of total 64 the majority of the patients were male i.e. 76.5% (49 patients). Female gender formed 23.4 % (15 patients) of the total patients. M: F = 3.2.

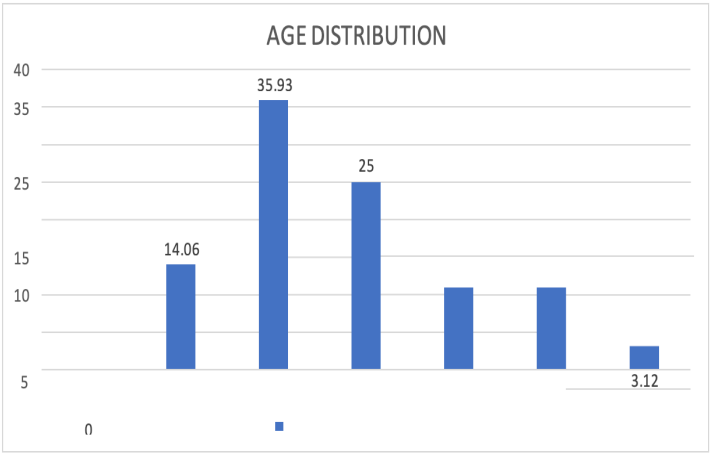


Graph 1: Gender Distribution

Table 2: Age Distribution of Total Leprosy Patients (N=64)

Sr. No	Age Group (Years)	No. of Patients	Percentage (N=64)
1	1 – 10	0	0
2	11 – 20	9	14.06%
3	21 -- 30	23	35.93%
4	31 -- 40	16	25.00%
5	41 -- 50	7	10.93%
6	51 -- 60	7	10.93%
7	61 -- 70	2	3.12%
Total		64	100 %

Out of total 64 patients, majority belonged to the age group 21 to 30 i.e., 23 patients (35.93%). This was followed by the age group 31 to 40 i.e., 16 patients (25%) and the age group 11 to 20 i.e., 9 patients (14.06%). Similar number of patients belonged to the age group41 to 50 i.e., 7 (10.93 %) and 51 to 60 i.e., 7 (10.93 %). There were only 2 patients in the age group of 61 to 70 years (3.12%). No patients in the study were less than 10 years old. The meanage was 33.73 (SD - 12.99) with minimum age 16 and maximum age 67 years.



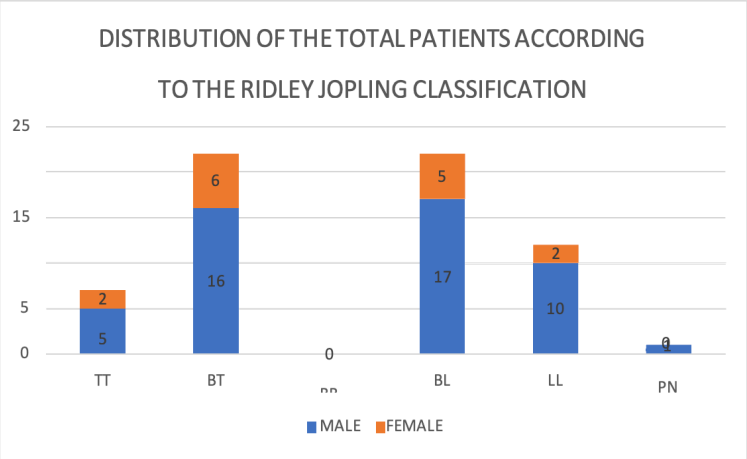
Graph 2: Age Distribution in Total Leprosy Patients (N=64)

Table 3: Distribution of the Total Patients According to the Ridley Jopling Classification (N=64)

Sr. No	Ridley- JoplingClassification	Male Patients	Female Patients	No. of Patients	Percentage (N=64)
1	TT	5	2	7	10.93%
2	BT	16	6	22	34.3%
3	BB	0	0	0	0%
4	BL	17	5	22	34.3%
5	LL	10	2	12	18.75%
6	PN	1	0	1	1.56%
Total		**49**	**15**	**64**	

Out of total 64 patients, maximum patients were 22 (34.3%) of borderline lepromatous type and borderline

tuberculoid type, followed by 12 (18.75%) in lepromatous leprosy and 7 (10.93%) in tuberculoid type. 1 patient was of pure neural type. (1.56%). 2 patients were relieved from treatment but presented with ENL reaction. No patient presented in the mid borderline spectrum.

