Health risks for the population living near petrochemical industrial complexes. 2. Adverse health outcomes other than cancer: A review of the scientific literature

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ABSTRACT

The present literature review was aimed at assessing whether living in the vicinity of petrochemical industries complexes – including oil refineries – is associated with a higher incidence of adverse health effects other than cancer. The available scientific literature on this potential association was reviewed by means of PubMed and Scopus databases. It is known that air pollutants such as sulfur oxides, nitrogen oxides, carbon monoxide and dioxide, volatile organic compounds, polycyclic aromatic hydrocarbons and various metals are commonly detected in the surroundings of these complexes. Most of the reviewed studies report increases in the prevalence of asthma and other respiratory problems for children and adults living in the surroundings of the petrochemical complexes, as well as reproductive outcomes in pregnant women. Based on this, as well as on similar conclusions also found for cancer incidence and mortality, we do recommend to conduct all the necessary studies for each specific complex in order -if necessary- to take the appropriate measurements to significantly reduce the levels of air pollutants can be achieved.

Keywords: petrochemical industries; air pollutants; human exposure; respiratory problems; reproductive outcomes.

1. **Introduction**

The recent development of the industrial civilization has had an important dependence on petroleum, being an issue of critical concern for many nations worldwide. In fact, general media recently reported that the global petrochemicals market size is projected to reach USD 958.8 billion by 2025, expanding in the meantime at a compound annual growth rate (CAGR) of 8.5% (PR Newswire, 2019). Petroleum-related activities are mainly focused on refineries and a wide set of industries whose raw material is oil itself, named petrochemical industries. Regarding these activities, it is also well established that petrochemical industries and oil refineries emit a number of air pollutants, which can negatively affect human health, especially for those people living in the surroundings (Chen et al., 2014; Broitman and Portnov, 2020). In the ambient air around petrochemical complexes, sulfur dioxide, particulate matter ($PM_{0.5}$, $PM_{2.5}$ and PM_{10}), polycyclic aromatic hydrocarbons (PAHs), some metals, as well as volatile organic compounds (VOCs), which include well known carcinogenic substances such as 1,3-butadiene, 1-2-dichloroethane and benzene, are frequently found (Nadal et al., 2009, 2011; Wichmann et al., 2009; Deger et al., 2012; Ramírez et al., 2012; Kongtip et al., 2013; dos Anjos et al., 2014; Chuang et al., 2018; Jephcote and Mah, 2019; Zheng et al., 2020). The human exposure to some of these pollutants may be also assessed by analyzing biomarkers in blood and urine (Fenga et al., 2017; Koh et al., 2018; Wang et al., 2019a).

Given the great magnitude and extension of the oil activities, there is a considerable number of individuals who -in different countries and regions- live in the vicinity of oil refineries, petrochemical industries and/or petrochemical complexes. For this reason, we have recently reviewed the scientific literature on the potential relationship between residing near that kind of facilities and both, cancer incidence and cancer mortality

(Domingo et al., 2020). We concluded that human exposure to carcinogenic pollutants emitted from petrochemical industries might increase cancer mortality and the incidence of some cancers, especially leukemia and other hematological malignancies, in some individuals residing in the neighborhood (Domingo et al., 2020). In order to have a global overview of the potential adverse health effects of residing in the surroundings of oil refineries, petrochemical industries and/or petrochemical complexes, studies aimed at analyzing a potential association between living in the vicinity of these facilities and the incidence of adverse health outcomes, other than cancer, were here reviewed. In March 2020, the available scientific literature was reviewed on PubMed (www.ncbi.nlm.nih.gov/pubmed) and Scopus (www.scopus.com) databases by using the following keywords: “adverse health effects", “reproductive outcomes”, “respiratory effects” and "petrochemical industries/petrochemical complex”. Information here presented has been classified according to the three main groups of adverse health effects. Table 1 shows a summary of the articles hereby reviewed.

2. **Asthma and respiratory symptoms**

Various epidemiological investigations have shown that air pollution is currently an important environmental public health issue. Thus, a number of studies have demonstrated that exposure to ambient air pollution is associated with several adverse outcomes, such as acute lower respiratory infections, chronic obstructive pulmonary disease, asthma, cardiovascular diseases and lung cancer (Sack et al., 2017; Shahadin et al., 2018; Wang M et al., 2019; Bergmann et al., 2020; Chen et al., 2020).

