LETTER TO THE EDITOR

LOW SEX HORMONE BINDING GLOBULIN: A POTENTIAL PREDICTOR OF FUTURE GLUCOSE DYSREGULATION IN WOMEN

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Previous work has suggested that a low sex hormone binding globulin (SHBG) concentration associates with insulin-resistance.[1] We previously showed that a low circulating SHBG level (<30 nmol/L) is associated with the presence of the metabolic syndrome in a multi-ethnic population with lower levels found in both men and women of Pakistan ethnic origin compared with Caucasian and African-Caribbean origin people. In that study SHBG correlated positively with insulin sensitivity as estimated by HOMA-S[3] and negatively with waist hip ratio, body mass index, and diastolic blood pressure across all ethnic groups, while in multivariate logistic regression analysis a low SHBG increased the likelihood of the metabolic syndrome being present. Furthermore, SHBG levels are often lower in women with polycystic ovarian syndrome (PCOS).[4–6]

There is therefore the potential for SHBG, given its relative ease of measurement (commonly by automated immunoassay), not requiring fasting status or special processing to have utility in identifying people at increased risk or developing impaired glucose handling in the future.

In the light of this, we looked at the predictive value of SHBG in relation to future development of impaired glucose handling in women in a preliminary study in 115 women, over an up to 10-year period. The women were normo-glycaemic at baseline. Outcome was either fasting glucose or glycosylated haemoglobin (HbA1c)[7], as measures of glycaemia.

The mean age of the women at the start of follow-up was 26.8 years (standard deviation 9.0, range 16–65). Over the up to 10-year follow-up period, 6% developed non-diabetic hyperglycaemia (defined as HbA1c 42–47 mmol/mol) to and 1% type 2 diabetes (T2DM, defined as HbA1c ≥48 mmol/mol). In multiple linear regression analysis, a lower SHBG was associated with a higher fasting glucose (normalised beta (β) -0.22, p=0.02) independent of age (β 0.28, p=0.01) and index of multiple deprivation (IMD) (β -0.11, p=0.06) and South Asian ethnicity (β -0.13, p=0.04). In logistic regression, we found that age was predictive of subsequent development of pre-diabetes/T2DM (odds ratio 1.08 (95% CI 1.02–1.15), p=0.01) independent of index of multiple deprivation (IMD)/SHBG/ethnicity.

In the light of these results, we suggest that a low SHBG level may have value as a risk marker for the development of future glucose dysregulation in women, with age also an independent predictor of non-diabetic hyperglycaemia / T2DM. Where someone has been found to have a low SHBG, there is the potential for targeted lifestyle measures to be implemented to prevent or delay the onset of glucose dysregulation.

In our study, a younger age profile of the group likely influenced the low cumulative incidence of T2DM over the 10-year follow-up period. Nevertheless, SHBG may prove to be a useful future marker for the impact of lifestyle change programmes to reduce metabolic risk those people found to have a low SHBG, including women with PCOS. We plan further work to improve our understanding of this and to continue to follow up this cohort of women in the coming years.

Keywords: SHBG; Non-diabetic hyperglycaemia; Type 2 diabetes; IMD

Learning Points

- Sex hormone binding globulin (SHBG) concentration associates with insulin-resistance.
- We looked at the relation between baseline SHBG concentration and future glycaemic status over an up to 10-year period, for women who were normoglycaemic at baseline.
- In multiple linear regression analysis, a lower SHBG was associated with a higher fasting glucose independent of age and index of multiple deprivation.
- These findings suggest that a low SHBG level, at a relatively young age is a risk marker for future impaired glucose handling in women.

Precis:

In a laboratory study, we found that low SHBG level is a risk marker for future relative dysglycaemia in women, with IMD also an independent predictor of future pre-diabetes/type 2 diabetes mellitus.

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