CHAPTER V

SUMMARY & CONCLUSION
Summary and conclusion

In the present study 134 subjects with muscular dystrophy (MDs) symptoms along with age-sex matched ninety healthy controls were incorporated. Subjects were classified into five major groups based upon the clinical condition, symptoms and provisional diagnosis which include DMD (94, 70.15%), BMD (14, 10.45%), carrier for D/BMD (20, 14.93%), LGMD (3, 2.24%) and SMA (3, 2.24%).

In the study clinical manifestations associated with D/BMD subjects include Gower’s sign, calf hypertrophy, scoliosis and state of ambulation indices. These marker signs were found enormous value to distinguish the condition as well severity of patients. Pedigree analysis, especially a maternal pedigree examination was found to be a monumental importance to identify individual at high risk who require specific consideration as well as evaluating the family members and to offer proper genetic counseling. In the study out of 108 D/BMD, 16 cases had a positive family history with 21 innate cases. Only single case with consanguineous marriage was observed.

Significantly increased levels of serum creatine phosphokinase (CPK), myoglobin (Mb) and lactate dehydrogenase (LDH) were observed in subjects with D/BMD compare to controls which might be due to absence or truncation of dystrophin; leading to disruption of myocyte organization that may result in an abnormal egress of these muscle components. It is also suggested that these biochemical profile can be used as an adjunct parameters in the screening cum diagnosis, prognosis and management of D/BMD patients when molecular study is not available or fails. Further the level of serum Ca (calcium) was found significantly decreased in DMD still in references range. This could be the result of reduced efflux and/or progressive elimination of dystrophic muscle fibers.
in patients. Though serum Ca level may not have potential diagnostic value, it may be useful for better management as well as understanding pathophysiology of the condition. In our study, the amplification of DMD gene was performed for 26 exons for detecting the deletion characteristics. In a total of 108, 71.30% patients had deletion of one or more exons in DMD gene. Out of these 90.90% DMD and 9.10% BMD were confirmed by M-PCR assay. In Gujarat population, the highest deletion rate was the del 45 (10.39%) followed by del 45-52 (9.10%) among DMD probands, out of total 33 observed deletions. One of the longest deletion includes exon 3-44 was found in clinically BMD proband. In the exonic study, exon 50 (50.65%) was one of the most frequently observed deletion found in our study. In all DMD gene mutation pattern deletions started with exon 45 were seen in 27.27%, which is as common. Further, M-PCR (26 exons) failed to identify duplication as well as deletion outside the selected hotspot region of DMD gene. This included 28.70% patients who were clinically confirmed as D/BMD.

Seventy seven (77) patients in our study had deletion mutation, of which 88.31% as OUT-frame and 5.19% IN-frame deletion pattern were found conforming to the reading frame rule. Only one proband with exceptional del 41-43 as OUT-frame mutation was found though clinically corresponded to BMD type. Only 6.49% deletion mutations could not be classified as either IN-/OUT-frame deletion due to lack of flanking exons in the study.

In the comparative indices, a significant correlation among serum CPK, Mb and LDH levels was found. In this study we also compared biochemical parameters with the proband’s age and their deletion pattern separately. Data revealed that these biochemical levels were gradually decreased with advancing age. It might be a result of the
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progressive elimination of dystrophic muscle fibers. Further the data also indicated there
was no significant correlation of elevation of these biochemical profiles with the gene
deletion pattern, severity as well as disease progression. A total 20 carrier females were
also analyzed where 90.00% carrier females had elevated serum CPK levels compared to
healthy controls.

Study also included health inequalities of D/BMD patients in connection with
socioeconomic position (SEP). It is found that brutality of disorders were more likely to
be found among patients with low SEP as well in lower educate family; might be due to
short of unique facility and facts regarding the condition. In our study, LGMD subjects;
serum CPK, Mb and LDH levels were high while in SMA only serum LDH enigmatically
elevates when compared to their respective reference ranges.

Genetic counseling was offered for all the subjects according to their clinical
manifestation; addition with studied investigation results. Familial D/BMD cases; were
advised to get further test viz. MLPA for sibs and other members especially of maternal
side.

**In conclusion**, our study thus opens new areas for potential research in DMD and BMD
patients of Gujarat population and strongly emphasizes the need for further investigation
into the genotype/phenotype aspects of these patents in order to provide better diagnostic,
prognostic, prenatal services and counseling to the suffering families by add-in of next
generation techniques such as MLPA, exome sequencing and arrayCGH. Thus, this study
provides a basis for a survey of these patients in Gujarat state.
Future lines of work

- The present study revealed the significance of molecular analysis of DMD and BMD patients in Gujarat population, India. In addition the clinical as well biomarkers will enable an early screening cum diagnosis and better management of the conditions.

- Further studies are required to validate the diagnostic efficacy of the studied parameters, likewise to investigate the molecular mechanism and also whole gene analysis for understanding the proper pathogenesis of the disease.

- This area also needs a large cohort with high resolution next-generation modus operandi to help in early diagnosis and to screen individuals at high risk for the disease, who could be benefited from early clinical management and for promoting new approaches for therapeutic developments.

- All maternal females of positive familial cases need to be analyses for carrier detection.

- Further studies are recommended to elucidate the underlying variations of genetic expressivity in the D/BMD patients. Additionally proteome profiles are warranted to uncover a correlation with the same.

- Selective segregation of DMD and BMD patients need to be done.

- Demographic studies need to be done in other states of India for better understanding of etiology along with distribution of the disease.

- Moreover D/BMD registry for Indian population need to be build up to obtain accurate burden of the condition.