COMMENTS AND RESPONSES

Response to Comment on: Hardikar et al. Spuriously High Prevalence of Prediabetes Diagnosed by HbA_{1c} in Young Indians Partly Explained by Hematological Factors and Iron Deficiency Anemia. Diabetes Care 2012;35:797–802

We are grateful to Schindhelm et al. (1) for their interest in our article. We measured HbA_{1c} during follow-up of a birth cohort in the hope of substituting it for an oral glucose tolerance test. We found a discrepancy between the results of the oral glucose tolerance test (World Health Organization, 1999) and HbA_{1c} (American Diabetes Association, 2009): A large number of individuals were classified as having "prediabetes" by HbA_{1c} when considered normal glucose tolerant by oral glucose tolerance test (2). This prompted us to investigate possible causes of this discrepancy. We found that a number of hematological parameters (lower hemoglobin concentration, lower mean corpuscular volume, lower mean corpuscular hemoglobin, and higher red cell distribution width) predicted higher HbA_{1c}. These hematological parameters were indicative of iron deficiency, so we measured serum ferritin concentrations. We found that lower ferritin concentrations also predicted higher HbA_{1c}, supporting an association with iron deficiency. We did not find an association of HbA_{1c} with another nutritional problem, i.e., vitamin B12 deficiency, which is quite common in this population. We searched the literature and found supportive data that HbA_{1c} is elevated in iron deficiency. We admit that our interpretation of previous studies (3,4) about prolonged erythrocyte survival in iron deficiency was not accurate.

Unfortunately, we do not have reticulocyte measurements in our study, nor do we have the expertise to perform the measurements that Schindhelm et al. suggest. We agree that the explanation for elevated HbA_{1c} concentrations in iron deficiency could be more complex than those suggested in the past. We would appreciate if Schindhelm et al. could transfer the technology to us to make relevant measurements.

Irrespective of the possible explanation, the basic findings and conclusions of our study remain valid; i.e., young nondiabetic individuals with iron deficiency have an inappropriately high HbA_{1c} concentration. In a subsequent study of 232 rural adolescents, we found a similar pattern: those with hemoglobin concentrations below 12 g% ($n = 116$) were 45% prediabetic by HbA_{1c} criteria compared with 15.5% in those with hemoglobin concentrations above 12 g% ($P < 0.001$) despite normal glucose tolerance. Use of HbA_{1c} to diagnose prediabetes and diabetes in nutritionally compromised populations might produce misleading estimates of prevalence.

PALLAVI S. HARDIKAR, BMTECH[1]
SUYOG M. JOSHI, MSC[1]
DATTATRAY S. BHAT, MSC[1]
DEEPA A. RAUT, BMTECH[1]
PRACHI A. KATRE, MSC[2]
HIMANGI G. LUBREE, MSC[1]
ABHAY JERE, PHD[2]
ANAND N. PANDIT, MD[3]
CAROLINE H.D. FALL, MB, CHB, DM, FRCP, FRCPH[4]
CHITTARANJAN S. YAJNIK, MD, FRCP[1]

From the [1]Kamalnayan Bajaj Diabetology Research Centre, King Edward Memorial Hospital Research Centre, Pune, India; [2]Persistent Systems Ltd., Pune, India; the [3]Pediatric Department, King Edward Memorial Hospital Research Centre, Pune, India; and the [4]Medical Research Council Lifecourse Epidemiology Unit, University of Southampton, Southampton, U.K.

Corresponding author: Chittaranjan S. Yajnik, diabetes@vsnl.com.

DOI: 10.2337/dc12-1439

Acknowledgments—This study was supported by The Wellcome Trust, London, U.K. (Grant 083460/Z/07/Z) and the Medical Research Council, London, U.K.

No potential conflicts of interest relevant to this article were reported.

The authors are grateful to the study participants for taking part in this study. The authors thank Dr. K.J. Coyaji, medical director of the KEMH, and Dr. V.S. Padbhidri, director, KEMH Research Centre, for providing research facilities. The authors thank P.C. Yajnik, L.V. Ramdas, T.M. Deokar, S.D. Chougule, A.B. Gaikwad, M.L. Hoge, S.N. Khemkar, S.B. Wagh, and B.S. Jadhav from the Diabetes Unit of KEMH Research Centre for their invaluable contribution to the study. The authors also acknowledge the support of Sneha-India.

References

1. Schindhelm RK, Schoorl M, van Pelt J. Comment on: Hardikar et al. Spuriously high prevalence of prediabetes diagnosed by HbA_{1c} in young Indians partly explained by hematological factors and iron deficiency anemia. Diabetes Care 2012;35:797–802 (Letter). Diabetes Care 2013;36:e23. DOI: 10.2337/dc12-1135
2. Hardikar PS, Joshi SM, Bhat DS, et al. Spuriously high prevalence of prediabetes diagnosed by HbA_{1c} in young Indians partly explained by hematological factors and iron deficiency anemia. Diabetes Care 2012;35:797–802
3. Coban E, Ozdogan M, Timuragaoglu A. Effect of iron deficiency anemia on the levels of hemoglobin A1c in nondiabetic patients. Acta Haematol 2004;112:126–128
4. Koga M, Morita S, Saito H, Mukai M, Kasayama S. Association of erythrocyte indices with glycated haemoglobin in premenopausal women. Diabet Med 2007;24:843–847