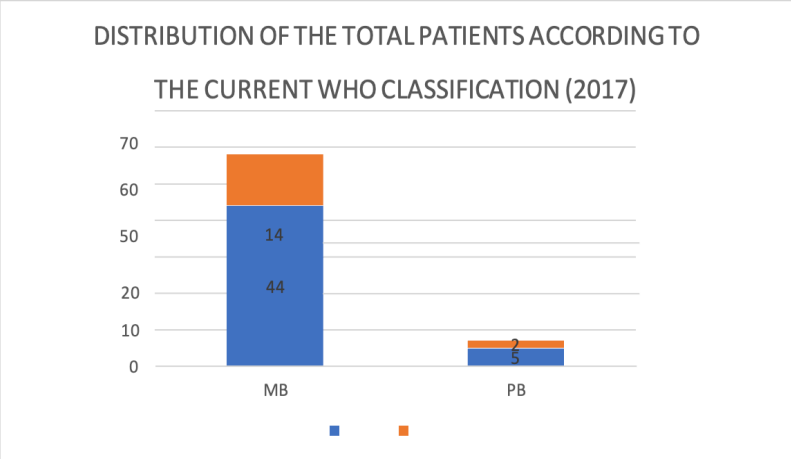


Graph 3: Distribution of the Total Patients According to the Ridley Jopling Classification

Table 4: Distribution of the Total Patients According To the current Who Classification (2017) (N=64)

Sr. No	Type of Leprosy	Male Patients	Female Patients	No. of Patients	Percentage (N=64)
1	PB	5	2	7	10.9%
2	MB	44	13	57	89.1%
Total		**49**	**15**	**64**	

Out of 64 cases, 89.1% (n=57) patients were mainly of multibacillary type. Out of 57 cases, 44were male and 13 were female. There were only 7 (10.9%) patients of paucibacillary type. Outof 7 PB, 5 cases were Male and 2 were female.



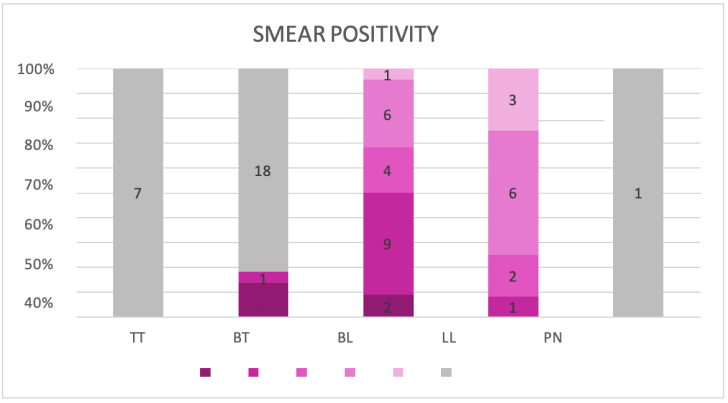
Graph 4: Distribution of the Total Patients According To the Current Who Classification (2017)

Table 5: Smear Positivity in Different Leprosy Types (N=64)

Sr. No	Ridley Joplings Type	Smear Positive Patients							Smear Negative Patients	Total Patients In Each Type	Percentage Of Smear Positive Patients
		1+	2+	3+	4+	5+	Total	% (N=64)			
1	TT	0	0	0	0	0	**0**	**0**	7	7	0%
2	BT	3	1	0	0	0	**4**	**6.25**	18	22	18.18%
3	BL	2	9	4	6	1	**22**	**34.38**	0	0	100%
4	LL	0	1	2	6	3	**12**	**18.75**	0	22	100%
5	PN	0	0	0	0	0	**0**	**0**	1	12	0%
	Total	5	11	6	12	4	**38**	**59.38**	**26**	**64**	**59.38**