In Taiwan, Yang et al. (1997) investigated whether there was an excess of adverse respiratory and irritant health outcomes in populations who lived near to petrochemical manufacturing facilities. Several indicators of respiratory health, including cough, wheezing and chronic bronchitis, did not show significantly different prevalence rates between the study subjects and the control populations. However, several acute irritative symptoms including eye irritation, nausea, throat irritation, and chemical odor perception, were found to be significantly more common in individuals living in the exposed area than in control subjects. Great differences in the perception of chemical odors (84.6% vs 2.1%) were especially remarkable. Also, the same research group (Yang et al., 1998) carried out a cross-sectional epidemiological study focused on investigating the respiratory health of school children residing in two areas of Taiwan. It was reported that the children residing in the petrochemical area showed more prevalence of asthma and other respiratory symptoms than those living in the control area. The concentrations of particulate matter, sulfur dioxide, nitrogen dioxide, and acid aerosols were found to be significantly higher in the petrochemical area. In another study, conducted also by the same Taiwanese research group (Chen et al., 1998), the effects of ambient air pollution on respiratory symptoms and diseases of school children were evaluated. For that study, 6 communities (1 rural, 2 urban, and 3 in petrochemical areas) were selected. As expected, children living in the urban communities had significantly more respiratory symptoms and other adverse effects such as sinusitis, wheezing, asthma, allergic rhinitis, and bronchitis, than those residing in the rural community. Notwithstanding, only nasal symptoms were more prevalent in children living in the communities close to the petrochemical industries than in those residing in the rural community. More recently, Chiang et al. (2016) assessed the relationship between exposure to sulfur dioxide and the incidence of respiratory diseases (allergic rhinitis, bronchitis and asthma) in children living near a petrochemical complex of Taiwan. It was found that the children residing in the vicinity of the petrochemical complex showed significant higher incidences of allergic rhinitis, twelve years after the petrochemical complex began regular operations. In addition, a significantly higher incidence of bronchitis and asthma was also observed in the high exposure group, in the four years after starting the operations in the complex. These children were exposed to significantly higher levels of sulfur dioxide.

In addition to the above investigations conducted in Taiwan, other studies have been also carried out in other countries. In Cape Town (South Africa), White et al. (2009) assessed whether asthma symptom frequency among children living in an area near a petrochemical refinery was associated with exposure to refinery emissions by means of a cross-sectional study. Another goal of that study was to determine whether children in the evaluated area showed a higher prevalence of asthma symptoms than those living in other locations of Cape Town. It was observed that children residing in the areas near the petrochemical refinery had a higher prevalence of asthma symptoms than those – of the same age and socioeconomic status – living in other areas of the city. The results supported the hypothesis of an increased prevalence of asthma as a result of the refinery emissions. In turn, Wichmann et al. (2009) investigated the effect of exposure to particulate matter and VOCs on the respiratory health of children (6-12 years), who lived in an area close to the petrochemical plants of La Plata (Argentina). The data were compared with those corresponding to children with exposure to heavy traffic, and those living in two relatively nonpolluted zones of the same area. The results showed that living in the areas with higher levels of particulate matter and VOCs was associated with an increased prevalence of asthma, asthma exacerbations, respiratory symptoms, and a lower lung function. These effects were primarily seen in children from an area under the exposure to pollution from the petrochemical plants. In Brazil, Moraes et al. (2010) conducted a cross-sectional study of wheezing in children (0-14 years) who lived in the vicinity of the Guamaré (State of Rio Grande do Norte) petrochemical complex. Children were divided into two groups: exposed and reference communities. Air concentrations of PM_{10}, $PM_{2.5}$, black carbon, SO_2, NO_2, O_3, benzene, toluene, and xylenes were daily measured at a fixed monitoring station. Even at low concentrations of these air pollutants, respiratory symptoms were related with living downwind of a petrochemical plant. In Italy, Rusconi et al. (2011) evaluated lung function and markers of inflammation and oxidative stress in children (6-14 years) with and without asthma, or wheezing symptoms, living in a petrochemical polluted area (Sarroch, province of Cagliari), where one of the largest Mediterranean refineries is located, versus a reference area (Burcei). Children living in Sarroch – versus children living in the reference area – showed an increase in wheezing symptoms, a decrease in lung function, an increase in bronchial inflammation, and also an increase in malondialdehyde-deoxyguanosine (MDA-dG) adduct levels in nasal mucosa. This was consistent with the role of the environmental contaminants detected in the polluted area on lung function and inflammation. Recently, the same research group conducted a longitudinal study in children/adolescents (8–14 years) living near a major oil refinery in Sarroch (Italy) (Barbone et al., 2019). The study involved repeated clinical evaluations, in conjunction with air quality. The main goal was to identify any potential association between the exposure to sulfur dioxide and respiratory outcomes, regardless of co-pollutants. It was found that short term effects of exposure to SO_2 were associated with a reduction of lung function, as well as an increase in airway inflammation.

