InsG791 mutation in cardiac myosin-binding protein C (MYBC3) gene: clinical characteristics in the Mennonite pediatric population, Manitoba, Canada

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Objective: Hypertrophic cardiomyopathy (HCM) is a common genetic and markedly heterogenous disease often associated with sudden cardiac arrest/death among young, otherwise healthy people. It is caused by more than 1400 pathogenic mutations in one of at least 11 genes encoding sarcomere proteins[1]. A unique mutation, InsG791, in the gene for cardiac myosin-binding protein C (MYBC3), is found to be responsible for cases of familial HCM among the Mennonite community population in the Province of Manitoba. Therefore, we are interested in conducting a study to determine some of the clinical characteristics of this unique mutation identified in Mennonite children living in our province.

Methods-Results: Retrospective study includes 35 Mennonite children (M:16, F:19), aged between 0-18 years, carrying identical mutations (InsG791) in the gene MYBC3 and managed at the Variety Children’s Heart Centre, Winnipeg, Manitoba. First echocardiogram was performed at median age 9.4 years (0.42-17.17). Five (5) were diagnosed with HCM in the form of septal hypertrophy on echocardiography. Incidental findings include Bicuspid Aortic Valve, small VSD and mild Pulmonic Valve stenosis in 3 non-HCM patients. All of the participants in this study remained asymptomatic throughout a median follow-up period of 7.5 years. No deaths were reported.

Conclusion: InsG791 mutation in the MYBC3 gene, identified in Manitoba’s Mennonite pediatric population, appears to be associated with, later age of onset of the disease and better survival, in contrast to other FHC mutations. Half of the Canadian Mennonite population resides in the Province of Manitoba. As we have shown in a previous study, Mennonite pediatric population contributes approximately for 81% the of the total reported pediatric HCM cases in the Province of Manitoba[2]. Therefore, we believe that it could have implications on diagnostic considerations and screening strategies for the children with this unique mutation in our province.