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Review Article

Leprosy and women

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ABSTRACT

Leprosy has an impact on the physical, social, and psychological health of affected people. Women in developing countries seek health care late for any health-related issues. Leprosy, a disease known for its stigma, adds further to these facts. Also, close contact between women and family members, especially children, increases the chance of transmission to others and thereby increases the disease burden in the society. Hence, leprosy in women is an important issue for the affected patient, their family members, and society as a whole.

Introduction

Leprosy is a chronic granulomatous disease caused by *Mycobacterium leprae*. The disease is mainly classified as paucibacillary (PB) or multibacillary (MB) leprosy, depending on the number of skin lesions and nerve involvement. PB leprosy is a milder form of the disease, characterized by few (i.e., up to five) hypopigmented, pale and reddish, hypo- or anesthetic skin lesions, which may at times be infiltrated. MB leprosy is associated with multiple (i.e., more than five) skin lesions that manifest as nodules, plaques, or diffuse skin infiltration (World Health Organization, 2002). (See Figs. 1–5).

According to the Ridley and Jopling classification (1966), leprosy can be divided into five groups: tuberculoid leprosy (TT), borderline tuberculoid leprosy (BT), mid-borderline leprosy (BB), borderline lepromatous leprosy (BL), and lepromatous leprosy (LL). Later, the leprosy was reclassified with the addition of pure neuritic leprosy and indeterminate leprosy. TT, BT, and indeterminate leprosy are considered PB leprosy, and BB, BL and LL Hansen's are classified as MB leposy. Pure neuritic leprosy can fall on both spectrums depending on the number of nerves involved and the bacillary load.

Indeterminate leprosy presents clinically as a vague hypopigmented patch with some degree of loss in tactile and thermal sensation that shows the presence of bacilli or perneural infitartion in histopathology. This is usually the first sign of leprosy in 20% to 80% of patients (Cardama, 1980). TT presents with well-defined anesthetic plaque with raised and clear-cut edges that slope inward. The surface looks dry with hair loss and sweating, and the feeder nerve may thicken. BT presents with an anesthetic patch with regular-to-irregular margins that have a pseudopodial extension and satellite lesions in the vicinity of patch. Several of the peripheral nerves are likely to be enlarged in an asymmetrical pattern, with hair loss and sweating on the patches.

BB is an unstable form of the disease that can present with features of both tuberculoid and lepromatous pole. The characteristic skin lesions are annular lesions with a well-defined, punched-out inner edge and an ill-defined outer-sloping edge that give the appearance of Swiss cheese. Nerve damage is variable and depends on whether the patient is upgrading from lepromatous pole or downgrading from tuberculoid pole. In BL, there are slightly infiltrated, round-to-oval macules of 2 to 3 cm in diameter that are distributed in an asymmetrical pattern with areas of apparently normal skin between macules. With the progression of disease papules, nodules and plaques may develop with slope-like margins merging into the surrounding skin. Peripheral nerve involvement is asymmetrical; however, the damage is less compared with BT and TT.

LL presents as macules, nodules, papules, and diffuse and infiltrated forms. Macules in LL are smaller compared with BL, with indistinct edges, shiny surfaces, and a symmetrical distribution. Diffuse LL has shiny and thickened skin that is better felt with touch by pinching the skin with fingers. Earlobes are shiny and thickened. The nodular form is the advanced stage of LL with nodules over the ear lobes, face, trunk, joints, and extremities. Symptoms also include madarosis, accentuation of skin folds, and bony deformities like nasal depression giving rise to leonine facies. Nerve trunks are rarely involved; instead, dermal twigs give rise to symmetrical loss of sensation initially over the extensors of the extremities in a glove and stocking pattern (Ridley and Jopling, 1966). Pure neuritic leprosy also presents with a loss of sensation and the involvement of nerves that supply those

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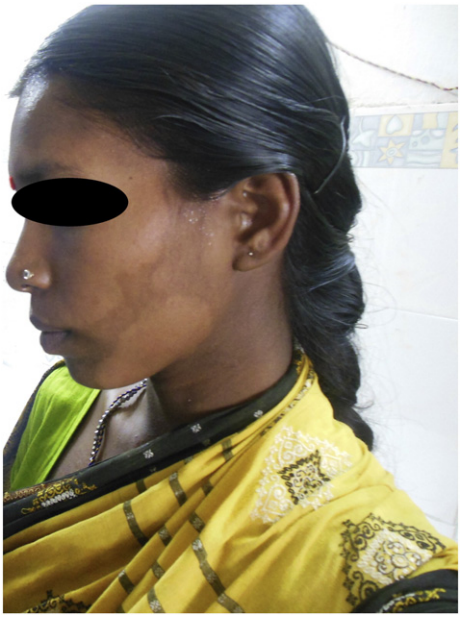

Fig. 1. Borderline tuberculoid leprosy with patch over face.

areas without any skin lesions of leprosy in the present or past (Dongre et al., 1976).