On the other hand, Tanyanont and Vichit-Vadakan (2012) conducted a population-based cross-sectional study, using data regarding respiratory problems among adults residing near a petrochemical complex in the Map Ta Phut Industrial Estate (MTPIE), which is located in the municipality of Map Ta Phut (Thailand). Data were obtained by means of a standardized questionnaire. The relationship between exposure to VOCs and human health was investigated, being the study focused on the potential association between living near the petrochemical complex and the increase of respiratory problems. It was found that residing near the complex was associated with more acute – but not with more chronic – respiratory problems than living farther from that complex. An increased risk of wheezing and upper respiratory symptoms was observed. The acute health effects of exposure to various air pollutants (PM_{10}, CO, total VOCs, ozone, SO_2 and NO_2) were also assessed for the population living near the area of MTPIE (Thailand) by Kongtip et al. (2013). Daily levels of air pollutants, as well as the daily percentage of respiratory (and other health) symptoms reported, were collected for 63 days. It was found that individuals residing near the MTPIE showed acute adverse health effects, shortness of breath, eye irritation, dizziness, cough, nose congestion, sore throat, phlegm, and weakness, as consequence of their exposure to air pollutants.

In residential areas near the industrial complex of the East End of Montreal (Canada), where two petroleum refineries are located, Kosatsky et al. (2004) reported that the annual rates of hospitalizations for respiratory health problems, among children 2–4 years old, were approximately 25% higher than those corresponding to Montreal Island children during the period 1996-2004. However, it could not be established if that excess was related to the emissions from the industrial complex, and if it was the case, whether the increased rates were related to short – or long – term exposures. In a subsequent study, Deger et al. (2012) used a case–crossover design to assess the risk of asthma episodes in children 2–4 years of age, who were exposed to SO_2 refinery stack emissions from the same industrial complex (East End of Montreal Island). According to the authors, their results suggested that same-day SO_2 peak levels – rather than daily mean levels – were associated with asthmatic episodes in children living in the vicinity of the refineries. In turn, Rodriguez-Villamizar et al. (2018) carried out a cross-sectional study to assess the potential associations between emergency department (ED) visits for childhood asthma and living near two industrial sources of air pollution in Edmonton (Alberta, Canada); a coal-fired power plant, and a petrochemical complex. In that city, studies conducted between 1992 and 2002 showed an increase in children's ED visits for acute asthma related to increased concentrations of nitrogen dioxide (NO_2), carbon monoxide (CO), ozone (O_3) and particulate matter ($PM_{2.5}$ and PM_{10}). However, these studies did not investigate the specific local sources of air pollution contributing to these potential associations. While the results indicated that there was a cluster of ED visits for asthma among children living near the coal-fired power plant, no asthma clusters were identified around the petrochemical industrial area. In this sense, Rovira et al. (2014) examined the prevalence of respiratory symptoms and lung function – in addition to asthma – in children (6-7 years) and adolescents (13-14 years) living near the petrochemical complex of Tarragona, which is the largest of Southern Europe. Children and adolescents living in the vicinity of that complex showed a significantly higher prevalence of respiratory hospitalizations the previous year, and of nocturnal cough, respectively, which would be related to short-term exposure to air pollutants. However, a higher prevalence of asthma in children and adolescents residing in the neighborhood of the petrochemical sites could not be demonstrated. Finally, Sopian et al. (2016), in review on respiratory effects, concluded that short-term petrochemical air pollutant exposure increases respiratory symptoms, reduces lung function, and increases the incidence of asthma, especially for children living within 5 km radius from this kind of industries.

