PEER REVIEW HISTORY

ARTICLE DETAILS

TITLE (PROVISIONAL)	Diabetes and intermediate hyperglycaemia in Kisantu, DR Congo: a cross-sectional prevalence study
AUTHORS	Buntinx, Frank ; Muyer, Muel; Muls, Erik; Mapatano, Mala; Makulo, Jean-Robert; Mvitu, Moise; Kimenyembo, Wivine; Mandja, Bien-Aimé; Kimbondo, Pierre; Bieleli, Chris; Kaimbo wa Kaimbo, Dieudonné

VERSION 1 - REVIEW

REVIEWER	Naomi Levitt Professor and Head Division of Diabetic Medicine and Endocrinology University of Cape Town and Groote Schuur Hospital Director:Chronic Diseases Initiative in Africa (CDIA) J47 Old Main Building Groote Schuur Hospital
REVIEW RETURNED	14-Sep-2012

GENERAL COMMENTS	This is clearly a well designed study that examined the prevalence and risk factors of diabetes mellitus and intermediate hyperglycaemia (IH) in Kisantu, a semi-rural town in Bas-Congo province, DR Congo. Given the paucity of diabetes prevalence data from central Africa, the study had considerable potential relevance in adding to the body of knowledge concerning the burden of diabetes in the region for the academic community, groupings lobbying for appropriate allocation of resources and health planners. The sampling methods were sound and there was an enviable response. The major problem in this reviewer's opinion is that the method used for measuring plasma glucose levels in this study was appropriate for assisting in determining glycaemic control in people with known diabetes and estimating the prevalence of diabetes for health planners, but not for academic studies. This problem could have been minimised had there been some attempt made to measure every 20th/50th sample in a laboratory to validate the capillary glucose method used, such as in the original study of the prevalence of diabetes in Tanzania by McLarty et al, but this was not done. Minor comments: The introduction adequately stated the background and rationale for the study Methods: sampling was appropriate, what method was used to assess alcohol consumption? Why was there a smaller proportion of individuals <50 e –is this because the households sampled had fewer <50s/ -this should be addressed in more detail. Results: Typo line 5 of pt characteristics, in the table the proportion overweight and obese should be added, was bmi also a significant risk factor if replaced waist in multivariate analysis

	There were some surprising results that should receive attention in the discussion: there was a surprisingly high proportion of previously diagnosed cases compared to other studies in subSaharan Africa- why should this be the case? The observation that the OGTT added so few cases of diabetes to those identified by fasting levels alone – is this the same as other studies in the region?t added so few cases of dm I note that HIV/ART was not an exclusion-what is the background prevalence of HIV in the district/proportion on ART – would this have impacted on your data. The finding of a much higher prevalence of IFG based on ADA criteria is expected-what would be the implications of using this lower level for the country

REVIEWER	Prof. Michel P. HERMANS MD PhD DipNatSci DipEarthSci DipGeogEnv PGCert(SocSc) Chef de Clinique Cliniques universitaires St-Luc Bruxelles I declare having no competing interests regarding this MS under revision
REVIEW RETURNED	30-Sep-2012

GENERAL COMMENTS	■ The authors state that the crude prevalence of the present survey may have been influenced by the structure of the study sample that contained relatively few individuals aged < 50 years in whom diabetes tends to be less prevalent; the underrepresentation of (young) men is also a potential confounder, especially on the relationship between (abdominal) obesity and prevalence of glucose homeostasis abnormalities; ■ The authors may further elaborate in the discussion on the unexpected low prevalence of undetected diabetes, which is odd; if due to above-normal level of diabetes care in Kisantu, how to demonstrate this and would it not actually restrict the scope of certain findings to this unique urban experience in the RDC; ■ The authors use the term risk factor for a variable with both a significant independent association with diabetes and a clinical suggestion about the direction of this association; since this is a transversal study, risk markers or another word may be preferable; ■ The authors mention their data suggesting the early stages of a diabetes epidemic in DRC; this comment may only apply to urban populations, still a minority in many parts of SSA, including the RDC; the use of “rural town” for Kisantu may in that respect be misleading; “the even higher prevalence of IDF suggest a large burden of the disease in rural Congo” is not really applicable, since rural Congo was not systematically sampled here; ■ To update the references on diabetes determinants in the RDC, the authors may consider a recent report on age and living in an urban environment as major determinants of diabetes among South Kivu Congolese adults (Katchunga et

	al. Diabetes Metab 2012).

