Hyperglycemia Phenotype as indicated by Salivary Glucose Biomarker

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Background

Early screening of type 2 *diabetes mellitus* (DM), a hyperglycemia phenotype associated condition, is essential for preventive treatment and effective delay of diabetes clinical complications [1]. However, testing for hyperglycemia phenotype (fasting blood glucose > 110 mg/dl) often requires invasive and painful blood testing, limiting its large-scale usefulness. To overcome this constraint salivary glucose assays have recently being applied with the purpose of screening hyperglycemia and type 2 DM [2]. Literature results regarding glycemia and salivary glucose relationship in diabetics or in healthy individuals are controversial. On the other hand, to the best of our knowledge no cross-validation has been done on type 2 DM / hyperglycemia detection models based on salivary glucose. We have performed a systematic review and meta-analysis on previous studies and cross-validated a type 2 DM / hyperglycemia phenotype predictor model based on salivary glucose.

Experimental Methods

We conducted a meta-analysis of peer-reviewed published articles that reported data regarding mean salivary glucose levels for type 2 DM and non-diabetic individuals combined with our own results [3]. Furthermore, we used our blood and salivary glucose data from type 2 diabetics and healthy individuals to build type 2 DM / hyperglycemia phenotype logistic prediction models. These models were cross-validated against external data (Brazil and India) and accuracy was evaluated through ROC curve analysis.

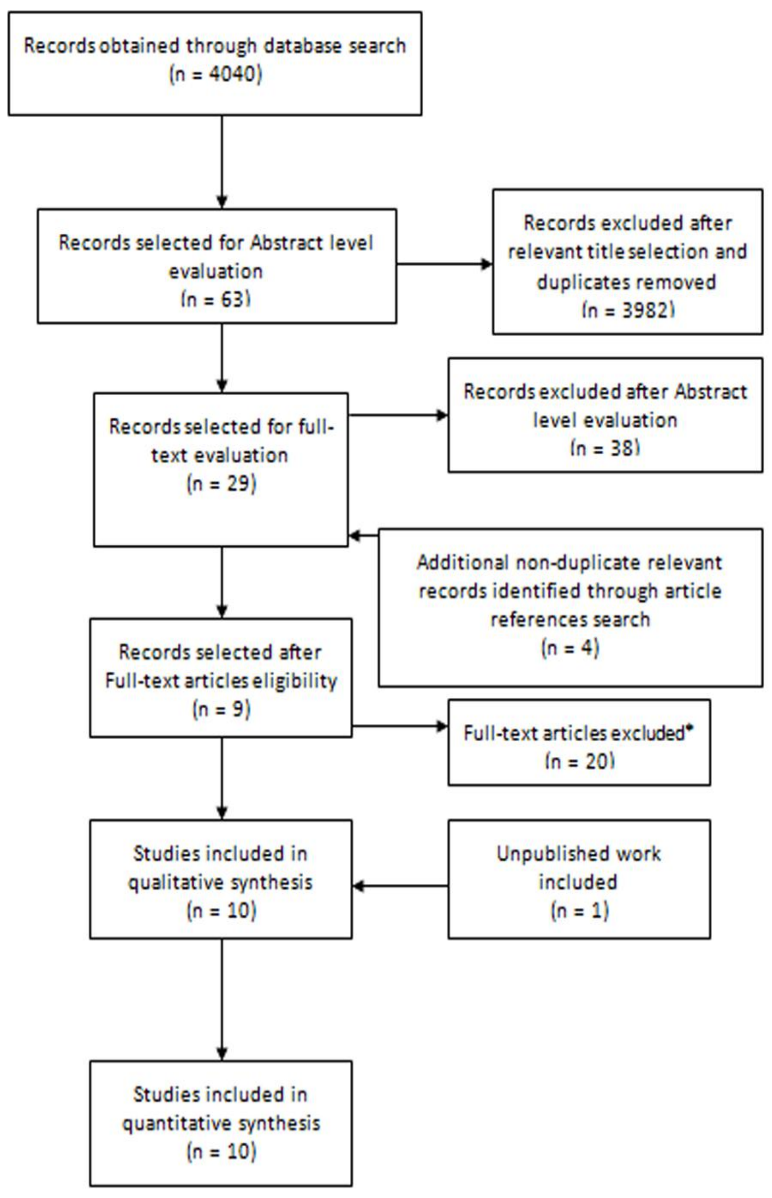

Figure 1 - Flow of study selection for mean salivary glucose levels. *Studies were excluded unless contained salivary glucose data (means, standard deviations and sample size) obtained from strictly diabetes mellitus type 2 patients and non-diabetic controls unstimulated whole saliva collected after a minimum fast period of 2 hours. Were also excluded if the full-text article were not available and the author(s) failed in sending a copy after contact request or failed in giving back supplementary required data inexistent in the original article. Records containing data already published in other article were also excluded.

