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ORIGINAL ARTICLE

The impact of air pollution to obesity

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Abstract

BACKGROUND: Air pollution in ambient air could affect the increase of obesity in children.
METHOD: Review analyze papers about the effect of polycyclic aromatic hydrocarbons (PAHs), fine particles (particulate matter < 2.5 μm, $PM_{2.5}$), and traffic air pollution (NO_2, NOx, $PM_{2.5}$).
RESULTS: Prenatal exposure to concentrations 1.73–3.07 ng/m^3 PAHs significantly increased obesity at age 5 and 7 years, up to 11 years. All studies indicate the significance of prenatal exposure with concentration > 0.3 ng/m^3 of B[a]P (benzo[a]pyrene). Prenatal exposure to $PM_{2.5}$ above concentrations 10.6–11.9 μg/m^3 increased obesity in children up to the age of 9 years.
Traffic air pollution was evaluated according to exposure to NO_2 and $PM_{2.5}$. Concentrations NO_2 higher 30 μg/m^3 affect adiponectin levels in cord blood, cholesterol metabolism, and therefore increase later the risk of overweight or obesity. $PM_{2.5}$ 9.2–11.6 μg/m^3 during pregnancy affect adiponectin. These concentrations from the traffic air pollution can affect the metabolism in newborns later related to obesity.
CONCLUSION: All these studies indicate that contemporary concentrations of PAHs, $PM_{2.5}$ and NO_2 in ambient air, especially during prenatal period, affect overweight and obesity in children.

INTRODUCTION

Obesity is a chronic noninfectious disease, which is combined with the risk of development of other diseases. Prevalence of overweight and obesity increases during childhood, it is therefore necessary to analyze various factors of this development already from the early life.

Prevalence of obesity in U.S. children has been increasing for more than 40 years (CDC 2011). According to Jerrett *et al.* (2010) the prevalence increased during the last 50 years twice. Similar increase is also observed n Europe (Olds *et al.* 2011). Obesity is related to dietary factors, physical activity, as well as lower socio-economic status. During last years was observed that environmental stressors as endocrine disrupting chemicals, could be responsible for childhood obesity (Blumberg *et al.* 2011).

Air pollutants in ambient air could affect the increase of obesity in children. We reviewed papers about the effect of polycyclic aromatic hydrocarbons (PAHs), fine particles (particulate matter < 2.5 μm, $PM_{2.5}$), and traffic air pollution (NO_2, NOx, $PM_{2.5}$).

PAHs AND OBESITY

Rundle *et al.* (2012) studied the effect of prenatal exposure to PAHs on obesity in African-American and Hispanic children from New York, USA, born in the years 1998–2006. Exposure to PAHs was measured in their mothers using personal monitors. These children were followed up to the age of 5 years (N=422) and 7 years (N=341). Mean levels of PAHs prenatal exposure for the group followed at 5 years was 2.34±2.05 ng/m^3, at 7 years 2.53±2.03 ng/m^3. The highest tertile of prenatal PAH exposure (> 3.08 ng/m^3) was significantly associated with higher BMI (body mass index) z score in both ages. In this tertile was the risk of obesity at age 5 years RR=1.79 (95% CI 1.09, 2.96), at age 7 years RR=2.26 (95% CI 1.28, 4.00), but obesity was increased also with PAH exposure 1.73–3.07 ng/m^3. This study suggests for the first time that prenatal exposure to PAHs causes increased fat mass gain during childhood and a higher risk of childhood obesity.

Previously was observed the association of maternal smoking during pregnancy, as a source of PAHs, with higher body weight in children (Oken *et al.* 2008; Power & Jefferis 2002).

Scinicarielo & Buser (2014) studied the association of urinary PAH metabolites with adiposity outcomes as BMI z score, waist circumference (WC) and rate of obesity in 3 189 individuals 6–19 years from 2001–2006 National Health and Nutrition Examination Survey (NHANES). They observed that ΣNAPHT (the sum of naphthalene metabolites) and Σmol PAHs (the sum of molar mass of all PAH metabolites) were positively and significantly associated with BMI z score, WC and obesity in the younger age group (6–11 years). Those results are in agreement with studies on mice, when Irigaray *et al.* (2006) observed that PAH exposure impaired adipose tissue lipolysis and increased weight gain and fat mass in mice. They found that the total molar sum of PAHs and naphthalene in urine were associated with obesity in children and adolescents. This study was the first report about the association of environmental PAH exposure and childhood obesity on nationally representative sample.