VERSION 1 – AUTHOR RESPONSE

Reviewer: Naomi Levitt

This is clearly a well-designed study that examined the prevalence and risk factors of diabetes mellitus and intermediate hyperglycaemia (IH) in Kisantu, a semi-rural town in Bas-Congo province, DR Congo. Given the paucity of diabetes prevalence data from central Africa, the study had considerable potential relevance in adding to the body of knowledge concerning the burden of diabetes in the region for the academic community, groupings lobbying for appropriate allocation of resources and health planners. The sampling methods were sound and there was an enviable response.

Thank you for the nice comments.

The major problem in this reviewer's opinion is that the method used for measuring plasma glucose levels in this study was appropriate for assisting in determining glycaemic control in people with known diabetes and estimating the prevalence of diabetes for health planners, but not for academic studies. This problem could have been minimised had there been some attempt made to measure every 20th/50th sample in a laboratory to validate the capillary glucose method used, such as in the original study of the prevalence of diabetes in Tanzania by McLarty et al, but this was not done.

We understand the reviewer's comment. A validation of the capillary testing method was not performed, indeed. However, quite some validation of the tests we used has been performed by others before the start of our study. We summarize some of the vast amount of reports in an added paragraph of the second paragraph of the limitations section of the discussion, which now reads: " We did not perform a validation study against venous samples ourselves. However, according to a recent WHO/IDF report [WHO. Definition and diagnosis of diabetes mellitus and intermediate hyperglycaemia. Report of a WHO/IDF consultation. WHO/IDF, Geneve: 2006.], fasting values of both methods are identical. Only postprandial values may differ (recommendation 5). With this device, there is no influence of hematocrite on glucose values within the normoglycaemia range, which is important in screening situations as during our study. [Arens et al, Clin Chem Lab Med 1998,36,47-52] The Glucocard X reports plasma glucose values. Testing showed that reproducibility is good, the device is robust, easy to use and without need of extensive training. [SKUP. Glucocard X-meter, Glucocard X-sensor: report from an evaluation organised by SKUP. Scandinavian evaluation of laboratory equipment for primary health care. University of Bergen, Bergen: 2006.] Additionally, according to the above mentioned WHO/IDF report, separation of plasma within minutes after sampling is required to obtain correct values when sampling venous blood. Even sampling in a container with NaF is not sufficient. Systematic separation would be totally impossible in our study setting"

Additionally, we changed the second item of the separate limitations section, which now reads: "We had to use (low-cost) capillary blood measures instead of venous samples processed in a laboratory, and did not formally validate the test characteristics ourselves."

Minor comments:

The introduction adequately stated the background and rationale for the study

Thanks

Methods: sampling was appropriate,
what method was used to assess alcohol consumption?

We asked people if they used alcohol (yes, never, stopped) and how many glasses each week. If they had stopped using alcohol, we registered since how many months. For the analysis, this was categorized as either current alcohol consumption or not (see methods section)

Why was there a smaller proportion of individuals <50 e –is this because the households sampled had fewer <50s/ -this should be addressed in more detail.

Reasons for the low proportion <50s can be on four levels: young (especially male) people died more frequently than average during the troubles in RDC in the last decennia, they left the region to work in Kinshasa or abroad, they still live in Kisantu but were absent and therefore unable to respond, because of work in the fields, they refused to respond for their own reasons. Without engaging in sociological research, we assume that the under-representation in our group is mostly due to the second and third reason. These reasons are discussed in the discussion section. We added a sentence referring to possible consequences of this under-representation: “As young men tend to be less obese, this under-representation may influence the crude – be it not the standardized – prevalence rate of diabetes and IH.”

Results: Typo line 5 of pt characteristics, in the table the proportion overweight and obese should be added, was bmi also a significant risk factor if replaced waist in multivariate analysis

This was corrected. Thanks

There were some surprising results that should receive attention in the discussion: there was a surprisingly high proportion of previously diagnosed cases compared to other studies in subSaharan Africa-why should this be the case?

