



BCG VACCINATION STATUS AMONG THE LEPROSY CASES IN LEPROSY ERADICATION ERA AT TERTIARY CARE HOSPITAL

Dermatology

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ABSTRACT

Background: Meta-analysis has confirmed that BCG vaccine is effective in preventing leprosy, but still there is no uniform policy for the adult BCG vaccination for the prevention of the leprosy in India. Low Proportion of the fully immunized individual might be at risk for the both tuberculosis and leprosy.

Aims: This study was designed to know the effect & status of the BCG vaccination among different types of leprosy.

Methods: All new untreated leprosy patients detected between April-2014 to March-2017 were included in study. Demographic Data with clinical characteristics of leprosy, slit smear, were collected. BCG vaccination status was noted by the presence or absence of the scar in deltoid region of the arm.

Result: Borderline leprosy was commonest 83 (40.29%) followed by Lepromatous Leprosy 49 (23.79%), Tuberculoid Leprosy 42 (20.39%), pure neural Leprosy 32(15.53%) out of 206 patients. Among 59 Pauci-Bacillary (PB) cases, BCG scar was present in 19 (32.20%) and absent in 40 (67.80 %). Out of 147 MB cases BCG scar was present in 40 (27.21%) and absent in 107 (72.79%). The difference between vaccinated and non-vaccinated group for different types of leprosy was not statistically significant.

Conclusion: Present study highlighted more number of Leprosy cases without previous BCG vaccination. Further Previous infant BCG vaccination is not appeared to have effect on disease evolution with increase age among leprosy cases.

KEYWORDS

BCG scar, Leprosy

INTRODUCTION:

Leprosy is a chronic granulomatous disease cause by Mycobacterium leprae. In India leprosy has been declared eliminated at the National Level in year 2005. Because of a long incubation period of disease, the new cases continue to occur in post eradication period for few more years. As per National Leprosy Eradication Programme annual report (1) of 2016-17, Prevalence Rate (PR) on 1st April 2017 was 0.66 per 10,000 populations. Annual new case detection rates (ANCDR) at national level for year 2014 to 2016 were static and below 1 per 10,000 populations with slight increase during 2016-17 that was 1.02 per 10000 populations. ANCDR for Gujarat was 10.85 per 10,000 populations with PR 0.57/ 10,000. There were Nine district with PR > 1 / 10,000 population. Therefore, timely diagnosis and complete MDT treatment of new leprosy cases is crucial for ultimate eradication of the disease at all the level.

BCG vaccine is part of universal immunization programme, for the prevention of the tuberculosis. Meta-analysis (2,3,4) has confirmed that BCG vaccine is effective in preventing leprosy, but still there is no uniform policy for the adult BCG vaccination for the prevention of the leprosy in India. As per the survey report (5) proportion of the fully immunized children is as low as 19%, and these may be one of the reason for the continue detection of the new leprosy cases among high prevalent region. Migrant population from high leprosy endemic state significantly contribute the number of new leprosy cases. There is possibility that many individuals were not covered under the immunization programme in past and they might be at risk for the both tuberculosis and leprosy.

Exact status of the BCG vaccination among the leprosy patient is not known. This study was designed to know the status of the BCG vaccine scar status among the newly detected leprosy patient, and to know the clinical difference among the leprosy patients with or without previous BCG vaccination.

MATERIALS AND METHODS:

This study was carried out after approval of institutional ethics committee, at department of Dermatology Venereology & Leprosy, Surat municipal institute of medical education & research. All new untreated leprosy patients detected between April-2014 to March-2017 were included in study. Other leprosy cases e.g. defaulter, relapse, release from treatment (RFT) & indeterminate Leprosy cases were excluded. All patients were screened at outpatient department by investigators and detailed clinical examination was noted as per

predefined proforma, and all cases were subjected to slit skin smear examination.

Leprosy cases were categorized as Pauci-Bacillary Leprosy (PB) (1-5 Patches and / or 1 Nerve Involvement), Multi-Bacillary Leprosy (MB) (≥ 6 patches; 2 or more Nerve Involvement) & Tuberculoid (TT), Borderline Leprosy (BL) – PB/MB, Lepromatous Leprosy (LL), and Pure Neural Leprosy (PN) –PB/MB as per National Leprosy eradication programme (NLEP) guideline. All newly diagnosed patients were treated with the standard WHO MDT regimes for PB or MB, and Lepra reaction patients were treated as per NLEP guideline. Data including age, sex, clinical characteristics of leprosy, skin slit smear for M. Leprae, were collected. Status of the previous BCG vaccination was noted by the presence or absence of the scar in deltoid region of the arm.