Jung *et al.* (2014) studied the impact of volatile and nonvolatile PAHs on asthma bronchiale, possible association with obesity on Columbia Center for Children Environmental Health birth cohort at the age of 5–6 years. PAHs were measured for two weeks as residential indoor monitoring (N=311). (Concentration of PAHs is given in Jung *et al.* 2010. Σnonvolatile PAHs indoor was 2.14±2.02 ng/m^3, outdoor 2.68±1.93 ng/m^3.) Obesity at age 5 ys was defined as the increase of BMI. Current asthma and wheezing at ages 5 and 7 were determined by questionnaires. They found that higher concentrations of methylphenanthrenes at the age of 5–6 ys were associated with asthma in obese children, but not in non-obese children. This study indicate that obesity may modify the effect of exposure to PAHs at age 5–6 ys, and specifically semivolatlile methylphenanthrenes, on asthma in children at the age of 5–6 ys. It seems that obesity may increase the vulnerability to PAH exposure, especially in nonatopic children and girls.

Cross-sectional analyses of the relationship among urinary concentrations of PAH metabolites, BMI and WC, used data for 1 985 subjects aged 6–18 years from the 2003–2008 NHANES (Kim *et al.* 2014). As PAH metabolites they analyzed 2 naphthalene metabolites, 3 fluorene metabolites, 3 phenathrene metabolites and 1-OH pyrene. Urinary PAH metabolites were higher in subjects with a lower poverty income ratio, lower parent education, and higher ETS (environmental tobacco smoke) exposure. The association between PAHs and obesity substantially strengthened with increasing ETS exposure. Among subjects with low ETS exposure, there was no significant association between PAHs and adiposity measures. The risks of general and central obesity were approx. 20–30 times higher among children and adolescents with both high ETS and PAH exposure than low PAH exposure without exposure to ETS. This study showed a significant synergistic interaction between PAHs and ETC to the risk of obesity.

Hendryx & Luo (2018) used latent class analysis for the association between PAH exposure and BMI, for NHANES 2013–2014 data, 2 354 subjects aged 6–80 years. They measured 7 OH-PAH metabolites and BMI. High multi-exposure to PAHs and naphthalene/phenanthrene exposure were associated with higher BMI (p<0.001) in all subjects. The PAH sum score was associated with higher BMI among young people, but in other ages. The latent classes indicate the importance of multiple exposures, new results may be seen in the relationship between naphthalene, phenanthrene, and pyrene exposure and BMI.

Choi *et al.* (2018) put forward the hypothesis about sexually dimorphic risk of obesity-associated asthma. Asthmatic and healthy control children were recruited from polluted urban (N=100+100) and rural areas (100+100). Exposure to benzo[a]pyrene (B[a]P) in polluted air was studied in the relationship to asthma, for groups as lean controls, overweight/obese (OV/OB) control, lean asthmatic, and OV/OB asthmatic children. Exposure to B[a]P was in the group of lean control (N=82) 4.3±2.4 ng/m^3, OV/OB control (N=11) 3.4±1.7 ng/m^3, lean asthma (N=72) 7.7±7.3 ng/m^3, OV/OB asthma (N=19) 9.5±8.5 ng/m^3 (p=0.002)..Compared to lean controls, the B[a]P exposure was associated with 4.3 times higher odds of asthma diagnosis (95% CI, 2.6–7.4; p<0.001), but similar diagnosis was 5.7 times greater (95% CI, 2.8–11.7; p<0.001) among OV/OB

children per (ln) unit exposure. When children were stratified according to their gender, the odds ratio of asthma was comparable between lean boys and OV/OB boys per unit exposure. However, the same unit increase among girls was associated with considerably higher odds of asthma among OV/OB girls (aOR=5.9; 95% CI, 1.9–17.7; p=0.002) than lean girls (aOR=3.8; 95% CI, 1.9–17.7; p=0.002) compared to lean controls. Increase in ambient B[a]P was associated with 10.5–times greater odds (95% CI, 2.6–39.6; p=0.001) in adolescent OV/OB boys, compared to lean controls. But the adolescent OV/OB girls were associated with highest adjusted odds of the asthma (aOR=15.4; 95% CI, 2.9–29.1; p<0.001) compared to lean control girls. This study proposes greater susceptibility of girls to airborne B[a]P for obesity associated childhood asthma.