The reviewer is correct that the percentage of previously known cases of diabetes is higher than found elsewhere (see Peer N, et al. Rising diabetes prevalence among urban-dwelling black South Africans. PLOS one 2012; 7: e43336). There is no evidence that enables us to formally explain this finding. It is tempting, however, to speculate that this is at least partially related to an increased awareness for diabetes in the regional population, following the building of a structured diabetes program in the previous years. This included a dedicated diabetes department within a well-organized regional hospital, sensibilisation programs towards the population, and training courses for diabetes teams. All this was made possible by a collaboration between the World diabetes foundation, the Flemish interuniversity council (VLIR) and the National diabetes programme (‘Le programme national de lutte contre le diabète’) of the Congolese government. Of course, this may influence response rates and the percentage of known cases, but not the total prevalence of diabetes. We added a statement in this sense to the discussion.

The observation that the OGTT added so few cases of diabetes to those identified by fasting levels alone –is this the same as other studies in the region?t added so few cases of dm

We are aware of one study in Angola in which this difference was examined. In that study (much

smaller and with a lower prevalence) five of the 12 cases of diabetes which were identified were diagnosed by OGTT (Evaristo-Neto AD et al. Diabetology & Metabolic Syndrome 2010).

I note that HIV/ART was not an exclusion-what is the background prevalence of HIV in the district/proportion on ART –would this have impacted on your data.

We realise that AIDS survival can be associated with increased Insuline resistance. However, during the data collection period of this study, no structured program of antiviral therapy was available in the Kisantu region. HIV testing was not performed in our study group.

The finding of a much higher prevalence of IFG based on ADA criteria is expected-what would be the implications of using this lower level for the country

In Europe, it has been shown that fasting glucose values between 5.6 and 6.1 mmol/l indicate increased cardiovascular risk. As far as we are aware, such relation has not been identified in an African population. Anyhow, we found a very high prevalence of IFG with both measures, indicating a real challenge for the Congolese national diabetes plan. The latter was added to the last paragraph of the discussion section.

Reviewer: Prof. Michel P. HERMANS

§ The authors state that the crude prevalence of the present survey may have been influenced by the structure of the study sample that contained relatively few individuals aged < 50 years in whom diabetes tends to be less prevalent; the underrepresentation of (young) men is also a potential confounder, especially on the relationship between (abdominal) obesity and prevalence of glucose homeostasis abnormalities;

We agree that the underrepresentation exists for young men especially. This is so discussed in the discussion section. We added: “As young men tend to be less obese, this under-representation may influence the crude – be it not the standardized – prevalence rate of diabetes and IH.”

§ The authors may further elaborate in the discussion on the unexpected low prevalence of undetected diabetes, which is odd; if due to above-normal level of diabetes care in Kisantu, how to demonstrate this and would it not actually restrict the scope of certain findings to this unique urban experience in the RDC;

There is no evidence that enables us to formally explain this finding. It is tempting, however, to speculate that this is at least partially related to an increased awareness for diabetes in the regional population, following the building of a structured diabetes program in the previous years. This included a dedicated diabetes department within a well-organized regional hospital, sensibilisation programs towards the population, and training courses for diabetes teams. All this was made possible by a collaboration between the World diabetes foundation, the Flemish interuniversity council (VLIR) and the National diabetes programme (‘Le programme national de lutte contre le diabète’) of the Congolese government. Of course, this may influence response rates and the percentage of known cases, but not the total prevalence of diabetes. We added a statement in this sense to the discussion.

§ The authors use the term risk factor for a variable with both a significant independent association

with diabetes and a clinical suggestion about the direction of this association; since this is a transversal study, risk markers or another word may be preferable;

We replaced “risk factor” with “risk marker” in the whole paper

§ The authors mention their data suggesting the early stages of a diabetes epidemic in DRC; this comment may only apply to urban populations, still a minority in many parts of SSA, including the RDC; the use of “rural town” for Kisantu may in that respect be misleading; “the even higher prevalence of IDF suggest a large burden of the disease in rural Congo” is not really applicable, since rural Congo was not systematically sampled here;

Indeed, a study published by the reviewer’s group this month indicates a large difference between diabetes prevalence in urban and rural regions in RDC (Katchunga et al Diabetes Metab 2012). Others have found similar findings elsewhere in the world, e. g. in China (Zhao J et al. J Endocrinol Invest. 2011) and India (Chow CK et al Diabetes Care 2006). We added: ”, probably more in urban than rural communities” with the Katchunga reference to the discussion section, and replaced “in rural Congo” with “in the region”
We kept however ‘rural town’ as we think this to be the best description for Kisantu.

§ To update the references on diabetes determinants in the RDC, the authors may consider a recent report on age and living in an urban environment as major determinants of diabetes among South Kivu Congolese adults (Katchunga et al. Diabetes Metab 2012).

This was added .