INTRODUCTION

Leprosy is a chronic disease caused by Mycobacterium leprae, acid-fast bacilli and usually presents with skin and nerve lesions [1,2]. Even today leprosy is an important public health problem. It can result in disfiguring complications in hand, feet, and face including blindness [3]. Early diagnosis, availability of effective drugs and strategies for the prevention of deformities has tremendously helped to effectively manage leprosy and to reduce the incidence of disease [1,4]. However, lepra reaction remains a common problem in patients receiving anti-leprosy therapy. Such reactions can be seen before or after completion of therapy [5]. In a study incidence of lepra reactions was 22.8% in multibacillary patients during multidrug therapy [6]. Two types of lepra reactions (Type 1 and Type 2) are known [7]. Type 1 lepra reactions, i.e., delayed hypersensitivity reactions seen in both paucibacillary and multibacillary cases can cause permanent damage to the peripheral nerves. Type 2 lepra reactions also known as erythema nodosum leprosum are acute inflammatory reactions seen only in multibacillary leprosy (usually in lepromatous leprosy or sometimes in borderline lepromatous leprosy). These reactions are result of immune complex response to M. leprae antigemic determinants [8,9]. Lepra reactions pose a significant burden in leprosy patients, hence their early identification and treatment is important to prevent further complications in the form of nerve damage and permanent disabilities [5,10]. There is limited data on the prevalence and management pattern of lepra reactions in real life setting in Indian patients.

Objective

The objective of this study was to find out the pattern of lepra reactions and medicines used in the treatment of lepra reactions in a tertiary hospital.

METHODS

In this retrospective study, we included patients treated for the management of lepra reactions. Prescriptions of the discharged patients were reviewed to examine the prevalence of Type 1 and Type 2 reactions. The mean and total number of medicines used in the patients with lepra reactions was recorded. The study was approved by the Institutional Ethics Committee.

Statistical analysis

Continuous data are presented as mean and standard deviation, whereas categorical data are presented as number and percentages.

RESULTS

In this study, we reviewed data of 66 patients of which 59.1% were male and 40.9% were females. The mean age of patients was 36.6±13.1 years (Table 1).

Out of 63 patients in whom type of leprosy was mentioned, 59 (93.7%) had multibacillary leprosy whereas 4 (6.3%) had paucibacillary leprosy (Fig. 1). In three patients, the classification was not mentioned. A total of 26 (40%) patients had Type 1 reaction while 39 (60%) patients had Type 2 reaction (Fig. 2). Data of one patient were missing. Of the 39 cases of Type 2 reactions, 11 (28.2%) were steroid-dependent cases and 6 (15.4%) were recurrent erythema nodosum leprosum (ENL).

A total number of medicines prescribed to study patients were 493. The mean number of medicines per patients was 7.5. Drugs used for the treatment of lepra reaction and leprosy are given in Table 2. Table 3 shows adjuvant drugs used in the treatment of lepra reaction.
Prednisolone was used in 62 (93.9%) patients with mean duration of 33.32±33.2 days whereas chloroquine was used in 52 (78.8%) patients for mean period of 36.6±27.9 days. Thalidomide, clofazimine, and colchicine were used in 25 (37.9%), 3 (4.5%), and 1 (1.5%) patients, respectively (Table 2). The mean duration of use for these three drugs was 75.7±41.0, 24.3±8.1, and 30 days, respectively. Clofazimine was also used in combination with rifampicin and dapson in 17 (25.8%) patients, whereas combination of rifampicin plus clofazimine was used in 2 patients. This was as a part of multidrug regimen for the treatment of leprosy. Analgesic and anti-inflammatory and anti-acidity drugs were used in 27 (40.9%), 27 (40.9%), and 35 (53.0%) patients, respectively (Table 3).

**DISCUSSION**

Lepra reactions represent a significant burden in patients with leprosy. Systematic data from India on the management of lepra reactions in real life settings are limited. In this study, we examined the prevalence and management pattern of lepra reactions in patients with leprosy. Most of the patients with lepra reactions had multibacillary leprosy in our study. We observed less common occurrence of Type 1 lepra reactions compared to Type 2 reactions. Neuritis, an important cause of deformities in leprosy can be managed in hospitals or outpatient settings, later being more beneficial in terms of cost reduction [11].