3. Reproductive outcomes

Exposure to air pollutants during gestational periods can cause adverse outcomes mainly affecting the fetal growth and gestational duration (Bonzini et al., 2010, Dadvand et al., 2013a,b; Pedersen et al., 2014). In this sense, it should be noted that a pregnant woman significantly increases the volume and oxygen consumption due to the respiratory adaptation to pregnancy (Chang and Streitman, 2012). Over the last 15 years, a significant number of reviews can be found in the scientific literature. The effects of ambient air pollution on adverse pregnancy and birth outcomes, basically low birth weight, preterm, and small for gestational age births are discussed (Maisonet et al., 2004; Srám et al., 2005; Wigle et al., 2008; Shah et al., 2011; Stieb et al., 2012; Kihal-Talantikite et al., 2017; Li et al., 2017; Li et al., 2019; Liu et al., 2017; Klepac et al., 2018). The reported adverse effects are mainly related to exposure to carbon monoxide, nitrogen dioxide, sulfur dioxide, ozone and particulate matter ($PM_{2.5}$ and PM_{10}) (Qian et al., 2016; Wu et al., 2016). However, in a recent paper on environmental and individual exposure and the risk of congenital anomalies, in which two systematic reviews with metanalyses, two multicenter studies, and nine single studies, were analyzed and discussed, the epidemiological evidence for a causal association between air pollutants exposure, and the risk of congenital anomalies was limited (Baldacci et al., 2018). Emissions of these air pollutants are caused by combustion processes from motor vehicles, solid fuel burning and industrial activities. In addition, certain industries such as petrochemical and oil refineries emit also specific contaminants such as volatile organic compounds (VOCs) - including BTEX and 1,3-butadiene-, as well as polycyclic aromatic hydrocarbons. In contrast to the abundant literature on the effects of general ambient air pollution on pregnancy and birth outcomes (Hehua et al., 2017; Li et al., 2017; Klepac et al., 2018; Porpora et al., 2019), information on the effects for pregnant women living near petrochemical complexes is much more limited.

Taiwan is probably the country where most of these investigations have been conducted. In fact, the petrochemical industry was being the main source of industrial air pollution in that country at the beginning of this century (Lin et al., 2001a,b; Yang et al., 2002a,b). Lin et al. (2001a) reported a significantly increased prevalence of delivery of preterm birth infants in mothers residing in a petroleum refinery area compared to controls of the same country. The prevalence of term low birth weight in the petrochemical and control areas was 3.22%, and 1.84%, respectively, being the adjusted odds ratio – after controlling for possible confounders – for term low birth weight, 1.767 in the petrochemical area (Lin et al., 2001b). In contrast, Yang et al. (2002a) reported that residential exposure to air pollution, specifically the pollution caused by the petrochemical industry, did not result in a significant increase of term low body weight (4.72% vs. 4.58% for controls) and preterm delivery (2.51% vs. 2.35% for controls). However, the same research group (Yang et al., 2002b) reported a significantly higher prevalence of delivery of preterm birth infants in mothers living near petrochemical industrial complexes than in control mothers. Notwithstanding, Yang et al. (2002a,b) remarked some methodological limitations of their investigations. In a subsequent study, a significant increased risk of preterm delivery was observed among infants of mothers living in the vicinity of three oil refineries of Taiwan (Yang et al., 2004). In turn, Tsai et al. (2003) reported also a significant high prevalence of delivery of preterm-birth infants in mothers living in an industrial area of Taiwan compared to control regions of that country. Infants with a lower birth weight were also significantly more prevalent in mothers, who during the gestational periods lived in a petrochemical industrial city (Kaohsiung), with an important air pollution, than in those living in a non-petrochemical industrial city (Taipei). Significantly higher concentrations of SO_2, O_3, and PM_{10} were found in Kaohsiung when compared with Taipei (Lin et al., 2004a). Maternal exposure to these air pollutants has been related with a higher risk of low birth weight in Taiwan (Lin CM et al., 2004b; Seo et al., 2010).

In addition to the investigations carried out in Taiwan, some studies conducted in other countries are also available in the scientific literature. In China, Xu et al. (1998) investigated the potential association between petrochemical exposure and spontaneous abortion in a large petrochemical complex of Beijing by means of a retrospective epidemiological study. An increased risk of spontaneous abortion was associated with exposure to benzene, gasoline and hydrogen sulfide. However, it needs to be highlighted that in contrast to the above revised studies, the pregnant women involved in this epidemiological study were employees of the complex. In Brazil, Oliveira et al. (2002) conducted a case-control study in an area adjacent to a petrochemical plant at the south of the country. That study was aimed at evaluating whether there was a relationship between adverse reproductive outcomes and the place of residence of the mothers. As outcomes for analysis, low birth weight newborns, stillborn, and newborns with major malformations, were selected as outcomes for analysis. The 15-year birth data analysis of congenital malformations, low birth weight, and stillbirths in the area under evaluation did not show significant increases in the incidence of the selected outcomes. On the other hand, Svechkina et al. (2018) carried out a study in the Haifa Bay area (Israel), where heavy industries, including chemical processing plants, and major oil refineries are located. That survey was focused on assessing the environmental risk factors associated with low birth weight. The results revealed an excess rate of low birth weight in residential areas located close to the petrochemical industrial complex, which was located in the central part of the study area. It was attributed to the potential exposure to VOCs and semivolatile organic compounds (sVOCs) emissions, which are known to be associated with adverse birth outcomes of the residents living near this petrochemical industrial complex. In another vein, but also potentially related with adverse effects during pregnancy, Ausili et al. (2008) reported toxicological risks for pregnant women, possibly involving an elevated frequency of neonatal malformations, when an ecotoxicological study was conducted in the petrochemical district of Priolo (Sicily, Italy). Elevated mercury concentrations were detected in marine organisms, which should mean potential risks for human health from seafood consumption. The incidence of neonatal malformations in that area was previously reported to be more than 3-fold higher than the national average (Bianchi et al., 2004).

