GENETIC INSIGHTS INTO β-THALASSEMIA: ASSOCIATION OF *LRP5* AND *VEGF* POLYMORPHISMS WITH SKELETAL AND VASCULAR COMPLICATIONS

B. NAEEM [1], W. NABEEL [1], U.-H. USMANI [1], N. HUSSAIN [1*], H. SAEED [1], N. AL-HOSHANI [2], R.A.EL H. MOHAMED [2], M.F. ELKHADRAGY [2], M.S. ALWETHAYNANI [3], G. NABI [4, *]

[1] Institute of Microbiology and Molecular Genetics, University of the Punjab, Lahore, Pakistan
[2] Department of Biology, College of Sciences, Princess Nourah bint Abdulrahman University, Riyadh, Saudi Arabia
[3] Department of Clinical Laboratory Sciences, College of Applied Medical Sciences, Shaqra University, Alquwayiyah, Riyadh, Saudi Arabia
[4] Department of Zoology, the University of Swat, Khyber Pakhtunkhwa, Swat, Pakistan

E-mail: bismanaeem2311@gmail.com; ummehaniusmani17@gmail.com; wareesha42002@gmail.com; nageen.mmg@pu.edu.pk; saaedhassan687@gmail.com; nialhoshanii@pnu.edu.sa; maalwethynani@su.edu.sa; ghulmnabiqau@gmail.com; rasdiigg@pnu·edu.sa; Mfelkhadragy@pnu.edu.sa

Corresponding author: Hussain N., Nabi C., e-mail:nageen.mmg@pu.edu.pk; ghulamnabiqau@gmail.com

Thalassemia is the most prevalent form of inherited anemia throughout the world. It is estimated by the World Health Organization that approximately 60,000 babies are born with significant thalassemia each year. This study uncovers the role of LRP5 (rs4988321, rs3736228) and VEGF (rs699947) genetic variants as genetic modifiers affecting vascular and skeletal complications by examining their frequency and association in β-thalassemia patients. The T allele of LRP5 gene SNP rs3736228 was more prevalent in patients (66%) than controls (24%) and exhibited strong relationships under different genetic models, confirming its contribution to disturbed Wnt signalling and decreased bone homeostasis. Similarly, patients had a higher prevalence of the A allele of VEGF rs699947 (9%) as compared to that in controls (4%), indicating its role in vascular dysfunction especially iron overload and disease vulnerability. These results highlight the potential of VEGF and LRP5 gene polymorphisms as predictive biomarkers for skeletal and vascular problems associated with thalassemia.

Key words: *β-thalassemia, Wnt signaling, bone homeostasis, angiogenesis, iron overload, predictive biomarker.*

ГЕНЕТИЧНІ ВІДОМОСТІ ПРО β-ТАЛАСЕМІЮ: ЗВ'ЯЗОК ПОЛІМОРФІЗМІВ *LRP5* І *VEGF* ЗІ СКЕЛЕТНИМИ ТА СУДИННИМИ УСКЛАДНЕННЯМИ

Таласемія — це найпоширеніша форма спадкової анемії у всьому світі. За оцінками Всесвітньої організації охорони здоров'я щороку народжується близько 60 000 дітей із значною таласемією. Це дослідження розкриває роль генетичних варіантів *LRP5* (*rs4988321, rs3736228*) та *VEGF* (*rs699947*) як генетичних модифікаторів, що впливають на судинні та скелетні ускладнення, шляхом вивчення їхньої частоти та асоціації у пацієнтів з β-таласемією. Алель Т гена *LRP5 SNP rs3736228* був більш поширений серед пацієнтів (66 %), ніж у контрольній групі (24 %), і демонстрував сильні взаємозв'язки в різних генетичних моделях, що підтверджує його вплив на порушену сигналізацію *Wnt* і знижений гомеостаз кісток. Аналогічно, у пацієнтів була вища поширеність алеля А *VEGF rs699947* (9 %) порівняно з контрольною групою (4 %), що вказує на її роль у судинній дисфункції, особливо в перевантаженні залізом та вразливості до захворювання. Ці результати підкреслюють потенціал поліморфізмів генів *VEGF* та *LRP5* як прогностичних біомаркерів скелетних та судинних проблем, пов'язаних із таласемією.

Ключові слова: β-таласемія, *Wnt*-сигналінг, кістковий гомеостаз, ангіогенез, перевантаження залізом, прогностичний біомаркер.

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