Poursafa *et al.* (2018) studied on the sample of 186 children aged 6–18 years association between PAH exposure, cardiometabolic risk factors and obesity. PAH exposure was analyzed in urine, determined 1-naphtol, 2-naphtol, 1-hydroxypyrene, 9-phenanthrol, and ΣOH-PAHs. As cardiometabolic risk factors were determined fasting blood glucose, total cholesterol, LDL-cholesterol, HDL-cholesterol, triglycerides. They observed increased risk of cardiometabolic risk factors associated with the second and third tertiles of 2-naphthol, 1-hydroxypyrene, and ΣOH-PAHs. For participants without cardiometabolic risk factors was exposure to 2-naphthol (p=0.02), 9-phenantrol (p=0.03), and ΣOH-PAHs (p=0.005) associated with increased risk of obesity. These finding suggest that exposure to PAHs could explain the existence of cardiometabolic risk factors in some normal-weight children as well as excess weight in some children without metabolic risk factors. This study showed PAHs role as endocrine disrupting compounds and their potential effect on obesity and metabolic impairments such as dyslipidemia, hyperleptinemia, and hyperglycemia in adults (Rajnbar *et al.* 2015; Zhang *et al.* 2016) and in children (Poursafa *et al.* 2014).

Rundle *at al.* (2019) further analyzed the effect of prenatal PAH exposure in their birth cohort to BMI in the longitudinal study, the age of 5–14 years. The prevalence of obesity was 20.6% at age 5 and increased across follow-ups until age 11 to 33.0%. Prenatal exposures to airborne PAH were associated with higher childhood BMI z scores at a young age, but growth trajectories converged by age 11 years. This study indicate the effect of PAH exposure to an earlier adiposity rebound in young children.

Canadian Health Measures Survey (CHMS) presented data on the asscociation of urinary PAHs and obesity in children aged 3–18 years (Bushnik *et al.* 2019). Study included 3 667 subjects, ages 3–5 N=1 242, ages 6–11 N=1 320, ages 12–18 N=1 105. As groups of PAH metabolites were determined fluorene, naphthalene, phenanthrene, and pyrene, as well as total PAHs. Obesity was measured as fat distribution – waist/to-height ratio (WHtR), BMI, WC and central obesity. BMI, WC, and WHtR were positively associated with total PAH and naphthalene metabolites in the total population aged 3–18 and in age groups 6–11 and 12–18. In 3–5 year old was WHtR significantly associated with total PAH, naphthalene, and phenanthrene metabolites. Urinary PAH metabolites were associated with measures of obesity in children as young as 3–5 years. Authors propose to use WHtR as the indicator of central obesity and predictor of health risk associated with obesity.

Acharya *et al.* (2019) studied in 45 mothers from Texas relationship between BMI and concentration of PAHs in breast milk. 24 women were obese (BMI>30), 21 women had BMI < 25 (18.5–24.9, normal). In 69% of samples was detected PAHs, especially phenanthrene, pyrene, fluoranthene. The mean concentration of total PAHs in the BMI > 30 group was 224.8 ng/g milk fat, in BMI < 25 group was 57.9 ng/milk fat. None of thes samples in BMI < 25 group contained 5–6 rings PAHs. The estimated total PAHs intakes by infants via obese and normal mothers' milk were 1.26 and 0.32 μg/kg/day. As PAH levels are high in breast milk of obese women, their babies may be at higher risk of exposure compared to babies of normal weight women. Higher molecular weight PAHs (> 4 rings) were found exclusively in obese group, they are listed as potential carcinogens/mutagens. It seems, that breastfed babies from obese mothers are potentially at higher risk of exposure to carcinogenic PAHs.