4. **Other adverse health effects**

Most studies concerning potential adverse health effects for the populations residing in areas surrounding petrochemical industries are mainly focused on cancer (Domingo et al., 2020), respiratory problems, as well as undesirable effects during pregnancy (see the above sections, 2 and 3). However, few studies have also investigated other potential adverse effects in other different organs/tissues. For example, Camargo et al. (2006) compared the prevalence of chronic autoimmune thyroiditis between people living in the vicinity of the petrochemical complex of Capuava and those residing in a control area (São Bernardo do Campo), both urban areas of metropolitan Sao Paulo (Brazil). The prevalence in the petrochemical complex was 14.6% and that in the control area 19.5%, but the difference was not statistically significant. In contrast, in a more recent study conducted in the same areas, de Freitas et al. (2010) found a prevalence of 9.3% and 3.9% ($p < 0.01$) in the complex area and in the control area, respectively. In order to avoid divergences between the results of both investigations, the data corresponding to the de Freitas et al. (2010) survey were classified according to the same criterion used by Camargo et al. (2006). After this, prevalence remained significantly higher in the petrochemical complex than in the control area: 31.3% and 19.7%, respectively. In turn, in recent years, Zaccarelli-Marino et al. (2016) compared the occurrence of primary hypothyroidism (PH) in children and adults of both sexes living also in the surroundings of the petrochemical complex of Capuava (Sao Paulo, Brazil). It was concluded that living near a petrochemical complex might be an important risk factor for PH, in both adults and children. It was found that the odds of PH for residents in the surroundings of petrochemical plants were larger than those for residents in a control area, having also an increasing trend over the study period (1989-2004). In a subsequent survey of the same group (Zaccarelli-Marino et al., 2019), the association between the atmospheric concentrations of nitrogen dioxide, carbon monoxide, particulate matter (PM_{10}), sulfur dioxide and various VOCs, and the primary PH occurrence odds, was investigated in residents living in the area of influence of the Capuava petrochemical complex. The odds for PH showed a clear trend to increase when NO_2, CO, and VOCs concentrations increased. However, a similar pattern was not observed for PM_{10} and SO_2. On the other hand, because the petrochemical industry is one of the most important sources of benzene (Verma et al., 2001; Bahadar et al., 2014), Silva et al. (2019) assessed the impact of benzene on the health of the population living near the municipality of Duque of Caixas (Rio de Janeiro State, Brazil), where there is a group of over 25 industries including the second largest oil refinery in Brazil. Urinary S-phenylmercapturic acid (S-PMA) and polymorphism (CYP2E1-1293G>C and NQO1 609C>T) were determined in residents near the refinery. The quantifiable presence of urinary S-PMA was associated with the detection of some specific hematological changes (e.g., leukocyte values, mean corpuscular volume, and neutrophils) in 60% of the participants, being also related to the environmental exposure to benzene. Moreover, the presence of the variant allele in the NQO1 genotype might be a risk factor for the detected hematological changes. Likewise, with respect to potential hematological changes, Chen et al. (2019) examined the effects of benzene, toluene, ethylbenzene and xylene (BTEX) on the hematologic system of elderly individuals living near petrochemical complexes in Nanjing (China), who were compared with a control group formed by residents in a community free of petrochemical air pollution. Higher blood BTEX levels, and decreased red blood cell counts, hemoglobin concentration, hematocrit, mean corpuscular hemoglobin concentration, and platelet counts, were found among the residents living in the vicinity of the petrochemical areas.

A couple of studies on visual-motor coordination deficit and short-term memory dysfunction have been conducted in children living near the MTPIE (Thailand). Aungudornpukdee and Vichit-Vadakan (2009) investigated the factors that affected visual-motor coordination deficit among 2956 children (6-13 years), who lived near the MTPIE. Although one-third of the children showed visual-motor coordination deficits, the factors causing these deficits were related with gender, monthly parental income, and household tobacco smoke, but not specifically with living near the MTPIE. However, in a second study conducted with 2158 children (6-13 years) of the same area, it was found that one-third of these children showed short-term memory dysfunction, which was related with the distance from residential areas to the sources of environmental pollution (Aungudornpukdee et al., 2010).