RESULTS:

Results are summarized in Table: 1 & 2.

Total 206 new leprosy cases were detected between April-2014 to March-2017. Out of 206 cases, 151 (73.30%) were male and 55 (26.70%) were female & average age was 31.77 years with median age of 30 years & standard deviation of 12.51. Out of total 206 new leprosy cases BCG scar was seen in 59 (28.64%) cases and rest 147 (71.36%) did not have BCG scar. Out of total 206 cases, borderline leprosy was commonest 83 (40.29%) followed by Lepromatous Leprosy 49 (23.79%), Tuberculoid Leprosy 42 (20.39%), & pure neural Leprosy 32 (15.53%). 147 (71.36%) cases were diagnosed as MB leprosy and 59 (28.64%) cases of PB leprosy. Out of 59 PB cases BCG scar was present in 19 (32.20%, n=59) and absent in 40 (67.80%, n=59). Out of 147 MB cases BCG scar was present in 40 (27.21% n=147) and absent in 107 (72.79%, n=147).

Table:1 Demographic characteristics of Leprosy cases

| Factors | Number of cases |
|-----------------|-----------------|
| Age | |
| Average | 31.77 |
| Median | 30 |
| SD | 12.5 |
| ≤ 15 years | 09 |

| | |
|---------------------|-----|
| >15 years | 197 |
| Sex | |
| Male | 151 |
| Female | 55 |
| Vaccinated * | 59 |
| M. Leprae Smear +ve | 27 |
| M. Leprae Smear -ve | 32 |
| Non-Vaccinated** | 147 |
| M. Leprae Smear +ve | 76 |
| M. Leprae Smear -ve | 71 |

*BCG scar present ** BCG scar not present

Among 42 Tuberculoid leprosy cases, BCG scar was seen in 15 (35.71%), while 27 (64.28%) cases did not have scar. Among 83 borderline leprosy cases BCG scar was seen in 24 (28.91%), and 59 (71.08%) did not have scar. In 49 Lepromatous Leprosy case, BCG scar was seen in 9 (18.36%), while in 40 (81.63%) cases did not have BCG scar. In 32 pure neural leprosy cases, BCG scar was seen in 11 (34.38%), while 21 (65.63%) cases did not have BCG scar.

Table: 2 Characteristics of Leprosy case with vaccination status

| | TT | BL- PB | BL- MB | LL | PN-PB | PN - MB | Total |
|--------------------|----|--------|--------|----|-------|---------|-------|
| Male | 31 | 02 | 58 | 38 | 08 | 14 | 151 |
| Female | 11 | 04 | 19 | 11 | 03 | 07 | 55 |
| Total | 42 | 06 | 77 | 49 | 11 | 21 | 206 |
| BCG vaccinated | | | | | | | |
| Male | 11 | 00 | 17 | 08 | 02 | 04 | 42 |
| Female | 04 | 00 | 07 | 01 | 02 | 03 | 17 |
| Total | 15 | 00 | 24 | 09 | 04 | 07 | 59 |
| M.Lepra e +VE | 00 | 00 | 21 | 06 | 00 | 00 | 27 |
| M.Lepra e -Ve | 15 | 00 | 03 | 03 | 04 | 07 | 32 |
| BCG non-vaccinated | | | | | | | |
| Male | 20 | 02 | 41 | 30 | 06 | 10 | 109 |
| Female | 07 | 04 | 12 | 10 | 01 | 04 | 38 |
| Total | 27 | 06 | 53 | 40 | 07 | 14 | 147 |
| M.Lepra e +VE | 00 | 01 | 43 | 32 | 00 | 00 | 76 |
| M.Lepra e -Ve | 27 | 05 | 10 | 08 | 07 | 14 | 71 |

TT-Tuberculoid Leprosy; BL-Borderline Leprosy; LL-Lepromatous Leprosy; PN - Pure Neural Leprosy; PB- Pauci-bacillary, MB - Multi-bacillary

DISCUSSION:

BCG vaccine is mainly used for the prevention of mycobacterium tuberculosis disease. Various study reports have highlighted its effectiveness in leprosy but protective effect of BCG for leprosy is variable. BCG vaccine induces cell mediate immune response with resultant stimulation of INF- γ , IL-2, IL-17 & 22 productions that provide protection against mycobacterial infection. BCG vaccine is part of universal immunization programme, for the prevention of the tuberculosis and the BCG scar (6) considered as a sensitive indicator of vaccination status.

