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Genotype–phenotype associations in Charcot-Marie-Tooth disease

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Background

Charcot-Marie-Tooth (CMT) disease is the most common inherited neurological disorder and affects peripheral nervous system. Disease is caused by mutations in more than 80 genes and most patients have a “classical” CMT phenotype characterized by onset in the first two decades of life, distal weakness, sensory loss, foot deformities (*pes cavus* and hammer toes), and absent ankle reflexes. However, the frequency of these disease manifestations and the variability between CMT types is poorly understood.

Aim

The goal of the study was to evaluate clinical phenotype differences in three CMT subtypes – CMT1A, CMTX1 and other CMT type.

Methods

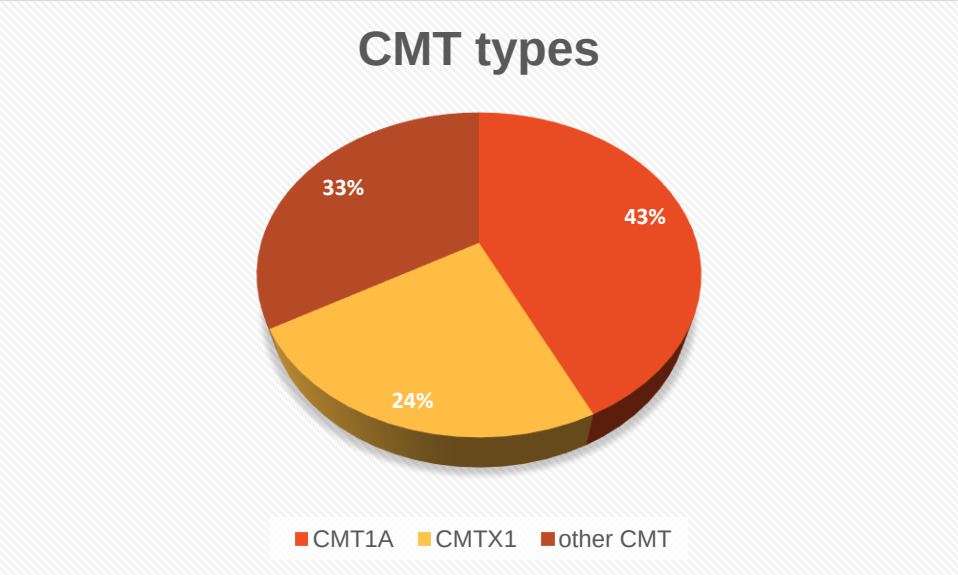
21 CMT patients were enrolled in the study. Patients completed a sociodemographic questionnaire. Clinical severity was assessed using the Charcot-Marie-Tooth neuropathy score (CMTNSv2) and 6-minute walk distance (6MWD).

Results

In our study group, (n=21) the mean age was 37.3±12.5 years, there was a slight female predominance: 62% (n=13) were females, and 38% (n=8) were males.

The majority of patients 42.9% (n=9) had CMT1A type, 23.8% (n=5) had CMTX1 type and 33.3% (n=7) had other CMT type.

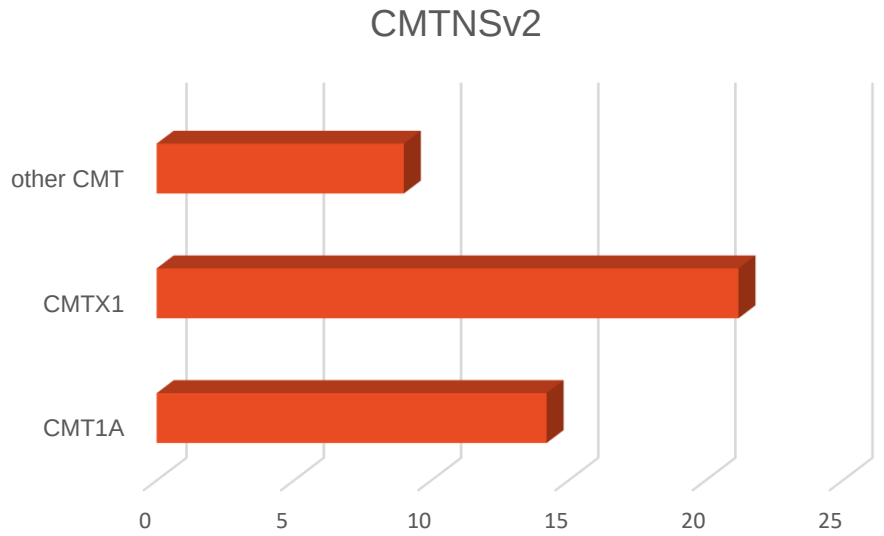
The mean age of first symptom development in CMTX1 type was 11.6±4.9 years, it was earlier in CMT1A patients (10.8±4.7 years), and later in other CMT type patients (12.4±6.5 years).

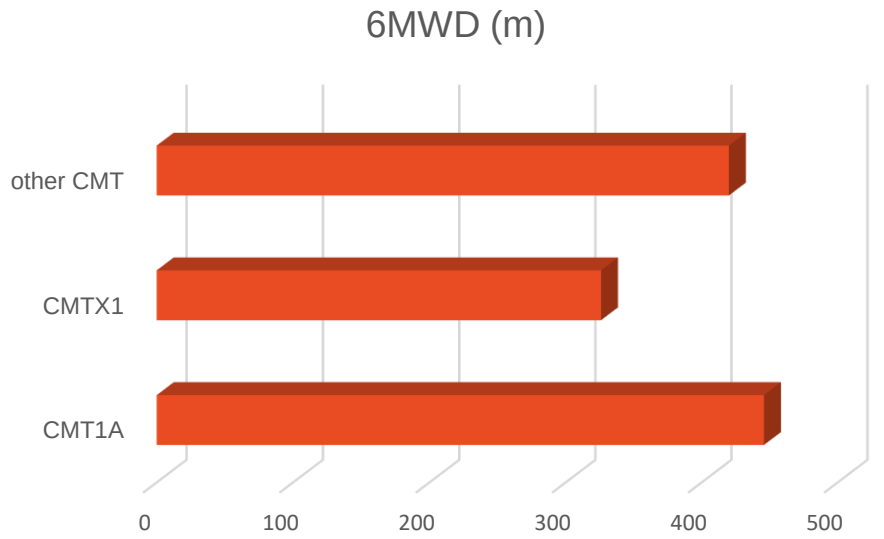


Results

CMTNSv2 revealed more severe clinical phenotype in CMTX1 type patients (21.2±7.6), in CMT1A group it was 14.2±3.8 and for other CMT types – 9.0±9.1, differences were statistically significant ($p<0.05$).

The shortest 6MWD was in CMTX1 type group (326.0±114.6 m), it was 445.8±59.8 m in CMT1A group and 420.0±139.4 m in other CMT types, differences were statistically significant ($p<0.05$).





Conclusion

CMTX1 type patients had a significantly more severe clinical phenotype compared to CMT1A and other CMT type assessed by CMTNSv2 and 6MWD.

Further characterising of the variability of disease severity between CMT types is important to increase genotype-phenotype