Although not life threatening, leprosy causes several stigmatizing deformities and thereby has a great psychosocial impact on affected people and their families. In developing countries like India, most women are housewives who are neglected within the family, especially where health is concerned. Women are always the last to seek healthcare, the most common being their financial dependence on men. Hence, leprosy in women has a great impact on the health of the affected patient and her family members, children, and community as a whole.

In this review, we discuss the various aspects of leprosy in women, including the prevalence; difference in clinical features; effects on pregnancy, lactation, menstruation, ovarian function, fertility status, and marital status; and response to treatment. However, not all forms of leprosy have stigmata.

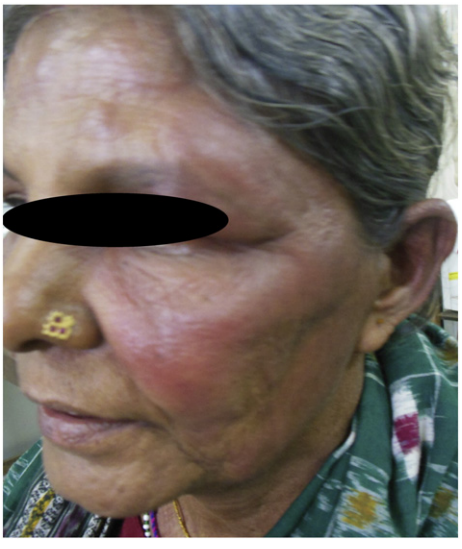

Fig. 2. Borderline tuberculoid leprosy with patch over face and plaque over forehead in type 1 reaction.

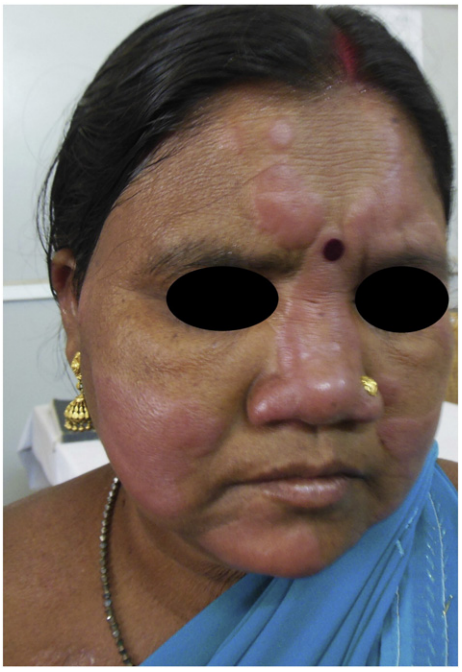

Fig. 3. Borderline tuberculoid leprosy with type 1 reaction.

Prevalence of leprosy in women

Although the prevalence of leprosy has declined and the disease was declared eliminated in 2005, endemic pockets remain in various parts of the world. In 2014-2015, the prevalence rate was 0.68/10,000; in 2013-2014, the proportions of women and children affected with leprosy were 36.81% and 9.04%, respectively. Traditionally, a male-over-female preponderance has been reported in various

Fig. 4. Nodular lepromatous leprosy with type 2 reaction along with clofazimine-induced pigmentation.

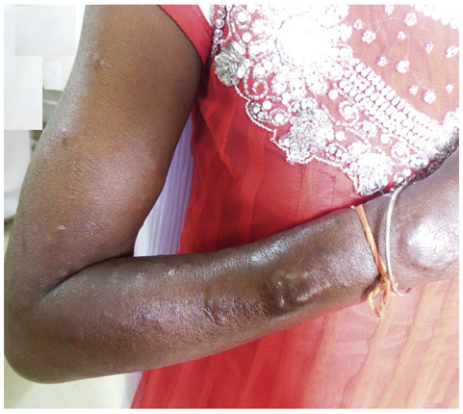

Fig. 5. Erythema nodosum leprosum lesions over the forearm.

epidemiological studies (Padhi and Pradhan, 2015; Peters and Eshiet, 2002; Rao et al., 1996; Van Veen et al., 2006). Traditional beliefs, the low status assigned to women, and women's limited mobility, illiteracy, and poor knowledge of leprosy have been suggested as important sociocultural factors responsible for underreporting of cases of women affected with leprosy.