Review of BCG vaccine protection (2) and clinical forms of leprosy showed pooled protection were 76% (95 CI: 69-83%) for MB forms, and 62% (95 CI: 51-73%) for PB forms with greater variability of the BCG vaccine effect against pauci-bacillary forms.

Study form Brasil (7) showed that BCG vaccine is effective in preventing leprosy among the contacts of leprosy cases. Study showed that BCG vaccine in contacts of leprosy patient induces macrophage activation and increased production of IFN- γ , TNF- ∞ , thus by mounting a cellular response effective against M. Leprae. BCG vaccinated individual can control subclinical leprosy infection and also managed to shift of MB leprosy to PB leprosy with decrease

incidence of lepra reaction and deformity. RCT Study by Richardus RA et al (8) shown that BCG vaccine among healthy contacts of index leprosy cases have increase appearance of PB cases in vaccinated contacts. These could possibly due to boosting of immune response against M. Leprae as a part of immune reconstitution in already exposed individual. Whether it is beneficial or harmful is question as most of the contacts who developed clinical symptoms, show some neurological deficit at the time of reporting.

In present study 59 (28.64%) cases had BCG scar and rest 147 (71.36%) did not have BCG scar. Vaccination status among the PB and MB cases were comparable with only marginal difference among PB & MB cases (PB vaccinated 32.20 %, Non-vaccinated 67.80 %; MB vaccinated 27.21 %, Non-vaccinated 72.79 %). These findings were comparable with the study done by Col P Ramadasan et al (9) (25.4% of leprosy cases were in BCG vaccinated & 74.6% non-vaccinated). Comparing BCG vaccinated and non-vaccinated group for PB and MB case, the difference among type of leprosy and BCG vaccine status was statistically not significant [p value = 0.4736]. Further comparing Vaccinated and non-vaccinated group for different types of leprosy (TT/BL/LL/PN) calculated P value was p=0.253, also suggested no significant difference among the different types of leprosy. Thus above data suggest that there is little effect of previous BCG vaccination on leprosy evaluation. Possible explanation of non-effectiveness of BCG vaccine in leprosy is related to age of infected patients and difference in immunological response after BCG vaccination.

Age factor: Under immunization programme BCG vaccine is offered immediately after birth, that stimulate protective immune response and produce scar formation at vaccine site. Weir RE et al (10) demonstrated that after infantile BCG vaccination that provide protective immune response up to 15 years and after these age BCG may fail to provide protection. In present study 9 cases were less than 15 years of age and BCG scar was absent in 7 (77.78%) cases, these explain the possibility of increase susceptibility for non-vaccinated children compare to vaccinated children. In 197 cases with age >15 years, 28.93% cases were vaccinated and 71.07% were non-vaccinated, these results is comparable to child cases. Median age in present study was 30 years with standard deviation 12.50, and thus previous BCG vaccination may not appear to have effect on evolution of leprosy.

Immunological factor: BCG vaccine is not 100 % effective in preventing pulmonary tuberculosis and also protection is not lasting (11). These may have related to different immunological response and cellular activation after BCG vaccination. There is a difference in antigen processing by different antigen presenting cells as Pattern Recognition Receptors (PRR) types & level are different among different antigen presenting cells. In case of BCG vaccine antigen is processed by epidermal macrophages, which is different form alveolar macrophage and thus immune response differs and may not be adequate to prevent pulmonary infection. Similarly, in Leprosy route of transmission of leprosy is through respiratory route and mucosal macrophages may play important role in resistance and prevention of Leprosy.

CONCLUSION:

Present study highlighted more number of Leprosy cases without previous BCG vaccination. As Meta-analysis has proven the effectiveness of BCG vaccination among the Leprosy, universal BCG vaccine coverage is one of the useful tool, until the availability of better and effective Leprosy vaccine for Leprosy protection. Further in BCG vaccinated leprosy group previous BCG vaccination was not appeared to have effect on disease evolution with increase age, so some uniform policy needed for adult BCG vaccination for Leprosy.

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