Out of the total 64 patients, 38 (59.38%) patients were smear positive. No tuberculoid type patient had smear positive. All borderline lepromatous leprosy (n=22) and lepromatous leprosy(n=12) cases were smear positive,

mainly of grade 4. While in borderline tuberculoid leprosy only 4 out of 22 patients (18.18 %) were smear positive in borderline tuberculoid type, and most of them had 1+ on Ridley's logarithmic grade.

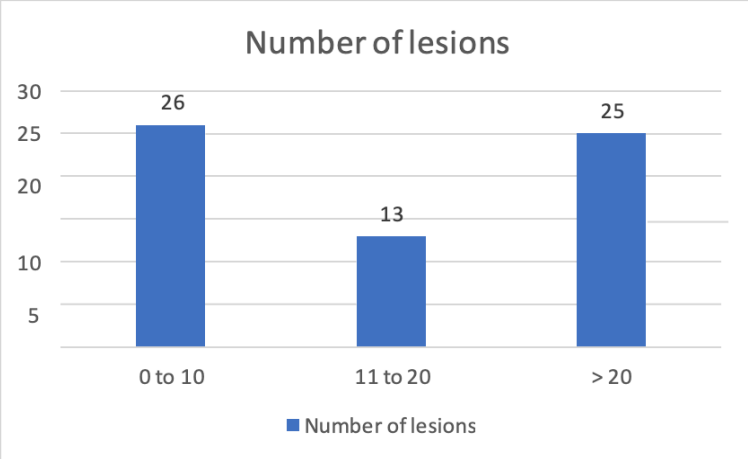


Graph 5: Smear Positivity In Different Leprosy Cases

Table 6: Distribution of the Number of Lesions amongst theTotal Patients (N=64)

Sr. No	Number of Lesions	No. of Patients	Percentage (N=54)
1	0 To 10	26	40.62%
2	11 To 20	13	20.31%
3	> 20	25	39.06%

Almost equal number of patients had up to 10 and more than 20 lesions i.e., 26 patients (40.62%) patients had upto 10 lesions, 25 patients (39.06%) had >20 lesions. 13 patients (20.31 %) had 11 to 20 lesions.

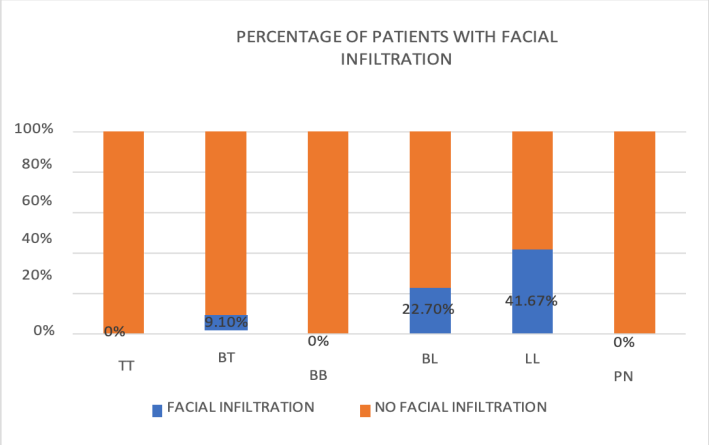


Graph 6: Distribution of the Number of Lesions amongst theTotal Number of Patients (N=64)

Table 7: Proportion of the Patients of Different Leprosy Types with Facial Lesions

Sr.No	Type of Leprosy	Total Patients	Patients With Facial Lesions	Percentage
1	TT	7	0	0%
2	BT	22	2	9.1%
3	BB	0	0	0%
4	BL	22	5	22.7%
5	LL	12	5	41.67%
6	PN	1	0	0%
Total		**64**	**12**	**18.75%**

Less than half of the patients of lepromatous leprosy had facial lesions i.e., 5 out of 12 patients(41.67%). 22.7% of the patients of borderline lepromatous leprosy i.e., 5 out of 22 and 9.1 % of patients of borderline tuberculoid leprosy i.e., 2 out of 22 also had facial lesions. None of the tuberculoid leprosy patient had it.



