Expanding Horizons in Familial Hypercholesterolemia: Insights and Implications for Healthcare Professionals

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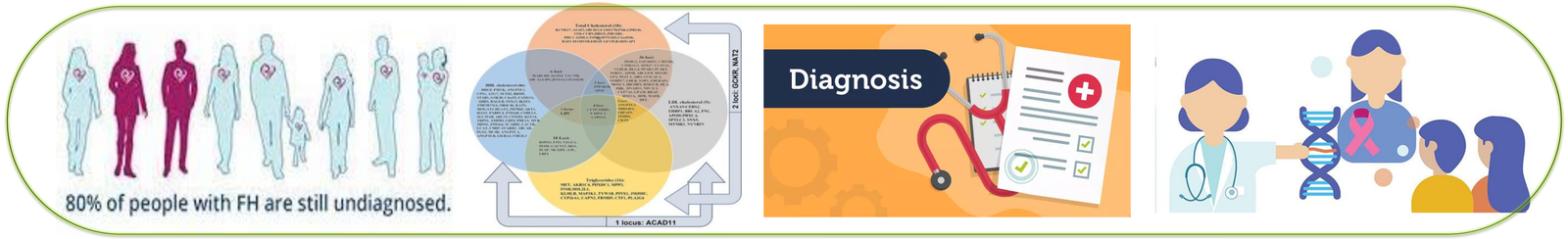
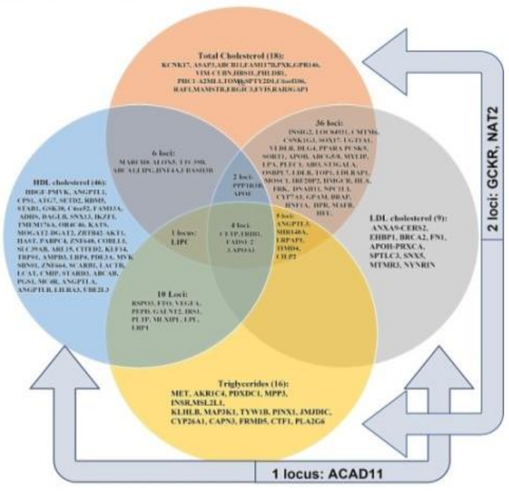
Abstract



Rationale

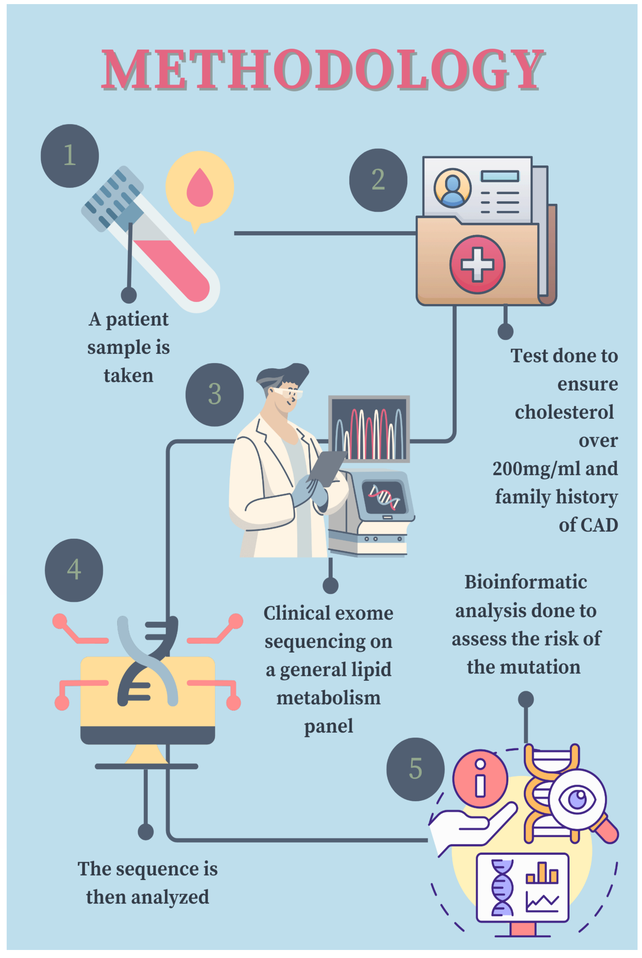
Familial hypercholesterolemia (FH) is a genetic disorder characterized by elevated cholesterol levels, increasing the risk of cardiovascular diseases. In the Indian population, conventional genetic testing for FH, focusing on mutations in major genes such as LDLR, APOB, and PCSK9, has often yielded negative results.

As there are no proper diagnostic methods and only handful of studies have been done in FH in India, we could not identify the recurrent mutations involved in FH in Indian population.



However, recent studies, including our own, have identified novel variations in non-classical genes not previously associated with FH. These findings suggest the presence of unique genetic variations in the Indian demographic, underscoring the need for a broader genetic investigation in FH research.

Methods

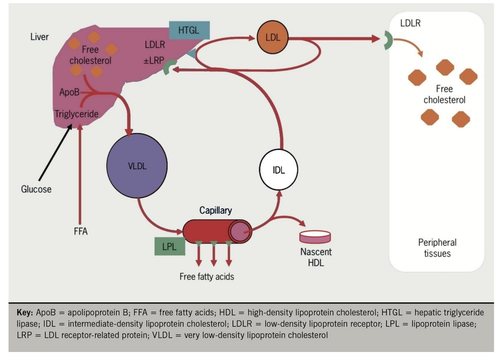


Results

We found some significant variations in "Other" genes such as

- **LDLRAP1**
- **LPA**
- **ALOX5**
- **LRP1**
- **LRP2**
- **LRP8**

LRP2 (Low-Density Lipoprotein Receptor-Related Protein 2): Often referred to as megalin, LRP2 plays a major role in endocytosis of lipids in kidney



Adapted from Lipids module 1: lipid metabolism and its role in atherosclerosis

LRP4 (Low-Density Lipoprotein Receptor-Related Protein 4): LRP4 plays indirect roles in metabolic regulation but is essential for the development of neuromuscular junctions and Wnt signaling. LRP8, sometimes referred to as ApoER2, has a role in lipoprotein absorption and lipid metabolism within cells.

Future directions

Clinicians and Genetic counsellors play a crucial role in this evolving landscape, helping patients understand their genetic risks and the implications of new findings. They will need to stay abreast of the latest research and methodologies to provide informed guidance. Integrating these novel genetic insights into clinical practice will improve the management of FH, offering more precise and effective interventions for affected individuals in the Indian population and beyond

References

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2.Ye, Y., Li, K., Liu, J., Li, M., Wang, W., Wang, R., Yuan, Z. (2013). Dysfunctional co-expression network analysis of familial hypercholesterolemia. J Cardiol, 62(1), 58-62.