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“Has air pollution any role in the incidence of congenital hypothyroidism?”

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In the last years the incidence of congenital hypothyroidism has grown progressively mainly due to the reduction of the limit level of thyroid-stimulating hormone (TSH) in the neonatal screening strategy and the higher percentage of newborns with risk factors of congenital hypothyroidism development such as preterm and twin babies. This has led to a rise of the incidence from 1:3000-4000 in the 90s and 1:2200 in the first decade of 2000, to the current 1:1090 in the Italian region of Piedmont in the observation period 2014-2019 [1]. The first effect of the observed increased incidence was the variation in the percentage of the different diagnostic categories of congenital hypothyroidism. Before the lowering of the TSH cutoff at screening in situ thyroid gland category had a percentage of 15-25% compared to the actual 40-50% (52.4% in the observation period 2014-2019 in Piedmont).

In the year 2020 the incidence of congenital hypothyroidism in the region of Piedmont was surprisingly almost halved to 1:1812 with an incidence of 1:625 in the first two months and 1:3125 in the following ten months when the Italian Government established the lockdown for the Sars-CoV-2 pandemic. Not only incidence varied during the year 2020 but also the percentage of the different congenital hypothyroidism categories: 18.7% of subjects had ectopic thyroid gland, 6.3% had thyroid hypoplasia, 6.3% had thyroid agenesis and 68.7% had in situ thyroid gland with dyshormonogenesis.

Many authors have observed an important role of air pollution in the thyroid hormone profile disorders. The most involved substances in the analysis were: Particulate Matter $< 2.5 \mu$ ($PM_{2.5}$), Particulate Matter $< 10 \mu$ (PM_{10}), nitrogen dioxide (NO_2), carbon monoxide (CO) and polycyclic aromatic hydrocarbons (PAH). Significant role of NO_2 and CO in TSH increase and free thyroxine (fT4) decrease was observed, whereas first-trimester exposures to $PM_{2.5}$ has been associated with mild thyroid dysfunction throughout early pregnancy. PAH was not associated to significant role in thyroid hormone profile dysregulation [2-4].

The data of the Environment Protection Regional Agency for the year 2020 indicate a higher mean concentration of both $PM_{2.5}$, and PM_{10} with respect of the year 2019, as well as the increase of the days with mean concentration overcome with respect of the established limits. On the other hand, NO_2 concentrations were significantly lower during the lockdown, probably due to the reduced traffic pollution, as it is the main substance delivered after combustion [5]. This fact, together with the obligation to carry on the masks, especially the filtering face piece-2 (FFP-2) may have contributed to reduce the effects of air pollution through pregnancy and consequently in the newborns.

Our observation arise many questions that interfere with the public health and the costs of the public health system itself as reported previously by studies in other countries. The exposure to air

pollution is widespread and quotidian thus the attention towards environment should be of main importance in the regional and national government agenda as many disruptors may interfere with the thyroid function in pregnancy and in the newborns, in which hypothyroxinemia may negatively influence the neurodevelopment.

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