**Table 1: Baseline demographics**

| Baseline parameter                  | Result                                      |
|-------------------------------------|---------------------------------------------|
| Total number of patients            | 66                                          |
| Mean age (±SD) years (range)        | 36.6 (±13.1) (Range 9-68 years)             |
| Male, N (%)                         | 39 (59.1)                                  |
| Female, N (%)                       | 27 (40.9)                                  |

SD: Standard deviation

**Table 2: Drugs used in the management of lepra reactions and leprosy**

| Class of medicine                  | N (%)                                      |
|------------------------------------|--------------------------------------------|
| Prednisolone                       | 62 (93.9)                                  |
| Chloroquine                        | 52 (78.8)                                  |
| Thalidomide                        | 25 (37.9)                                  |
| Clofazimine                        | 3 (4.5)                                    |
| Colchicine                         | 1 (1.5)                                    |
| Rifampicin plus clofazimine        | 2 (3)                                      |
| Rifampicin, clofazimine plus dapsone | 17 (25.8)                              |
| Analgesic and anti-inflammatory    | 63 (95.5)                                  |
| Paracetamol                        | 41 (62.1)                                  |

**Table 3: Adjuvant therapies used in the management of lepra reaction**

| Class of medicine                  | N (%)                                      |
|------------------------------------|--------------------------------------------|
| Anti-acidity                       | 63 (95.5)                                  |
| Antihistamine                      | 29 (43.9)                                  |
| Antimicrobial                      | 27 (40.9)                                  |
| Calcium                            | 12 (18.2)                                  |
| Iron                               | 10 (15.2)                                  |
| Vitamins                           | 35 (53.0)                                  |
| Iron plus folic acid               | 1 (1.5)                                    |
| Vitamin plus mineral               | 30 (45.5)                                  |
| Others                             | 12 (18.2)                                  |
in patients with ENL [18] and represents a promising agent for the treatment of ENL; however, it is not recommended for use in pregnancy.

Cofazimine has been shown to be effective in the dose of 100 mg 3 times daily for 12 weeks [14]. The benefits of clofazimine include anti-inflammatory and steroid sparing effect [19]. The effective is usually seen after 4 weeks [9]. Cofazimine is used in both, i.e., treatment of leprosy, mainly lepromatous leprosy as well as treatment of lepra reactions, i.e., erythema nodosum leprisum [17,20].

In our study, duration of clofazimine was 24.3 days, mainly in the treatment of leprosy and rarely in the treatment of lepra reaction.

Pentoxifylline is another effective agent for the treatment of Type 2 reactions. Pentoxifylline is effective in reducing initial severity, whereas clofazimine has comparatively slower onset of action [14]. In our study, pentoxifylline was not used. The use of colchicine has also been reported in the management of in the management of erythema nodosum lepromatum due to its anti-inflammatory and immunoregulatory action [16]. In our study, the use of colchicines was very low. It was used only in one patient in this study. Overall, steroid, analgesic anti-inflammatory drugs, paracetamol, chloroquine, thalidomide, and clofazimine were the major drugs used in the treatment of lepra reactions. In addition to these major medicines, use of adjuvant therapies including anti-acidity medicines, anti-histamines, antimicrobial therapy and vitamins and minerals was common mostly for preventing adverse events and improving general health of the patients.

Our study has some limitations. Cross-sectional, retrospective analysis of data from single center limits the generalization of findings to whole population. The safety of medicines in the treatment of lepra reactions and outcomes of the patients are not evaluated. Considering these findings, the observations should be carefully extrapolated.

CONCLUSION
Lepra 2 reaction is more common than lepra 1 reaction. Prednisolone and chloroquine are the two most commonly used medicines in the treatment of lepra reaction whereas colchicine use is uncommon. Thalidomide, older drug is commonly used for the treatment of lepra reaction in government tertiary hospital set up.