Some studies on the adverse effects on renal and hepatic functions for individuals living in the vicinity of petrochemical complexes are also available in the scientific literature. The most common environmental air pollutants emitted by petroleum industries are SO_2, nitrogen oxides, VOCs, PM and PAHs. Nevertheless, various heavy metals are also emitted (Nadal et al., 2004, 2007, 2011; Relić et al., 2019), being arsenic, cadmium, mercury and thallium, and PAHs, associated with kidney impairment. To assess the potential association between renal functions and pollutants exposure in adults living in the neighborhood of a big petrochemical complex in Taiwan, Yuan et al. (2020) determined the urinary levels of arsenic, cadmium, mercury, thallium, and 1-hydroxypyrene (1-OHP) (a known marker of PAH exposure) of these individuals. The subjects with the highest urinary concentrations of arsenic and 1-OHP – who were potentially contaminated from the petrochemical complex – showed a lower renal function and a higher risk of chronic kidney disease. It has been also demonstrated that emissions from a petrochemical complex in Taiwan could increase particle-phase PAH concentrations in surrounding areas, while increased the urinary 1-OHP levels of adults living nearby (Yuan et al., 2015). PAH exposure and its potential genotoxic effects were also evaluated in children living near a petrochemical complex in Coatzacoalcos County (Veracruz, Mexico) (Sánchez-Guerra et al., 2012), a region with many petrochemical industries, representing up to 80% of the total petrochemical activity of Mexico. The results for urinary levels of 1-OHP revealed that children living in one of the main petrochemical areas of Mexico were exposed to high PAH concentrations, which might induce genetic damage and represent a significant health risk factor for these children.

On the other hand, Huang et al. (2016) evaluated whether the concentrations of urinary thiodiglycolic acid (TDGA) in school-aged children, decreased depending on the distance of their schools to a nearby petrochemical complex in central Taiwan. The median urinary level of TDGA for school-aged children was significantly increased with shorter distances between the schools and the different factories of the petrochemical complex, mainly those producing vinyl chloride/polyvinyl chloride. The median urinary TDGA level for the children during school time, was four times higher than that observed during the summer vacation. In the same line, Wang et al. (2019a) assessed the non-alcoholic fatty liver disease (NAFLD) by determining urinary TDGA in children (6-13 years) residing near a petrochemical complex of central Taiwan. NAFLD is a chronic liver disease, in which excessive fat (> 5%) is accumulated in the liver. Interestingly, it can develop into end stage liver disease, with consequent increase risk of liver transplantation, being required during adolescence or early childhood. The results supported the hypothesis that the children living near the petrochemical complex, who had higher urinary TDGA concentrations, also had significantly increased NAFLD risks. A similar conclusion was also reached with the results of a second study conducted by the same researchers (Wang et al., 2019b) in the same cohort of children (6-13 years). These children lived within 10 km nearly a petrochemical complex in central Taiwan. The potential association between urinary TDGA and abnormal liver function and hepatic fibrosis index, with the place of residence of the children was assessed. The results were consistent with the hypothesis that urinary TDGA level in children living near this petrochemical complex was associated with the children's susceptibility to hepatotoxicity. On the other hand, recently Zheng et al. (2020) studied the composition (especially the halo hydrocarbons), sources, and human health risks of a number of VOCs in petrochemical industrial parks of China. Alkanes were the predominant group, which was followed by alkenes, oxygenated VOCs, halo hydrocarbons, aromatics and acetylene. The non-cancer risks of four VOCs sources were above the safe levels, with regional background contributing most to the hazard ratio (HR). Compound-specific health risk results showed that acrolein and 1,3-butadiene had the highest non-carcinogenic risk (HR: 22.8).

Conclusions

Despite the tremendous importance of petrochemical industries/oil refineries worldwide, there is a lack of scientific information regarding the potential adverse health effects for the population living in their neighborhood. Main human health risks are related with the increases in the number of cancers – mostly hematological – and in cancer mortality, as well as in the cases of asthma and other respiratory problems. In this paper, we have reviewed the association between the adverse effects on the respiratory system, reproduction, as well as other than cancer for those individuals residing near petrochemical complexes. Similar to the results found in our recent Review on cancer (Domingo et al., 2020), most of the above reviewed studies have reported increases in the prevalence of the examined adverse health effects, for the populations (children, adults, and pregnant women) living in the surroundings of the complexes. The results here summarized, clearly indicate that living near petrochemical complexes increases health risks. Therefore, we strongly recommend conducting all the necessary studies for each specific petrochemical complex to significantly reduce the levels of air pollutants, and consequently, decrease human health risks. For that purpose, different approaches, such as investigations focused on air emissions or health risk assessment, can be simultaneously followed.

