IOCCR 2025 Conference
The 1st International Online Conference on Clinical Reports
19–20 March 2025 | Online
MDPI

Association BetweenTFR2 Gene Variant rs7385804 and Hemochromatosis and Its Role in Iron-Related Carcinogenesis in Pakistani Population

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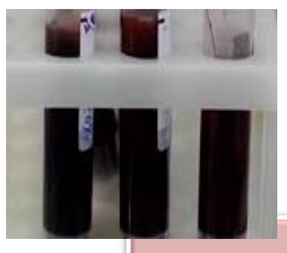
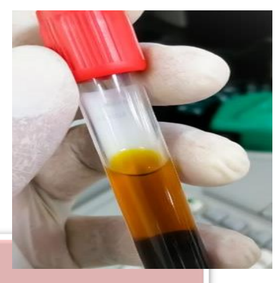
INTRODUCTION & AIM

Hemochromatosis (HH) is a hereditary disorder characterized by excessive iron accumulation in the body, primarily affecting the liver, heart, and pancreas. While extensively studied in European populations, its genetic prevalence in South Asia remains underexplored. The most common mutation, C282Y in the HFE gene, is rare in South Asians, whereas H63D and S65C mutations occur at higher frequencies. Environmental and dietary factors may also influence iron overload in this region. This systematic review aims to assess the prevalence and distribution of HH-related genetic mutations in South Asian populations (India, Pakistan, Bangladesh, Nepal, and Sri Lanka). By synthesizing existing research, we seek to enhance understanding of the epidemiology, genetic variations, and potential diagnostic gaps in HH within this diverse region. Findings from this review will contribute to improving diagnostic strategies, guiding public health interventions, and informing genetic research to optimize HH management in South Asia. Early detection and targeted healthcare strategies can mitigate severe complications such as liver cirrhosis, diabetes, and cardiovascular diseases.

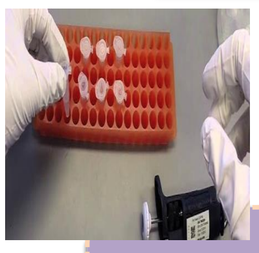
METHOD



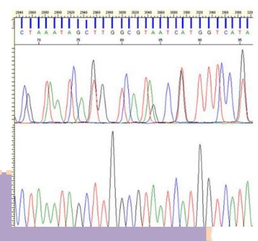
Blood/Sample Collection



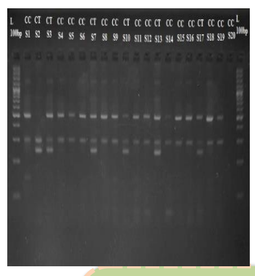
DNA Extraction



Procedure of DNA Extraction by organic method



Sanger's Sequencing



Gel Electrophoresis

Polymerase chain Reaction

RESULTS & DISCUSSION

Figure 1. (**a**)Genomic DNA on 1% agarose gel; Well No. 1 contains standard DNA samples (St) at 20 ng/20 µL, and Wells No. 2-201 contain DNA samples (S1-S200) from case and control samples. (**b**)Electropherogram showing DNA sequencing results for SNP rs7385804 in the TFR2 gene. The peaks represent nucleotide bases (adenine, thymine, cytosine, and guanine) detected in the sequence.

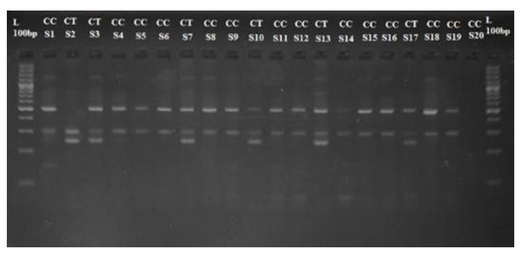
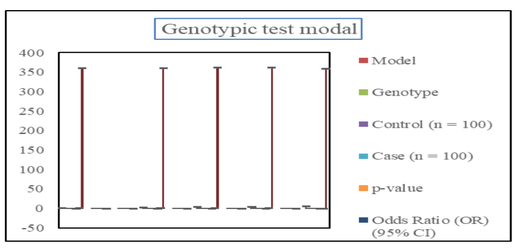


Figure 2. (**a**) The PCR products are compared with the DNA ladder (L), with the optimal amplification observed at a 1:1 primer ratio and an annealing temperature of 60°C. (**b**)TETRA-ARMS PCR amplification of TFR2 gene variant rs7385804 on a 2% agarose gel. The main PCR product size is 490bp, with the reference C allele at 298 bp and the mutant T allele at 248bp



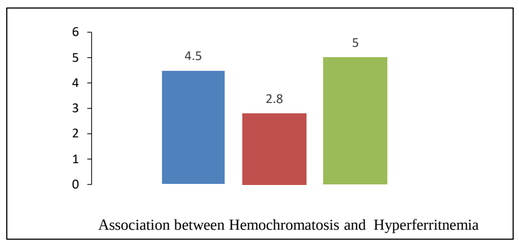


Figure 4.(**a**) Frequencies of TFR2 in case and control (**b**)Association between Hemochromatosis and Hyperferritnemia

Discussion

This study identified a significant association between the rs7385804 SNP in TFR2 and hemochromatosis in a South Asian population, with the Log-additive model being the strongest predictor (OR = 2.34, p = 0.0013). The C/T genotype showed the highest risk, suggesting heterozygosity plays a key role in disease susceptibility. Functional implications indicate that rs7385804 may influence TFR2 expression and hepcidin regulation, contributing to iron overload. These findings emphasize the need for genetic screening to enable early diagnosis and intervention.

CONCLUSION

This study's results suggest a very significant association between the SNP rs7385804 in the TFR2 gene and the risk of hemochromatosis in a South Asian population. The results clearly highlight the significance of heterozygous genotypes and propose that the Log-additive model is the best predictor of the risk of developing disease. The present findings could lay a platform for further studies to understand genetic and molecular mechanisms in the case of hemochromatosis, which has a potential effect on improving diagnostic and management approaches.

FUTURE WORK / REFERENCES

- ❑ Whole-genome sequencing to identify additional risk variants.
- ❑ Longitudinal studies to track disease progression in individuals with risk genotypes.

1. Adams PC, Reboussin DM, Barton JC, McLaren CE, Eckfeldt JH, McLaren GD, et al. Hemochromatosis and iron-overload screening in a racially diverse population. New England Journal of Medicine. 2005;352(17):1769-78.
2. Kanwar P, Kowdley KV. Diagnosis and treatment of hereditary hemochromatosis: an update. Expert review of gastroenterology & hepatology. 2013;7(6):517-30.
3. Fernandes A, Preza GC, Phung Y, De Domenico I, Kaplan J, Ganz T, et al. The molecular basis of hepcidin-resistant hereditary hemochromatosis. Blood, The Journal of the American Society of Hematology. 2009;114(2):437-43.