INFECTIOUS DISEASES (BACTERIAL, FUNGAL, VIRAL, PARASITIC, INFESTATIONS)

EVALUATION OF POLYMORPHISM OF TLR1, TLR2, TLR4, NRAMP, TAP1 AND TAP2 AS MARKERS OF HOST-SUSCEPTIBILITY IN LEPROSY: MOLECULAR EPIDEMIOLOGICAL STUDY IN HIGH ANCDR DISTRICT IN EASTERN INDIA

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Introduction: In post-elimination era, certain pockets in Eastern India still exist with high ANCDR despite continuing anti-leprosy programmes.

Objective: To assess TLR1, TLR2, TLR4, NRAMP, TAP1 and TAP2 polymorphism in patients of leprosy in high ANCDR areas as a measure of host-susceptibility and to compare with genetically linked and non-genetically linked controls from the same community in the study area.

Materials and Methods: Cross-sectional molecular epidemiological field-study on all leprosy cases residing in 4 specified blocks as present in monthly field camps alongwith their appropriate controls, after obtaining informed consent. Cases were confirmed by clinico-histopathological correlations and blood samples were collected. Restriction Fragment Length Polymorphism (RFLP) was done to assess Single Nucleotide Polymorphisms (SNPs) within TLR1(I602S), TLR2(Arg753Gln, Arg677Trp), TLR4(Asp299Gly, Thr399Ile), NRAMP(3-UTR', allele TGTG+), TAP1(A/G exon10) and TAP2(Ala665Thr).

Results: Study population comprised of 161 cases(mean age=36.34±13.96years,M:F=1:1.2) with 135 genetically-linked controls(mean age=28.522±16.813years,M:F=1:1.4) and 124 non-genetically-linked controls(mean age=34.919±12.454 years,M:F=2.1:1) with majority (76%) in tuberculoid spectrum. For TLR1 SNPs, 9/161(6%) cases showed allele length at 129bp and 151bp, suggestive of 602S allele which was absent in control groups. The 602I allele was found in 152/161(94%) cases when compared to controls (100%) (P<0.001, Fischer's exact test). 35/161(21.7%) patients with leprosy showed heterozygous genotype (Aspartic Acid (A)/Glycine (G)) for TAP1. Remaining 78.3% patients and 100% control had homozygous AA genotype (P<0.001, Fischer's exact test). The Hardy-Weinberg equilibrium was not consistent with TAP1 (p=0.122). No Polymorphism was seen for TLR2, TLR4, NRAMP1 and TAP2 for the tested SNPs in either cases or controls. No association was found with TLR1/TAP1 SNPs with leprosy spectrum.

Conclusion: Contrary to previous reports, allele 602S of TLR1 was not found to have protective role in leprosy. Heterozygous AG genotype of TAP1 was found to be significantly associated with leprosy. Further studies are needed to probe other genetic factors as host-susceptibility markers.