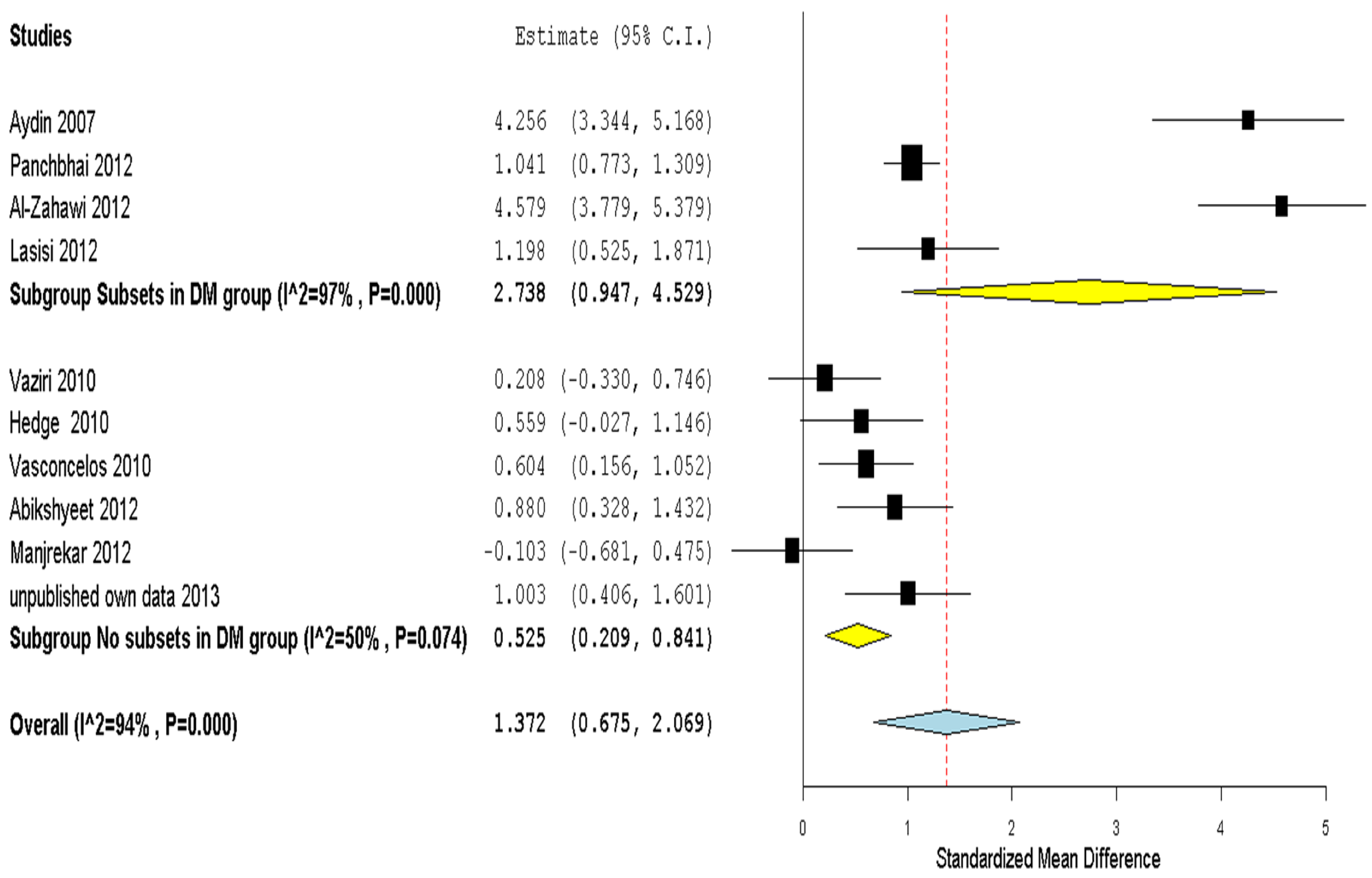

Figure 2 - Subgroup forest plot of type 2 DM mean salivary glucose levels studies. Studies have been grouped according to the type 2 DM group allocation: with or without subsets. Hedge's *g* (standardized mean difference) effect size estimates have been calculated with 95% confidence intervals and are shown in the figure. Area of squares represents sample size, continuous horizontal lines and diamonds width represents 95% confidence interval. Yellow diamonds center indicates the subgroup pooled estimates while the blue diamond center and the vertical red dotted line both point to the overall pooled estimate.

Results

- Meta-analysis results show a significant increase of salivary glucose concentration on type 2 DM individuals (Hedge's *g* > 1).
- The fitted models show a good accuracy within the training sample for predicting both hyperglycemia (81,0%) and type 2 DM (84,5%), while in the external data cross-validation the prediction accuracy was lower: hyperglycemia (68,1%) and type 2 DM (65,5%).

Prediction model	Prediction accuracy (%)	
	Internal data* (n=84)	External data** (n=229)
Hyperglycemia	81,0	68,1
Type 2 DM	84,5	65,5

Table 1 – Predictive logistic models accuracy (%). * Portuguese training dataset; ** External cross-validation dataset (Brazil and India data)

Conclusions

- Salivary glucose has potential to be used as a hyperglycemia phenotype biomarker combined with other salivary biomarkers and associated with sensitive portable technology.
- Salivary glucose don't show enough cross-validation performance to be used as a hyperglycemia phenotype global biomarker and therefore predictions should be based on region specific models.

References

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- [3] Mascarenhas P, Fatela B, Barahona I (2014) Effect of Diabetes Mellitus Type 2 on Salivary Glucose – A Systematic Review and Meta-Analysis of Observational Studies. PLoS ONE **9(7)**: e101706

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