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Table 1
A summary of international scientific studies with associations between negative health outcomes and proximity to petrochemical industries.

Location	Period of time	Population under study	Health outcome	Results	Reference
Taiwan	1996	Adults (30-64 years) living near the petrochemical industrial area of Sanwei	Irritant health outcomes	Acute irritative symptoms occurs more frequently in individuals living near to petrochemical manufacturing facilities than in control subjects	Yang et al. (1997)
Taiwan	1994-1995	Children (primary school) living close to the petrochemical complex of Linyuan	Respiratory symptoms and illness	Asthma and other respiratory symptoms were more prevalent in children living near the petrochemical area than those living in the control	Yang et al. (1998)
Taiwan	1994	Children (primary school) living in the surroundings of the petrochemical complexes of Toufen, Jenwu and Linyuan	Respiratory symptoms and diseases	Children living close to the petrochemical industries presented more nasal symptoms than those residing in the reference areas	Chen at al. (1998)
Taiwan	1999-2010	Children (11-14 years) living within 10 km of the Petrochemical complex No. 6 Naphtha Cracking.	Respiratory diseases	Higher incidence of bronchitis and asthma in children living close to the petrochemical complex 4 years after it started the operations. Higher incidence of allergic rhinitis in children after 12 years	Chiang et al. (2017)
South Africa	Not available	Children (11-14 years) living in the vicinity of the petrochemical complex in Cape Town	Asthma symptom frequency	Increased prevalence of asthma in children living near the petrochemical refinery	White et al. (2009)
Argentina	2005-2006	Children (6-12 years) living close to the petrochemical plants of La Plata	Asthma, asthma exacerbations, symptoms	Children living near the petrochemical plant had more asthma, asthma exacerbations and respiratory symptoms, but lower lung function, than those living in reference regions.	Wichmann et al. (2009)
Brazil State of Rio Grande do Norte	2006	Children (0-14 years) living in the vicinity of the Guamaré petrochemical complex	Wheezing	Wheezing in children and adolescents was associated with living downwind of a petrochemical plant, being male preschoolers the most vulnerable group	Moraes et al. (2010)

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Italy	Not available	Children (6-14 years) living in Sarroch (petrochemical area)	Asthma symptoms, lung function and markers of oxidative stress and inflammation	Children living in the petrochemical polluted area of Sarroch vs. those of Brucei area showed an increase in wheezing symptoms, a decrease in lung function, an increase in bronchial inflammation, and an increase in MDA-dG adducts.	Rusconi et al. (2011)
Italy	2007	Children (8-14 years) living in Sarroch, Sardinia.	Respiratory function, respiratory symptoms	Exposure to SO_2 is strongly associated with reduction of lung function and an increase in airway inflammation.	Barbone et al. (2019)
Thailand	2007-2008	Adults (>13 years) living near a petrochemical complex in Map Ta Phut Industrial Estate (MTPIE)	Chronic respiratory symptoms, respiratory symptoms and acute respiratory symptoms	Residing near the complex was associated with more acute -but not with more chronic- respiratory problems than living farther from that complex. An increased risk of wheezing and upper respiratory symptoms was observed.	Tanyanont et al. (2012)
Thailand	2009-2010	Adults (18-60 years) living near a petrochemical complex in Map Ta Phut Industrial Estate (MTPIE)	Respiratory symptoms and other health symptoms	Individuals residing near the MTPIE showed acute adverse health effects, shortness of breath, eye irritation, dizziness, cough, nose congestion, sore throat, phlegm, and weakness, as consequence of their exposure to air pollutants.	Kongtip et al. (2013)
Canada	1996-2004	Population (0-74 years) living near the industrial complex of the East End of Montreal, where two petroleum refineries are located	Respiratory health problems	The annual rates of hospitalizations for respiratory health problems, among children aged 2–4 living the industrial complex, were approximately 25% higher than those corresponding to Montreal Island children. However, excess could not be related to chemical emissions by the industrial complex	Kosatsky et al. (2004)

