Reviewer’s report

Title: Susceptibility of Prediabetes to the Health Effect of Air Pollution: a Community-Based Panel Study with a Nested Case-Control Design

Version: 1 Date: 13 May 2019

Reviewer: Rossella Alfano

Reviewer's report:

The study addresses an important question as investigates if changes in cardiovascular, pulmonary, and inflammatory biomarkers and in BP triggered by air pollution are larger in prediabetic population than in non-diabetic population. Overall results show air pollution related changes in BP and in inflammation and metabolic biomarkers are larger in prediabetic rather than in non-diabetic.

The study explores cardiovascular outcomes (BP) and biomarkers in prediabetic patient. In the cohort description there is no mention about participant being normotensive or not but it seems that a considerable amount of the population is taking antihypertensive drugs so it is likely that they may have been diagnosed suffering from hypertension. Sensitivity analysis excluding subject suffering from hypertension should be performed in order to evaluate the effects of PM on subjects with exclusive glicemic control impairment.

The paper is well written and easy to follow. The report of the results could benefit addressing the following comments.

Title

The title leads the reader imagine that in the paper "Health Effect of Air Pollution" (eg cardiovascular or pulmonary diseases) are assessed. However, apart from BP the other study outcomes are all biomarkers.

Abstract

In the methods authors first state they are going to look at "20 pulmonary and cardiometabolic outcomes" and in the following line they mentioned they are going to estimate "associated effect on multiple biomarkers". I suggest to be more detailed and to declare immediately which are the outcomes under study (both xx biomarkers and xx health effect) and maybe mention the 4 groups described in the methods (xx cardiopulmonary, xx inflammation and xx glucose metabolism biomarkers, and xx measurements of BP).
In the results are presented as "significant" also changes in the diastolic blood pressure and augmentation pressure that are not significant judging from the confidence intervals (1.2% [CI: -0.1%-2.4%], 5.7% [CI: -0.1%-11.8%]).

Methods

Description of the health outcomes at page 10 is not consistent with ST1. Outcomes are grouped in 4 groups in the text and in 3 groups in the ST1.

P values <0.05 were considered significant. Multiple testing adjusted p values should also be added.

Results

At page 13 authors decide to show only 12 cardiopulmonary and metabolic outcomes. It is not clear why and how these outcomes have been selected. Also, note that in the methods at line 15 it seems that cardiopulmonary outcomes measured are only 6 and metabolic are 4 for a total of 10.

At page 14 line 12 WBC and neutrophils are mentioned among the inflammatory biomarkers while in methods are included among the cardiopulmonary biomarkers.

At page 16 line 12 authors state the no significant difference was found in pulmonary biomarkers. Please specify which are these biomarkers.

At page 16 Figure 3 is presented. In the legend there is no explanation of the meaning of the grey background (that should identify the significant difference between prediabetic and non-diabetic). Also, from the moment 3 out of the 3 BP outcomes resulted significantly different in prediabetic and non-diabetic it would be interesting to show results also excluding subjects actually suffering from hypertension (if not available this information use of anti-hypertensive drug could be used as proxy). Results from this analysis may be useful in interpretation of the findings as it is expected that the effect of air pollution on BP is larger in pre-diabetic that suffer from hypertension.

Discussion

At page 17 it is not clear if the sentence starting at line 19 refers to baseline difference between prediabetic and non-diabetic or to the difference between the two groups with increased exposure to PM2.5?
At page 19 line 15 the authors state that results support that the progression of glucose metabolic disorder may aggravate the PM-induced elevation in arterial BP. It is of importance that in the analysis almost half of the prediabetic population takes drugs (including anti-hypertensive). It could be of interest to explore BP elevation in prediabetic normal tensive patients vs prediabetic patients suffering from hypertension in order to support the sentence above. Also, more elaborate discussion on the possible mechanisms underlying this association is needed (also based on the results of the present paper).

At page 20 line 31 authors state that the study suggests that elevated glucose and HOMA-IR occur in preDM but not in not diabetic subjects. However, looking at the results (Fig 3) it seems that no significant difference was detected for HOMA-IR.

In the discussion there is no mention of pulmonary biomarker results. Please, elaborate more on this negative finding.

Conclusions

Only cardiometabolic is mentioned while from the results also inflammation biomarkers seem to be relevant.

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Please indicate how interesting you found the manuscript:

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