FINE PARTICLES AND OBESITY

Mao *et al.* (2017) studied the effects of early-life ambient $PM_{2.5}$ exposure and maternal prepregnancy obesity on childhood overweight or obesity in 1 446 mother-infant pairs recruited at birth from 1998 and followed through 2012 at the Boston Medical Center, Mass., USA. Obesity was diagnosed by pediatric staff, who measured height and weight within the age 2 and 9. Exposure to $PM_{2.5}$ during all trimesters was in the forth quartile > 12.32 μg/m^3, at the age of 2 years > 11.99 μg/m^3 (RR=1.3 (95% CI 1.1, 1.5). Children of mothers who were obese at conception and who were exposed to $PM_{2.5}$ at or above concentrations of 10.5–10.9 μg/m^3 were at least twice the risk of over-weight or obesity compared with children of mothers of prepregnancy body mass index in the normal range and low $PM_{2.5}$ exposure. They observed that early life exposure to $PM_{2.5}$ to children overweight or obesity in concentrations below the U.S. standard for PM2.5 of 12 μg/m^3 (U.S. EPA 2013).

Rodent studies indicate that $PM_{2.5}$ exposure induces inflammatory response in visceral adipose tissue (de Melo *et al.* 2015; Sun *et al.* 2009; Xu *et al.* 2010) or epidermal fat (Wei *et al.* 2016).

The impact of air pollution to obesity was studied in China in 13 414 respondents, mean age 61 years, from 125 cities in the year 2014 (Yang *et al.* 2019).

They studied the relationship of BMI to air pollutants as $PM_{2.5}$, PM_{10}, NO_2, CO, O_3 and SO_2. Concentration of $PM_{2.5}$ for the group with BMI < 18.5 was 34.68 μg/m^3, BMI 18.5–23.9 36.12 μg/m^3, BMI 24–27.9 39.18 μg/m^3, BMI > 28 41.07 μg/m^3; OR for overweight = 1.025 (95% CI, 1.018, 1.032), for obese = 1.034 (95% CI, 1.027, 1.041). Exposure to $PM_{2.5}$ represents a significantly positive impact on the BMI score. They also identified that women, the middle aged, and those with low levels of education were especially susceptible (Li *et al.* 2015).

In South Korea 5 114 subjects were analyzed for the effect of PM_{10} and NO_2 to obesity, diagnosed as BMI, waist circumference, percent body fat, total adipose tissue, visceral adipose tissue, and subcutaneous adipose tissue (Hwang *et al.* 2019). Mean age of this population was 53.5 years, annual concentrations of PM_{10} was 49.4 μg/m^3, NO_2 was 57.0 μg/m^3. No relationship between PM_{10} or NO_2 exposure and the markers of obesity was observed. These findings provide the evidence that exposure to PM_{10} and NO_2 in concentrations determined in Korea is not associated with any widely used obesity-measuring parameters.

TRAFFIC AIR POLLUTION (TAP)

First paper about TAP exposure and BMI in children was published by Jerrett *et al.* (2010). Cohort of 3 318 children aged 9–10 years from 12 communities in Southern California was enrolled to longitudinal study followed until age 18. Air pollution was evaluated according to the traffic density, the distance from child´s home within 150, 300 or 500 m. For increased traffic exposures within 150 m of the home, there was a significant increase in attained BMI for both sexes. Results confirm the hypothesis that proximate exposures to traffic exert the largest effect on BMI growth. The traffic density within 150 m increased 5% BMI at age 18. As possible reasons are understood sense of danger among parents and children that inhibits mobility on foot or bicycle (Timperio *et al.* 2006) as well TAP decrease lung function growth (Gauderman *et al.* 2007), and increase the incidence of asthma (McConnell *et al.* 2006; Jerrett *et al.* 2008). Higher traffic exposure in California is also associated with lower socioeconomic status (Green *et al.* 2004). This analysis yields the first evidence of significant effects from traffic density on BMI levels at age 18 in a large cohort of children.

Jarrett *et al.* (2014) further studied impact of TAP on cohort of children (N=4 550) aged 5–11 years from 13 communities in California, children were followed for 4 ys. Traffic density at 150 m radius had borderline significance for BMI increase (p<0.1). More significant was traffic air pollution by NO_x (non-freeway exposure, 92.9 μg/m^3), which was at the age 10 significantly associated with BMI, 13.6% increase in the rate of average annual BMI growth. In this study air pollution by NO_x exerted a stronger effect on BMI growth than traffic density. The observed changes are related to hypothesis, that the inflammatory effects of air pollution predispose children to obesity in a similar way as was observed already in mice (Sun *et al.* 2009).

