INVITED COMMENTARY

Duchenne Muscular Dystrophy – Renewed Enthusiasm as We Enter the Era of Therapeutics!

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From the first descriptions of the disease in 1830s by physicians, Giovanni Semmola and Gaetano Conte, and a full clinical narrative by Dr. Guillaume BB Duchenne in 1861, Duchenne Muscular Dystrophy (DMD) has found a consistent reference in the literature as a progressive debilitating muscular disorder [1]. The notable Gower sign was first described in 1879. The interest in the disorder grew with discovery of the Dystrophin gene in 1986, after which not only was the genetic diagnosis made possible, but also prenatal diagnosis became feasible.

Since the turn of the century, and more recently in the last decade or so, there is a renewed enthusiasm regarding the disorder, with optimism shining in view of the current and proposed treatments that are fast becoming available [2]. Alongside the therapeutics, there are now efforts to perform carrier screening as well as newborn screening in general population on research basis [3,4].

Riding high on this enthusiasm, the paper by Singh et al comes at an opportune time, informing us of the enormity of the situation closer home [5]. Singh et al describe clinical and molecular profile of DMD from case records of population from eastern Uttar Pradesh. The authors provide an account of 112 boys presenting in the first decade with progressive proximal muscle weakness. A lag in diagnosis of 30 months (mean age of onset of symptoms and diagnosis being 60 and 90 months, respectively) is notable, and leaves a ground for improvement, as early diagnosis and initiation of therapies, including physiotherapy as well as steroid therapy has proven efficacious beyond doubt [2]. A fifth of the families already had another individual affected with the disorder (either maternal uncle or brother), which emphasizes the need for increasing awareness among families for preventive measures and early diagnosis.

However, there are a few concerns regarding the diagnostic yield provided in the study. The study recorded the highest percentage of deletions (94.59%) in DMD. This statement holds true only if we consider the copy number variants including deletions as well as duplications of single or multiple exons in the gene. This leaves out 20-30% of boys whose DMD would be due to a sequence error, requiring next generation sequencing, which was not part of the study. Deletions or duplications are typically noted in 70-80% of DMD boys, leaving the rest with sequence variants [6].

A confirmed diagnosis provides many benefits to the family, helping to streamline the treatment of the patient with timely and appropriate steroid and supportive treatment. It also benefits female relatives, who would be eligible for testing for carrier status. Ultimately, the specific genetic defect will open the doors for treatment as exon skipping therapy is dependent upon the extent and boundaries of exon deletion/duplications.

Overall, the article has brought forth the discussion on rare genetic disorders like DMD as we pin our hopes and aspirations upon researchers in bringing more robust treatments on to the table. The possibility of these newer treatments to reach the average Indian is not far away, thanks to the recently introduced National Policy on Rare Diseases (NPRD). With a strong political will, hard work and dedication by doctors and families of DMD warriors, this will soon see the light of the day.

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