Graph 7: Percentage of the Patients of Different Leprosy Types with Facial Lesions.

Discussion

Leprosy or Hansen's disease is an ancient chronic bacterial disease that, although curable, is still a significant health problem in developing countries. Caused by Mycobacterium leprae, it has varied clinical presentations depending on the immune response of the host. Reactions are states of heightened immune response. There emerging concept of innate immunity and IL-17 T cells in pathogenesis of leprosy which have different pro-inflammatory and inflammatory consequences. Chronic inflammatory state in leprosy is associated with raised cytokine levels e.g., IL-2, IL-4, IL-5, IL-6, IL-10, IL-17 TNF- α, IFN-γ etc., which can be associated with varied systemic effects and present study was taken to evaluate these changes in leprosy and lepra reaction cases. In present study, mean age of leprosy patient was 33.73 years with majority of the people were in the age group 21 to 30 i.e., 23 patients (35.93%).

This was followed by the age group 31 to 40 i.e., 16 patients (25%) and the age group 11 to 20 i.e., 9 patients (14.06%). Similar number of patients belonged to the age group 41 to 50 i.e., 7 (10.93 %) and 51 to 60 i.e., 7 (10.93 %). Most of the patients were male i.e., 76.5% (49 patients). Female gender formed 23.4 % (15 patients) of the total patients. Male female ratio was 3.2. This was comparable with study by Martoreli et al where majority of cases were male (58.37%), with a predominant age of 15 to 59 years (87.55%).[10] Most common age group noted in a study done by Prasannan et al was 21-40 years (44.4%) and male to female ratio was 2:1.[11] In study of Shah et al, the male: female ratio was 1.93:1.175 In a study by Gupta et al, more than 2/3 (67%) were between 20-49 years of age - 24.35%were in the age group of 30-39 years, followed by 20-29 years (23.49%) and 40-49 years (19.39%), comparable with our study.[12] Being a tertiary care centre in rapidly developing urban area with possibility of greater number of young and middle-aged male migrant form endemic region for employment may be the reason of male predominance. In present study, equal number of patients were present in borderline lepromatous type and borderline tuberculoid type i.e., 22 (34.3%), followed by 12 (18.75%) in lepromatous leprosy and 7 (10.93%) in tuberculoid type. 1 patient was of pure neural type. 2 patients were relieved from treatment but presented with ENL reaction. No patient presented in the mid borderline spectrum, as it is unstable form and usually it progresses to either side e.g., with treatment and rising immunity it progresses towards tuberculoid pole and without treatment and spreading infection with inadequate immunity it progresses towards lepromatous pole. This was almost similar to the findings of Gupta et al where maximum numbers of patients are in borderline spectrum (BT+BB+BL) with major proportion of BT cases. 29.31% belonged to Borderline Tuberculoid (BT) group, followed by Lepromatous Leprosy (21.12%) and closely by Borderline Lepromatous (BL) (17.02%).1271.42% cases in Type I reaction belonged to the borderline lepromatous spectrum, as compared to 92.85 % in Kumar et al study belonging to borderline tuberculoid type. In Type II reaction 100% of patients the belonged to the lepromatous spectrum, as compared to 65% cases in Kumar et al study.13Out of total 64 patients, our study had almost three-fourth of the patients without any lepra reaction cases i.e. 47 (73.4 %) and one fourth of the total patients with lepra reaction i.e. 17 (26.5%). Out of the total 17 lepra reaction patients, a greater number of patients were of type2 reactions i.e., 10 (58.8%). The number of patients of type 1 reaction were 7 (41.2%).In the study of Gupta et al, 34.91% of the patients had signs and symptoms of reactions andout of total reaction cases, 44.85% patients had lesions suggestive of type 1 reaction and 59.25% had lesions suggestive of type 2 reactions comparable with our study.[12] In present study, recurrence was more common in type 2 reaction, with 5 patients showingmultiple recurrences of type 2 reaction and 1 patient with recurrence of type 1 reaction. Similarto

this finding, in a study of Shah et all, recurrence was more commonly seen with ENL (69.6%)than type 1 reaction (25%).[14]