Kim *et al.* (2018) studied the effect of TAP in utero and first year of life in the cohort of 2 318 children, recruited from 2002 to 2003 from kindergarten and 45 public schools across 13 Southern California Communities. At study entry, the mean age was 6.5±0.7 years, approx. 29% of children were overweight or obese. Mean NO_x exposures from freeway roadways during in utero, first year of life, and childhood were 31.3±37.8 μg/m^3, 30.5±36.7 μg/m^3, and 28.4±35.5 μg/m^3, mean NO_x exposures from non-freeway roadways during in utero, first year of life, and childhood were 19.4±13.9 μg/m^3, 17.5±12.6 μg/m^3, and 11.7±8.8 μg/m^3. First year of life exposures to TAP from freeway roads were positively associated with BMI at age 10 years that were independent of later childhood exposures. These finding suggest that elevated early life TAP exposures contribute to increased obesity risk in children.

One mechanism for the increase of childhood obesity by air pollution may be an altered metabolic function, predisposing affected children to the development of obesity (Grun & Blumberg 2006; Newbold*et al.* 2008). Elevated adipokine levels in cord blood are considered as predictors of early development of obesity (Karakosta *et al.* 2011). Leptin and adiponectin are hormones secreted by adipocytes, correlate with fetal adiposity and childhood weight gain (Tsai *et al.* 2004; Mantzoros *et al.* 2009). Lavigne *et al.* (2016) therefore investigated the association between maternal exposure to ambient air pollution (4th quartile $PM_{2.5}$ 9.2–11.6 μg/m^3, NO_2 38.9–77.8 μg/m^3) and umbilical cord blood levels of leptin and adiponectin in the cohort of 2 001 mother-infant pairs from Maternal-Infant Research on Environmental Chemicals (MIREC) Study from Canada. $PM_{2.5}$ was positively associated with cord blood adiponectin levels, IQR increase (3.2 μg/m^3) was associated with 11% (95% CI: 1, 21) higher adiponectin levels. Similar increase was observed for the effect of NO_2, IQR increase (25.6 μg/m^3) was associated with 12% (95%CI: 2, 23) higher adiponectin levels. These results indicate that air pollution during pregnancy may affect fetal metabolic function, which may be later associated with obesity.

Alderete *et al.* (2018) hypothesized that increased prenatal exposure to TAP and ambient air pollution are associated with higher levels of cord blood leptin and HMW adiponectin. Study included 136 mother-infant pairs from Los Angeles County. Ambient air pollution was determined 9 months before delivery ($PM_{2.5}$ 12.3±0.8 μg/m^3, NO_2 35.2±4.1 μg/m^3). TAP exposure during pregnancy were positively associated with adipokines in cord blood. A 1-SD (3.8 μg/m^3) increase in NOx was associated with a 33% higher leptin level (p=0.001), 9% higher HMW adiponectin level (p=0.07). Cord blood leptin levels were higher in mothers who lived near major roadways. They found that cord blood

adipokine levels were associated with increased growth from birth to 6 month of age and have implications for future obesity risk.

Fioravanti *et al.* (2018) followed cohort of 719 infants from Rome, Italy, at 4 years (N=581) and 8 years (N=499). The prevalence of overweight/obesity was 9.3% and 36.9% at 4 and 8 years. Exposure levels of NO_2 between birth and 4 years for was 43.3±10.1 μg/m^3, to 8 years 43.4±10.2 μg/m^3, of $PM_{2.5}$ 19.5±2.03 μg/m^3 and 19.5±2.02 μg/m^3, respectively. In this study was not observed any evidence of an association between exposure to air pollutants and overweight/obesity in children enrolled at birth and followed to 8 years of age.

Frondelius *et al.* (2018) studied the effect of prenatal exposure to NOx and traffic density to childhood overweight and obesity at 4 years in Malmo, Sweden. Final population consisted of 5 815 children. Concentration of NOx between 1999 and 2005 averaged around 20 μg/m^3. Similar to previous Italian study (Fioravanti *et al.* 2018), these authors did not observe any association of increased risk for childhood overweight and obesity through low level NOx prenatal exposure.

