Open Access Letter to the Editor

Sir,

It is an immense pleasure to read the articles published by our national haematologists in our national journal of Haematology, *Journal of Haematology and Stem Cell Research (JHSCR)*. In the coming few minutes, I shall communicate to you regarding an article published with the title "Frequencies of Hemoglobinopathies in Pakistan: A Single Center Study" by Hina Maryam and Badar e Alam in Vol. 5 No. 1 (2025): January-June in *JHSCR*. It is a good study conducted to detect frequencies of haemoglobinopathies in Rawalpindi and I hope that it will be a beacon for future endeavours. But I have few observations which I humbly want to present:

1. My first observation is that 'normal results of 88% referrals' mean that such referrals were not useful for patients. Or in other words, 88% of the test requests were not justified! This may be due to lack of any selection criteria of patients to test them for Haemoglobin Variant Analysis. It is a dilemma to proceed to advanced testing without carefully screening the baseline analyses. *The physicians should be educated about when to screen for Haemoglobinopathy to avoid wastage of resources and time of patients*.

2. My second observation is that although the mentioned study is acceptable for frequencies of haemoglobinopathies among anaemics, it cannot infer about prevalence of haemoglobinopathies because healthy population was not included i.e. it was not based on random selection of population. The impact of this disparity is that the prevalences of different haemoglobinopathies are over-estimated and may not be useful for decision making at governmental level: The Inference should match with the inclusion criteria & the purpose of the study. *If the purpose is to determine prevalence of a disease in a population, random population should be selected, and to avoid over-estimating disease burden, the symptomatic population should not be selectively included.*

3. My third observation is that in the study, the WHO sample size calculator used to determine the sample size, was based on population prevalence of 9.7%. If you give the reference of *Shaikh IA, Zubair R, Siddiqui IA, Ahmad AH, Sheikh U. Hematological Parameters and Demographic Distribution of Hemoglobinopathies and Various Hemoglobin Variants. Cureus. 2022 Dec 29;14(12):e33115. doi: 10.7759/cureus.33115. PMID: 36721613; PMCID: PMC9884327.,* then that study was also flawed by the selection bias according to the principle presented in the 2nd observation. *I would request the authors to cite any valid reference of 9.7% prevalence of haemoglobinopathies upon which the sample size was calculated.*

4. My fourth observation is that it appears that out of 5961 specimens, Haemoglobin Variant Analysis performed on 5254 (88%) specimens revealed no haemoglobinopathy! Which means that either their CBCs were normal or not fit for further screening by HVA. It could have been better if the data in the study included their CBCs as well. If those cases were normal, *which Standard Operating Procedure of proceeding to Haemoglobin Variant Analysis was opted when a person had a normal CBC? And which Standard Operating Procedure of proceeding to Haemoglobin Variant Analysis was opted when a person had anaemia?*

5. My fifth observation is that the list of haemoglobinopathies provided included diagnostic entities as well as clinical ones. *Thalassaemia intermedia could have been elaborated* as this is a clinical diagnosis and not a diagnostic entity per se. There are many haematological diseases under the umbrella of Thalassaemia intermedia eg β Thalassaemia with Coinheritance of α-Thalassaemia, Compound heterozygous with low synthesis variant such as HbE, Homozygous HbE disease, Hereditary persistence of fetal haemoglobin, homozygous δβ Thalassaemia, Gγ XMN1 Polymorphism, unusually severe β Thalassaemia trait and HbH. (1) Furthermore, it was not mentioned that how Thalassaemia intermedia was diagnosed.

6. My sixth observation is that the prevalence of haemoglobinopathies differs in different ethnic groups and regions of Pakistan, as detected by Khattak MF, Saleem M. (2) where they found beta Thalassaemia trait to be higher in NWFP compared to that in Punjab. This has implication on making Provincial policies to prevent Thlassaemia. *It would be better if the authors mentioned the ethnicities and geographical distribution of patients.*

I wish that if the author finds my observations justified then the relevant changes may be made in the text of the article to make this heavy data of 5961 cases more useful.

References

Genetic Haemoglobin Disorders in Pakistan. Suhaib Ahmed. 1st edition. 2018.
2. Khattak MF, Saleem M. Prevalence of heterozygous beta-thalassaemia in the northern areas of Pakistan. JPMA 1992;42:32-4

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