Fabry disease (FD) is an X-linked inherited lysosomal storage disorder that results from mutations in the alpha-galactosidase A gene (GLA), leading to deficient alpha-galactosidase A (alpha-GaLA) activity and subsequent accumulation of globotriaosylceramide (Gb3) in a variety of tissues. The estimated prevalence of classic FD in males ranges from 1:8000 to 1:117,000, likely an underestimation given its non-specific manifestations. The mutation IVS4 +919G>A (c.936 +919G>A) associated with founder effect in East Asia was first described in Taiwan. Left ventricular hypertrophy (LVH) is a hallmark of the later-onset cardiac variant of FD. The prevalence of FD among adult patients with LVH is unknown. In an ongoing FD screening programme from August 2017 to 2018, we measured plasma alpha-GaLA activity using dried blood spot testing in 143 consecutive male patients with LVH (defined as maximal LV wall thickness ≥13 mm on echocardiography). Patients with low alpha-GaLA activity underwent GLEA gene sequencing analysis and endomyocardial biopsy. Four of 143 patients with LVH (2.8%) had low plasma alpha-GaLA activity (0.4±0.2 μmol/L wb/hr; 3%-15% of the mean in normal controls). All 4 unrelated patients (aged 53-74 years) shared the same IVS4 +919G>A mutation with maximal LV wall thickness ranging from 14-29 mm. None had extracardiac manifestations but presented with hypertrophic cardiomyopathy, hypertension, heart failure, or aortic stenosis. Endomyocardial biopsy performed in one patient showed hypertrophic cardiomyocytes with sarcoplasmic vacuolisation. Our results suggest that FD should be considered as a cause of LVH in adult men even when other more usual causes of LVH are present.

REFERENCES

EMPIROLOGY OF HEART FAILURE IN SOUTH ASIA
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South Asia has seen rapid epidemiological transition in the last two decades with a rapid rise in cardiovascular diseases, which have emerged as the leading cause of mortality in this region. In India the leading cause of disability adjusted life years is ischaemic heart disease which has seen a 104% increase between 1990 and 2016. Similarly the burden of obesity, hypertension and diabetes mellitus has increased markedly over this time and with poor control rates for these risk factors leading to a fertile soil for rise in incidence of heart failure. In the absence of active surveillance mechanisms reliable estimates of heart failure burden is missing. However, one study estimates it to the tune of 4.6 million which is probably a severe under-estimate given the risk factor burden. The study of the heart failure patients in two large registries, INTER-CHF and Trivandrum Heart Failure Registry, revealed disturbingly high mortality rates of 23% and 31%, respectively. This was much higher than that of patients from other low and middle income countries. The chief driver of this mortality seems to be suboptimal medical management of these patients with a large percentage not receiving beta-blockers and renin-angiotensin aldosterone inhibitors; drugs known to improve survival. Thus, quality improvement program using guideline-directed medical therapy will go a long way in improving survival of these patients.