Kim *et al.* (2019) analyzed in period 2014–2018 158 young adults from Southern California, who were followed as cohort in the Children Health Study already from 2002. They studied the impact of air pollution (NO_2, O_3, $PM_{2.5}$, and traffic density) to cardiometabolic health (fasting glucose, fasting insulin and lipid profiles). One month regional ambient air pollution was 30.3±10.7 μg NO_2/m^3 and 12.4±4.3 μg $PM_{2.5}$/m^3, one year exposure was 30.0±7.3 μg NO_2/m^3 and 12.4±2.5 μg $PM_{2.5}$/m^3, Higher long-term ambient NO_2 exposure was associated with higher fasting total cholesterol and LDL-cholesterol, which was affected by obesity status. The associate estimates between prior 1-year NO_2 exposure and total cholesterol amongst obese participants were nearly 5-fold larger (21.4 mg/dL vs. 4.7 mg/dL) than none-obese participants, between NO_2 exposure and. LDL-cholesterol were 9-fold larger (19.9 mg/dL vs. 2.2 mg/dL). These findings suggest that higher long-term NO_2 exposures may increase risk of dyslipidemia in young adults, especially in obese young adults.

Previously Yang *et al.* (2018) published study on 15 447 participants aged 18–74 years from China on the impact of air pollution to lipid level and dyslipidemia. Exposure to $PM_{2.5}$ corresponded to 82.02 μg/m^3, NO_2 35.28 μg/m^3. They detected higher $PM_{2.5}$ and NO_2 concentrations and OR for hypercholesterolemia. Association between air pollutants and dyslipidemias were greater in participants, who were overweight or obese.

Ambient air pollution and overweight and obesity was studied in 2 660 children aged 7–10 years during 2012 in Barcelona (Bont *et al.* 2019). The prevalence of overweight was 26%, obesity 16%. NO_2 levels were similar at homes and schools (median = 44.4 and 48.5 μg/m^3, respectively), $PM_{2.5}$ levels were higher at schools (median = 25.0 μg/m^3) than at homes (median = 13.4 μg/m^3). At schools, children exposed to levels of NO_2 and $PM_{2.5}$ in the second exposure tertile had a higher OR of being overweight or obese, versus normal weight children of the first tertile of exposure (NO_2 OR=1.28, 95% CI = 1.03, 1.61, $PM_{2.5}$ OR = 1.35, 95% CI = 1.01, 1.60). This study suggests that exposure to ambient air pollution, particularly at schools, was associated with an increased risk of being overweight or obese.

DISCUSSION

PAHs are understood as obesogens. An animal experimental study exhibited that chronic exposure to B[a]P in mice directly inhibits lipolysis in adipocytes and causes fat mass gain (Irigaray *et al.* 2006). Another mechanism may be related to their endocrine-related activity as estrogenic receptor activation (Sievers *et al.* 2013), thyroid receptor inhibition (Sun *et al.* 2008), and PPAR (peroxisome proliferator activated receptors, Kim *et al.* 2005). Hydroxy-PAHs are structurally similar to estrogens and have shown to have estrogenic activities (Wenger *et al.* 2009).

Exposure to PAHs was determined by mother´s personal monitoring (Rundle *et al.* 2012; Rundle *et al.* 2019), residential indoor monitoring (Jung *et al.* 2010), ambient air monitoring (Choi *et al.* 2018), or related to urinary PAH metabolites (Scinicario and Buser 2014; Kim et al 2014; Hendryx and Luo 2018; Poursafa *et al.* 2018; Bushnik *et al.* 2019) as well as in the breast milk (Acharya *et al.* 2019).

Prenatal ambient air exposure to PAHs in Columbia Center studies (Rundle *et al.* 2012; Jung *et al.* 2014; Rundle *et al.* 2019) seems to be very low, concentrations of B[a]P are on average lower than 0.3 ng/m^3. May be, that those results are simultaneously affected by the low social-economic situation in the studied population. In Choi *et al.* study on asthmatic children (2018) exposure to B[a]P was in different groups between 4.3–9.5 ng/m^3. According to Guerreiro *et al.* (2016) acceptable risk level is 0.12 ng B[a]P/m^3. EU standard for annual exposure is related to 1 ng B[a]P/m^3.

Studies by Rundle *et al.* (2012; 2019) and Jung *et al.* (2014) indicate the significance of already prenatal exposure to PAHs, which later increased overweight and obesity in children in the longitudinal study up to 14 years. Prenatal exposure to PAHs is extremely important for the future child development as was also proved for their neurodevelopment (Sram *et al.* 2017).

