CONCLUSIONS

The present study mainly deals with the evaluation of oxidative stress, autoimmune and neurochemical hypotheses in Gujarat vitiligo patients compared to controls, where the prevalence of vitiligo is alarmingly high. Our results on oxidative stress hypothesis showed that patients of different age groups and different clinical types of vitiligo exhibited significant increase in oxidative stress compared to controls. However there were minor changes observed in the antioxidant status among different clinical types of vitiligo. No significant differences were observed in the antioxidant status between active and stable vitiligo. This study showed impairment in the systemic antioxidant system resulting in oxidative stress in all types of vitiligo. Thus, systemic oxidative stress may have a pathophysiological role in precipitation of vitiligo in Gujarat population.

Based on our biochemical results we selected catalase and glutathione peroxidase as the candidate genes for genetic association studies. The well-documented two SNPs i.e. *CAT* exon 9 T/C in vitiligo, and *GPX* exon 2 C/T polymorphism in cancer were analyzed in Gujarat population. Our results showed that the *CAT* exon 9 T/C and *GPX* exon 2 C/T polymorphisms may not be associated with Gujarat vitiligo patients and suggest for the presence of novel SNPs in Gujarat vitiligo patients.

Increased oxidative stress in Gujarat vitiligo patients could be because of significant increase in SOD 1 activity. We monitored whether the higher SOD 1 activity obtained in vitiligo patients was due to the increased amount of SOD1 protein content. Our SOD 1 western hybridization results suggested that increased SOD1 activity in vitiligo patients was not due to increase in the SOD1 protein levels suggesting for the presence of SNP/s in the *SOD1* gene, which could enhance the SOD 1 activity.

Our results on autoimmune hypothesis showed that all age groups and clinical types of vitiligo showed significant increase in the antimelanocyte antibody levels compared to controls. Vitiligo patients showed a prominent band of approximately 200 kDa melanocyte surface protein in the western blot

analysis, which might be playing a major role in the pathogenesis of vitiligo in Gujarat population.

Our results on neurochemical hypothesis showed a significant decrease in acetylcholine esterase activity in vitiligo patients compared to controls. The decrease in acetylcholine esterase activity might be due H_2O_2 mediated oxidation of AChE, thus emphasizing the role of oxidative stress in precipitating vitiligo in Gujarat population.

Overall, this study shows that oxidative stress plays a major role in the precipitation of vitiligo in Gujarat population. The evaluation of oxidative stress and autoimmune hypotheses in patients at the onset of vitiligo (< 3 months) showed a significant increase in LPO levels but exhibited significant decrease in antimelanocyte antibody levels. These results strongly suggest that oxidative stress is playing a major role in the initiation of disease in Gujarat vitiligo patients. The high levels of oxidative stress generated in Gujarat vitiligo patients may be because of the mutation/s in the *SOD*1 gene, which resulted in its increased activity. The higher oxidative stress may cause H_2O_2 mediated oxidation of AChE and the accumulation of acetylcholine may aggravate the process of depigmentation in vitiligo, thus emphasizing the role of oxidative stress in precipitating vitiligo. Oxidative stress could also result in the destruction of melanocytes and the melanocyte proteins thus released could act as antigens for the formation of antimelanocyte antibodies. Antimelanocyte antibodies thus formed could also destroy melanocytes by complement mediated cytotoxicity and antibody dependent cellular cytotoxicity, which might lead to the progression of the disease.