REFERENCES
1. Desikan KV. Elimination of leprosy & possibility of eradication - The Indian scenario. Indian J Med Res 2012;135:3-5.
2. Vinod KV, Chandramohan R, Dutta TK, Rajesh NG, Basu D. Type 2 lepra reaction as a cause of pyrexia of unknown origin. J Assoc Physicians India 2012;60:70-2.
3. Arun S, Balachandar V, Sasikala K, Subramanian A, Abilash VG. Comparative and cross sectional study of success of leprosy elimination strategy before (2000 to 2005) and after (2006 to 2010) eradication period in referral hospital of Tamil Nadu. Indian J Pharm Clin Res 2013;6 Suppl 3:182-5.
4. Kumar B. World leprosy day 2015: Renewing commitment for a leprosy free world! Indian J Med Res 2015;141(1):1-4.
5. Kahawita IP, Walker SL, Lockwood DN. Leprosy Type I reactions and erythema nodosumlepromatum. An Bras Dermatol 2008;83(1):75-82.
6. Vijayakumaran P, Jenudasan K, Manimozhi N. Fixed-dose therapy (FDT) in multibacillary leprosy; Efficacy and complications. Int J Lepr Other Mycobact Dis 1996;64(2):123-7.
7. Raffe SF, Thapa M, Khadge S, Tamang K, Haggie D, Lockwood DN. Diagnosis and treatment of leprosy reactions in integrated services - The patients’ perspective in Nepal. PLoS Negl Trop Dis 2013;7(3):e2089.
8. Treatment of Lepra Reaction. Available from: http://www.apps.who.int/medicinedocs/en/d/Jh2988e/6.html#Jh2988e.6. [Last accessed on 2017 Jan 14].
9. Yogeesh HR, Chankramath S, Yadalla HK, Shariff S, Ramesh SB, Sreekantaiah SB. Type 2 lepra reaction (ENL) presenting with extensive cutaneous ulcerations. Our Dermatol Online 2012;3(1):17-20.
10. Pandhi D, Chhabra N. New insights in the pathogenesis of Type 1 and Type 2 lepra reaction. Indian J Dermatol Venereol Leprol 2013;79(6):739-49.
11. Remme HN, George R, Eapen EP, Pulimood SA, Gnanamuthu C, Jacob M, et al. A comparison of economic aspects of hospitalization versus ambulatory care in the management of neuritis occurring in lepra reaction. Int J Lepr Other Mycobact Dis 2004;72(4):448-56.
12. Walker SL, Lockwood DN. Leprosy Type 1 (reversal) reactions and their management. Lepr Rev 2008;79(4):372-86.
13. Sarita S, Muhammed K, Najeeba R, Rajan GN, Anza K, Binitha MP, et al. A study on histological features of lepra reactions in patients attending the Dermatology Department of the Government Medical College, Calicut, Kerala, India. Lepr Rev 2013;84(1):51-64.
14. Roy K, Sil A, Das NK, Bandopadhayay D. Effectiveness and safety of clofazimine and pentoxifylline in Type 2 lepra reaction: A double-blind, randomized, controlled study. Int J Dermatol 2015;54(11):1325-32.
15. Lakalim AV. Spectrophotometric method for estimation of chloroquine in bulk and tablet dosage form. Asian J Pharm Clin Res 2013;6 Suppl 1:156-8.
16. Girdhar BK. Immunopharmacology of drugs used in leprosy reactions. Indian J Dermatol Venereol Leprol 1990;56:354-63.
17. Use of Thalidomide in Leprosy. Available from: http://www.who.int/lep/research/thalidomide/en. [Last accessed on 2017 Jan 21].
18. Patil US, Jaydeekar AV, Bandawane DD. Immunomodifiers: A pharmacological review. Int J Pharm Pharm Sci 2012;4 Suppl 1:30-6.
19. Pai VV. Role of clofazimine in management of reactions in leprosy: A brief overview. Indian J Drugs Dermatol 2015;1(1):12-5.
20. Saxena S, Singh HD, Agrawala VK, Rai J, Singh S. Estimation of clofazimine in capsule dosage form by using UV-VIS spectroscopy. Int J Pharm Pharm Sci 2013;5 Suppl 3:126-34.