Determination of urinary PAH metabolites is very informative about PAHs exposure from ambient air as well as diet. In all studies OH-PAH metabolites levels were associated with obesity (Scinicarielo & Buser 2014; Kim *et al.* 2014; Hendryx & Luo 2018; Poursafa *et al.* 2018; Bushnik *et al.* 2019).

All studies are very informative about PAHs exposure and possible health risk related to obesity already in children, especially the significance of prenatal

exposure. As data from USA and Canada corresponds to lower PAHs exposure from ambient air, the significance to PAHs exposure e.g. in some countries in Europe may be more important, than was judged until now. E.g. in the Czech Republic is 37% of population is exposed to annual concentrations of B[a]P higher than 1 ng/m^3. Therefore, we may anticipate, that PAHs exposure from ambient air may in some polluted countries also affect the overweight and obesity in children.

Prenatal exposure to $PM_{2.5}$ above concentrations 10.6–11.9 μg/m^3 increased obesity in children in Boston, USA, up to the age of 9 years (Mao *et al.* 2017).

Study in China analyzed the relationship between BMI and $PM_{2.5}$ in adults. At the highest BMI was exposure to $PM_{2.5}$ 41.07 μg/m^3, they observed a higher impact in obese population (Li *et al.* 2015).

Study in Barcelona followed children at age 7–10 years detected association with $PM_{2.5}$ (25.0 μg/m^3) and NO_2 (48.5 μg/m^3) exposure in schools in the second tertile of both concentrations (de Bont *et al.* 2019).

However, study in South Korea with subjects with mean age 53.5 years and annual concentrations PM_{10} 49.4 μg/m^3 and NO_2 57.0 μg/m^3 did not observe any association with any increase in obesity parameters (Hwang *et al.* 2019).

Study from USA (Mao *et al.* 2017) postulate the risk for obesity due to early life exposure in $PM_{2.5}$ concentrations lower than U.S. annual standard 12.0 μg/m^3.

Traffic air pollution was originally evaluated according to the traffic density, increase of BMI in children was observed within 150 m of the home (Jerrett *et al.* 2010).

Later was analyzed the traffic density and ambient air exposure to NO_x, NO_2 and $PM_{2.5}$.

Effect of TAP in utero related to obesity was observed at NO_x concentrations 92.9 μg/m^3 (Jarrett *et al.* 2014) as well as 31.7±37.8 μg/m^3 in California (Kim *et al.* 2018), no effect was observed at NO_x concentrations 20 μg/m^3 in Malmo, Sweden (Frondelius *et al.* (2018).

NO_2 concentrations 38.9–77.8 μg/m^3 increased adiponectin levels in cord blood (Lavigne *et al.* 2016), 35.2±4.1 μg/m^3 leptin as well as adiponectin (Alderete *et al.* (2018). According to Kim *et al.* (2019) NO_2 concentrations 30.3±10.7 μg/m^3 increased total cholesterol and LDL cholesterol in young adults. Yang *et al.* (2018) observed the effect of 35.28 μg NO_2/m^3 to increase hypercholesterolemia in adults in China. In school children in Barcelona, Spain, NO_2 concentrations 44.4–48.5 μg/m^3 was associated with an increased risk of being overweight or obese (de Bont *et al.* 2019).

According to these studies NO_2 concentrations higher 30 μg/m^3 may already increase obesity.

Concentration of $PM_{2.5}$ 9.2–11.6 μg/m^3 during pregnancy are associated with higher adiponectin levels in newborns, which may be later related to obesity (Lavigne at al. 2016). No effect of prenatal exposure to $PM_{2.5}$ 19.5±2.03 μg/m^3 to obesity in 4 and 8 years old children was recognized in Italian study (Fioravanti *et al.* 2018). Concentration of $PM_{2.5}$ 25.0 μg/m^3 at schools in Barcelona was associated with obesity among 7–12 years old children.

Concentrations of $PM_{2.5}$ 9.2–11.6 μg/m^3 during fetal development from TAP can affect metabolism in newborns. It corresponds to Mao *et al.* (2017) results about the significance of prenatal concentration to later obesity. Those results support WHO recommendation for $PM_{2.5}$ standard: 10 μg/m^3.

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AUTHORS CONTRIBUTION

All the authors made important intellectual contributions to the manuscript and all authors approved the final version before submission.

CONFLICT OF INTEREST

The authors declare no conflict of interest.

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