In a study from Nepal, it was determined that most of the women were illiterate, married at an early age, had a heavy workload, and had poor knowledge and awareness of the clinical signs of leprosy and its treatment. Affected women had to seek permission from their mother-in-law or husband to leave the homestead and needed escort and money for transportation and sometimes treatment. All of these factors impeded women in reporting for an early diagnosis and treatment (Varkevisser et al., 2009).

Gender-related difference

In various studies, it has been reported that women affected with leprosy were of a younger age group compared with men (Arora et al., 2008; Lockwood and Sinha, 1999). Hormonal imbalance related to pregnancy and/or puerperium might be a possible cause of such occurrence (Arora et al., 2008). With regard to MB prevalence, women are in an advantageous position compared with men and comprise a lower percentage of MB cases according to existing data (Arora et al., 2008; Chisi et al., 2003; Hussein et al., 2010; Peters and Eshiet, 2002; Varkevisser et al., 2009). Most published data show that the incidence of chronic neuropathic ulcer is higher in men compared with women, which may be due to underdiagnosis in women (Kunst, 2000; Lema et al., 2012; Tiendrebeogo et al., 1999).

In a study from Southeast Nigeria, a higher proportion of women had various deformities compared with men, and the duration gap between appearance of signs and symptoms and diagnosis of leprosy was almost double (Peters and Eshiet, 2002).

Because of the late presentation, there are more chances for severe deformities in women. In countries like India, because a significant proportion of females are housewives, they engage in cooking and other household activities and are vulnerable to repeated trauma, ulceration, and other severe-grade deformities in leprosy.

Leprosy and pregnancy

Leprosy and pregnancy affect each other's course. The clinical signs and symptoms of leprosy are mostly due to the role of immunity and depend on the immunological status of the host. Hormonal changes during puberty or pregnancy lead to alteration in the host's immune status. The first appearance of leprosy, reactivation of the disease, and relapse in "cured" patients are likely to occur particularly in the third trimester of pregnancy due to decreased immunity (Duncan et al., 1981, 1982). Due to the variation in cell-mediated and humoral immunity, lepra reactions are triggered by pregnancy (Duncan et al., 1982). A type 1 reaction (reversal reaction) occurs during postpartum phase, whereas a type 2 reaction (erythema nodosum leprosum) peaks during late pregnancy. Both types of reaction can continue long into lactation. Hence, affected women are vulnerable to sequelae both due to leprosy and lepra reactions. Up to 20% of children born to mothers with leprosy may develop leprosy by the time they reach puberty. If marriage and childbearing occur at an early age in the leprosy-affected daughters of mothers who have leprosy, they are likely to experience the adverse effects of pregnancy on leprosy (Duncan, 1993).

Effect of leprosy on fetus and children

Existing evidence shows that babies of mothers with leprosy have a lower birth weight and smaller placentae, grow more slowly, and experience more infections and higher infant mortality than those of non-leprous mothers. Mothers affected with LL have more of these findings compared to mothers with other variants of leprosy. In a study by Duncan et al. (2007), it was found that children of mothers affected with LL had more serious infections compared with other groups of children. The pubertal skeletal growth spurt and menarche in girls was delayed in children who were studied in comparison with a healthy control group; they caught up by the late teen years. These findings were mostly marked in children of LL-affected mothers (Duncan et al., 2007). Impaired growth in utero and infancy due to immunological factors have been suggested as a possible cause for this observation.

Effect of leprosy on menstrual cycle and fertility status

Data are more scarce regarding the involvement of gonads in female patients with leprosy. Existing studies show contradictory findings. Mitsuda (1936); Mitsuda and Ogawa (1937) and Hardas et al. (1972) suggested that leprosy does not have any effect on the menstrual cycle or fertility. However, Sharma et al. (1981) found that 10% of women affected with leprosy had primary infertility, which was higher than the prevalence of infertility in the general population in India (Jejeebhoy, 1995; Sharma et al., 1981). Similarly, Fleger et al. (1963) found that 54% of female patients with leprosy were sterile, and gross menstrual abnormalities were reported by King and Marks (1958) in patients with leprosy. Bogush (1976) also reported menstrual dysfunction in patients with leprosy, which could be prevented by early institution of therapy.

In a study from India by Khanna et al. (2014), a significantly larger number of female patients with MB leprosy had irregular periods postdating the onset of leprosy than patients with PB leprosy. The study also found that gonadotropic hormone levels were elevated in significantly more patients with MB leprosy vis-à-vis patients with PB leprosy, and that the mean levels of these hormones showed an increasing trend from controls to patients with PB to patients with MB leprosy.