Systematic review 15 noted multiple episodes range from 39% to 77.3% of ENL patients in hospital-based studies & 44 to 63% in field study of all ENL case. Our study showed a greater number of patients of type 1 reaction of borderline lepromatous and borderline tuberculoid types, 5 and 2 patients respectively out of total 7, type 1 reaction patients. Type 2 reaction was seen in borderline lepromatous and lepromatous type, 4 and 6 patients respectively out of total 10, type 2 reaction patients.

These findings were also reflected in the study done by Shah et al where most common type of leprosy showing type 1 reaction (reversal reaction) was borderline tuberculoid leprosy (75%) followed by borderline lepromatous leprosy (25%), while most common type of leprosy showing type 2 reaction (ENL) was lepromatous leprosy (97.8%) followed by borderline lepromatous leprosy (2.1%) 16 Singla P et al (2021)[17] reported 50 (37.3%) BL & 84 (62.7%) LL with T2R. Padhi T et al (2019)[17] reported 72 (74.22%) LL cases with T2R.

Systematic review also highlighted more proportion of ENL reaction in LL cases compare to BL cases. Mean haemoglobin level was lowest in lepromatous leprosy (10.78 ± 1.97) followed by type 2reaction cases (10.94 ± 1.32) g/dl and followed by type 1 reaction cases (11.78 ± 1.32) g/dl. Mean Hb was 12.92 g/dl in non-reaction cases and was 11.21 ± 1.55 g/dl in reactions (TT1R & T2R) cases. Low mean Hb was statistically significant in lepromatous leprosy & reactions cases ($p < 0.05$) compared to non-reaction leprosy cases and comparison group. Average haemoglobin values observed in a study of Freitas et al, were 7.36 g/dl in moderate tointense episodes of ENL and 11.6 g/dl in mild ENL episodes.[18] In a study by Ambalia et al, out of 77 leprosy cases Hb < 10 gm/dl was seen in 11 (14.29%). Out of 11 cases, 7 (63.63%) were T2R cases and 2 (18.18%) BL without reaction cases and rest were 1 each in tuberculoidand pure neural type. Raised inflammatory cytokines in leprosy e.g., IFN-γ, TNF- α, IL-6, have been implicated in development of anaemia and altered iron homeostasis. Cytokines such as IL-1 beta, IFN-gamma, TNF-alpha and IL-6 inhibit erythropoiesis via direct suppression of erythroid precursors or promotion of apoptosis of precursor cells.[19] TNF-α cause down-regulation of erythropoietin (EPO) receptors and blunt the erythropoietic effect of erythropoietin (EPO) directly.[20]

IFN-gamma causes macrophage iron retention through transcriptional inhibition of ferroportin expression, which is a sole cellular iron exporter.[21] IFN-gamma causes macrophage iron retention through transcriptional inhibition of ferroportin expression, which is a sole cellular iron exporter.

Conclusion

Total 64 patients were included in the study, out of which 17 (26.5%) were patients withreaction. Mean age in this study was 33.73 years. Majority of the patients were male. Male to female ratio was 3.26.Most of the patients belonged to 20 to 40 years age group. Mean age was 33.73 years. Patients mostly were of MB type i.e., 57. Only 7 patients belonged to PB type. Equal number of patients were present in borderline lepromatous and borderline tuberculoid type (22 patients, 34.3%), followed by lepromatous type (12 patients, 18.75%) and tuberculoid type (7 patients, 10.93%). 1 patient belonged to pure neuritictype.

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