Correspondence

The pattern of fetal hemoglobin changes in patients with malignancy on chemotherapy

To the Editor

We have read with interest the report of Omoti et al[1] and their effort to find association between levels of fetal hemoglobin (HbF), cancer and its response to chemotherapy. This interest in finding such association is old and probably not clinically relevant. The authors' methodology in the reported trial suffered from major problems. The study was designed to have 3 different groups; namely, pre-chemotherapy group, post chemotherapy group and the control group. The testing of the differences in the mean of HbF and hematological values between pre and post chemotherapy should have been performed in the same group to avoid the possibility of detecting differences due to the between-group variation in patients' characteristics, such as, age, stage of the disease, existing medical illness and others. The reported results showed significant differences between the pre-chemotherapy group and post-chemotherapy group in hemoglobin (Hb) and HbF values. The between-group differences in HbF and Hb values were comparable to the within group variations in both pre-chemotherapy and post-chemotherapy groups. This could be contributed to the design and the use of a Mann-Whitney U test, which performs an overall comparison of distributions in the 2 groups, in terms of both shape and location, [2] and does not specifically test for a difference in means. We computed the 95% confidence intervals associated with the mean of HbF and Hb using the t-distribution, since the sample size is large enough and assuming the distribution of HbF and Hb are not very skewed. **Table 1** presents the mean ± SD with the 95% confidence intervals. We observed that there is no gap between the 95% CI associated with the pre-chemotherapy mean and the corresponding one for the post-chemotherapy in each of Hb and HbF values. This point confirms the above comment, that is, the between-group differences could be due to the variation in patients' characteristics similar to what was found in the within-group variation. Additionally, we do not agree with what the authors concluded by stating that the drop in previously high HbF levels may be a useful tool for monitoring response to chemotherapy. We must state that neither the data presented by the authors, nor any prior study can support this conclusion.

Table 1 - Hemoglobin and fetal hemoglobin summary statistics.

Status	Hemoglobin		Fetal Hemoglobin	
	Mean ± SD	95% CI	Mean ± SD	95% CI
Pre-chemotherapy	11.62±2.26	(10.64, 12.6)	1.71±0.7	(1.41, 2.01)
Post-chemotherapy	9.7±2.4	(8.73, 10.67)	1.23±0.5	(1.03, 1.43)

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Reply from the Author

We thank Dr. Hikmat Abdel-Razeq for his keen interest in our work. We differ with his opinion that the association between HbF levels in patients with malignancy and response to chemotherapy is not clinically relevant. There is always an on going effort to identify simple, reliable and possibly affordable ways of monitoring patient response to therapy than existing ones, keeping in mind the needs of resource deficient nations. Our findings are also of clinical value to corroborate the results of other parameters for monitoring response especially where there are conflicting results. We acknowledge that there has been some interest in the subject in the past but there is still a lack of information conclusively supporting or disputing the hypothesis that there is a consistent and predictable drop in HbF levels with chemotherapy. We note that there are various alternative statistical methods for determining differences in numerical outcomes. We agree with the fact that the Mann Whitney U test is a less sensitive tool than the t-test for assessing differences between populations and as such is likely to underestimate the differences between groups.[3] However, considering the strong possibility of skewing of the distribution of the parameters, our choice of the Mann Whitney U test is still valid and the differences noted between the pre- and post- chemotherapy groups stand as reported.[4]

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