Common Genetic Variants of the NBN Gene Associated With Risk and Survival in Pakistani Acute Lymphoblastic Leukemia Patients

A.Naveed[1], K.Nawab[1], A.Tahir [1], A.Amar[2], K.Qamar[1]

[1]University of Health Sciences, Lahore, Pakistan.
[2]Pakistan Kidney and Liver Institute and Research Center, Lahore, Pakistan

Introduction

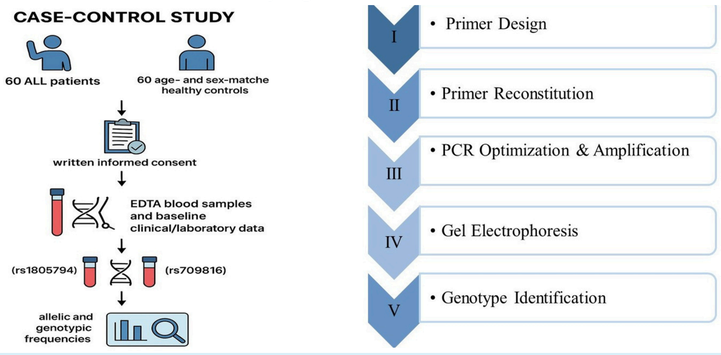
Acute lymphoblastic leukemia (ALL), a common childhood cancer characterized by uncontrolled lymphoblast proliferation, has been linked to DNA damage from ionizing radiation and chemotherapy, with SNPs in the DNA repair gene NBN—which encodes the double-strand break repair protein nibrin—potentially serving as diagnostic and prognostic biomarkers.[1,2,3]

Objective

This study was conducted to determine the association of NBN SNPs (rs1805794 and rs709816) with risk and clinical outcomes in ALL patients of Pakistani origin.

Methodology

This case-control study included 60 ALL patients and 60 age- and sex-matched healthy controls recruited from Jinnah Hospital, Lahore, over 1 year. After obtaining written informed consent, EDTA blood samples and baseline clinical/laboratory data were collected from newly diagnosed ALL patients. Following DNA extractions, genotyping of the target NBN SNPs was done by custom-designed PCR-restriction fragment length polymorphism (rs1805794) and amplification refractory mutation system (rs709816) assays. The allelic and genotypic frequencies of the NBN rs1805794 and NBN rs709816 SNPs were compared between patients and controls as well as among patient subgroups to determine their diagnostic and prognostic potential using SNPStats, SPSS, and GraphPad Prism statistical analysis tools. P-values of ≤0.05 were considered statistically significant.



Results

The median age of the ALL patients was 14 (IQR, 12) years, and 73.8% were male. Diagnostically, risk allele (G) of the NBN rs1805794 SNP was found to be more prevalent among ALL patients (60%) compared with healthy controls (42%), reflecting a significant association with ALL risk (OR, 2.07; P=0.007) (Figure 1). Prognostically, the variant (GG) genotype of the NBN rs709816 SNP was significantly associated with longer overall survival of ALL patients (32 months) compared with the GA+AA genotype (7.5 months, P=0.05). However, the NBN target SNPs did not modulate demographic, clinicopathological, laboratory, hematologic, or treatment response characteristics in ALL subgroup analyses (all P>0.05). The results of Cox regression and Kaplan-Meier survival curve analyses rendered CNS involvement, total lymphocyte count of $<50\times10^9$/L, and negative day-29 remission status as additional significant predictors of poor prognosis in ALL patients (all P≤0.05).

Table 01:

Genetic variant	Genotype /Allele	Controls n=60n(%)	Cases n=60n(%)	OR (95%CI)	p-value (corrected)*
NBN Rs1805794 C/G	C/C	23 (38.3%)	10(16.9%)	REFERENT	
	C/G	26 (43.3%)	29(49.1%)	1.41 (0.38-5.28)	0.28
	G/G	11 (18.3%)	20(33.9%)	3.20 (0.69-14.9)	
	C	49 (39%)	69(58%)	REFERENT	0.007
	G	75 (60%)	51(42%)	2.07(1.24-3.45)	
NBN Rs709816 G/A	G/G	10 (16.4%)	4(7.3%)	REFERENT	0.26
	A/G	42 (68.8%)	38(69.1%)	2.46 (0.52-11.6)	
	A/A	9 (14.8%)	13(23.6%)	5.03 (0.69-36.7)	
	G	65 (51%)	46(41%)	REFERENT	0.16
	A	63 (49%)	66(59%)	0.67(0.40-1.12)	

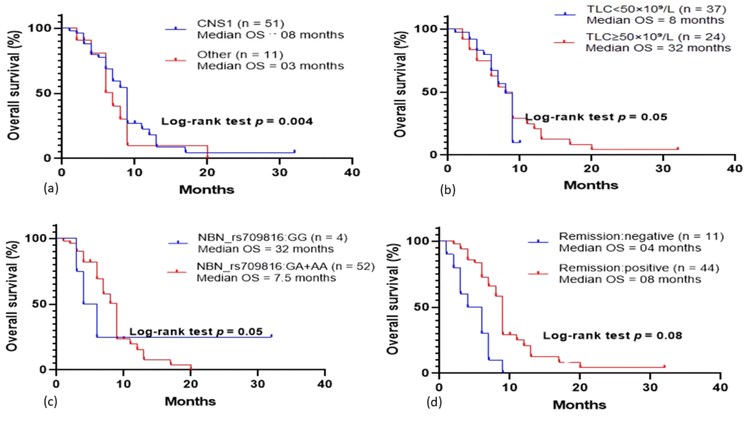


Figure 01:

Conclusion

In conclusion, our results suggest that the NBN rs1805794 and rs709816 SNPs may hold clinical value as potential biomarkers predicting risk and survival, respectively, in Pakistani ALL patients, but have no potential effect on therapeutic response.

References

1. Genetic basis of acute lymphoblastic leukemia, *Journal of Clinical Oncology*
2.Functional and structural insights into the MRX/MRN complex, a key player in recognition and repair of DNA double-strand breaks, *Computational and Structural Biotechnology Journal*
3.Risk of acute lymphoblastic leukemia: Results of a case-control study, *Asian Pacific Journal of Cancer Prevention*

© 2025 Asif Naveed. This poster may be used for educational purpose only. All rights reserved.