Autoimmune disorders of the ovary often cause ovarian dysfunction, resulting in irregularity of the menstrual cycle and infertility (Nandedkar and Wadia, 1998; Nelson et al., 2005). MB leprosy is often associated with an autoimmune phenomenon with various autoantibodies, such as anti-neutrophil cytoplasmic antibodies (ANCA), A-ANCA, anti-mitochondrial antibodies, and anti-phospholipid antibodies, found in the sera of patients (Freire et al., 1998; Garcia-De La Torre, 1993; Guedes Barbosa et al., 1996; Park et al., 1992). Hence, it has been suggested that autoantibodies directed against components of the ovary might be a cause of ovarian failure.

Table 1
World Health Organization multidrug therapy regimen for paucibacillary and multibacillary leprosy

	Paucibacillary Leprosy	Multibacillary Leprosy
Adult	Once a month: Day 1: rifampicin 600 mg + dapsone (100 mg) (supervised dose) Days 2–28: 1 tablet of dapsone (100 mg) once daily Full course: 6 months	Once a month: Day 1: rifampicin 600 mg + clofazimine 300 mg (100 mg X 3) + dapsone 100 mg Once a day: Days 2–28 1 capsule of clofazimine (50 mg) and 1 tablet of dapsone (100 mg) Full course: 12 months
Children	10–14 years: Once a month: Day 1: rifampicin 450 mg + dapsone 50 mg (supervised dose) Days 2–28: 1 tablet of dapsone (50 mg) Full course: 6 months For children younger than 10 years of age, the dose must be adjusted according to body weight.	10–14 years: Once a month: Day 1: rifampicin 450 mg + clofazimine 150 mg (50 mg X 3) + dapsone (50 mg) Once a day: Days 2–28: clofazimine every other day (50 mg) and 1 tablet of dapsone (50 mg) Full course: 12 months For children younger than 10 years of age, the dose must be adjusted according to body weight.

Leprosy and marital status

Various studies have proved that the level of stigma is quite high in women affected by leprosy compared with men (Mankar et al., 2011; Rafferty, 2005; Singh, 2012; Try, 2006; Vlassoff et al., 1996; World Health Organization, 2002). The social and psychological complications due to leprosy persist even after completion of treatment. The effect of leprosy on marital relationships is an important example of a social complication. A qualitative study of the psychological needs of men and women with leprosy in South Africa revealed that one third of leprosy patients are abandoned by their spouses (Scott, 2000). Another study from Nepal found that 48% of community members thought that people affected by leprosy would encounter marital problems (Adhikari et al., 2013).

A similar study from Nepal found that leprosy affected the marital status of women in various ways. They face significant problems during treatment, which often lasts a full year. They do not have intercourse at all due to the fear of contagion, are kept distant from loved ones, and both spouses sleep in separate beds. Also, most of the leprosy-affected women are abandoned or sexually abused by their husbands even after treatment (van't Noordende et al., 2016).

Intolerance to multidrug therapy in women

Multidrug therapy (MDT) instituted by the Word Health Organization in 1981 has been considered the gold standard treatment for leprosy. The regimen has undergone different modifications regarding duration of therapy and doses. However, the currently recommended duration is 6 months for PB and 12 months for MB (Table 1).

MDT includes rifampicin, dapsone, and clofazimine. Each drug has its own side effect profile, which varies by individual. However, there is some evidence of gender-related differences in tolerance to MDT. In one study, 23.6% of women were found to have MDT intolerance to the PB regimen, leading to a greater change in the MDT regimen. Anemia was the cause in 13.8% of cases (Dupink et al., 2013). Goulart et al. (2002) found that reported incidence of hemolytic anemia related to dapsone was higher in women compared with men.

Among the three drugs in MDT, clofazimine is well known for causing visible, long-lasting changes in skin in the form of icthyosis and hyperpigmentation. These changes are mostly cosmetically disabling and unacceptable by many women, which further adds to psychological stress (Hastings et al., 1988; Jamet et al., 1992; Singh et al., 2011).

Nutritional status in women with leprosy

Recent studies regarding the nutritional status of leprosy patients suggest that poor nutrition can indirectly lead to progression of the clinical disease due to an indirect impact on cell-mediated immunity, but they do mention gender-related differences. However, women are the most affected by poor nutrition in a family and hence have more chances for progression of the disease. More studies are needed to document this.

Conclusions

This paper highlights the various aspects of leprosy in women in developing countries over the last few decades (Le grand, 1997), including prevalence, clinical features, complications, social aspects and treatment-related issues. It highlights that screening, treating, and rehabilitating women with leprosy is an important aspect of leprosy programs, and counseling women and their spouses and family members will go a long way in enabling female patients to return to their normal lives.

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