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Canada	2006	Children (6 months – 12 years) living under the influence of the oil refineries of Montreal east-end industrial complex	Asthma and poor asthma control	A relationship between exposure to refinery stack emissions of SO2 and the prevalence of active and poor asthma control in children living and attending school in proximity to refineries	Deger et al. (2012)
Canada	2004-2010	Children (2-14 years) with asthma diagnosis in a hospital emergency department in the Edmonton metropolitan area	Asthma	A cluster of ED visits for asthma among children living near to the coal-fired power plant was found, but not for those living in the vicinity of the petrochemical complex	Rodriguez-Villamizar et al. (2018)
Spain	2010	Children (6-7 years) and adolescents (13-14 years) living near (north and south) the petrochemical complex of Tarragona, Tarragona city and rest of the county (reference)	Lung function, asthma, rhinitis and eczema, hospitalizations by respiratory disease	Children and adolescents living near a petrochemical site only showed a higher prevalence of respiratory hospitalizations in the previous year and of nocturnal cough	Rovira et al. (2014)
Taiwan	Not available	Mothers residing in communities in close proximity to a petroleum refinery plant	Delivery of preterm birth infants	The prevalence of delivery of preterm birth infants was significantly higher in mothers living in a petroleum refinery area compared to controls in Taiwan	Lin et al. (2001a)
Taiwan	Not available	Mothers residing in communities in close proximity to a petroleum refinery plant	Low birth weight	The prevalence of low birth weight in the petrochemical and control areas was 3.22% and 1.84, respectively.	Lin et al. (2001b)
Taiwan	1993-1996	Mothers living near the three petrochemical complexes in the north of Kaohsiung county (Complex A, Ta-sher and Jen-Wu)	Delivery of preterm birth infants	Higher prevalence of delivery of preterm birth infants in mothers living near petrochemical industrial complexes than in control mothers	Yang et al. (2002b)

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Taiwan	Not available	Mothers living close to the petrochemical industrial city (Kaohsiung)	Delivery of preterm-birth infants	Infants with a lower birth weight were also significantly more prevalent in mothers, who during the gestational periods lived in a Kaohsiung than in Taipei, a non-petrochemical industrial city	Tsai et al. (2003)
China	1993	Pregnant women, employees of a large petrochemical complex in Beijing	Spontaneous abortion	An increased risk of spontaneous abortion was associated with exposure to benzene, gasoline and hydrogen sulfide	Xu et al. (1998)
Brazil	1983-1998	Children born in the adjacent area to the Southern Petrochemical Complex (Complexo Petroquímico do Sul – COPESUL)	Congenital malformations, low birth weight, stillborn babies	A correlation between low birth weight and geographical proximity of mother's residence to the petrochemical plant or residence on the way of preferential wind direction was found	Oliveira et al. (2002)
Israel	2015	Children born in the Haifa Bay Area (distance to industrial facilities from 1 to 5 km)	Low birth weight	Significant decrease in the low birth weight rate as a function of the distance from the petrochemical industrial complex	Svechkina et al. (2018)
Brazil	Not available	Individuals (males and females) > 20 years living in the vicinity of the petrochemical complex of Capuava (Sao Paulo)	Hashimoto's thyroiditis	The prevalence of chronic autoimmune thyroiditis in the petrochemical complex was higher than in the control area	Freitas et al. (2010)
Brazil	1989-2004	Children and adults living in the surroundings of the petrochemical complex of Capuava (Sao Paulo)	Primary hypothyroidism	Living near a petrochemical complex might be an important risk factor for primary hypothyroidism, in both adults and children	Zaccarelli-Marino et al. (2016)
Brazil	2017	Residents living in the area of influence of the Capuava petrochemical complex (Sao Paulo)	Primary hypothyroidism	Primary hypothyroidism increases as concentrations of NO2, CO and VOCs increase	Zaccarelli-Marino et al. (2019)

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Brazil	Not available	Population living near the municipality of Duque of Caixas	Hematological changes	The presence of urinary S-phenylmercapturic acid and the variant allele in the NQO1 genotype were associated to hematological changes	Silva et al. (2019)
China	2016	Residents living near the petrochemical complex of Nanjing (Jiangsu)	Hematologic system	The increased blood BTEX levels in residents are associated with the reduction in red blood cells counts, hemoglobin concentration, hematocrit, mean corpuscular hemoglobin concentration, and platelet counts	Chen et al. (2019)
Thailand	Not available	Children (6-13 years) living near	Short-term memory dysfunction	Short-term memory dysfunction was found to be related with the distance from residential areas to the sources of environmental pollution	Aungudornpukdee et al. (2010)
Taiwan	2009-2012	Adults (>35 years) living at the same address during the previous 5 years	Renal functions	The subjects with the highest urinary concentrations of arsenic and 1-hydroxypyrene, potentially contaminated from the petrochemical complex, showed a lower renal function and a higher risk of chronic kidney disease	Yuan et al. (2020)
Taiwan	2013-2014	Children (6-13 years) residing near a petrochemical complex of central Taiwan	Non-alcoholic fatty liver disease	Children living near the petrochemical complex showed higher concentrations of urinary thiodiglycolic acid and significantly increased non-alcoholic fatty liver disease	Wang et al. (2019a)
Taiwan	2013-2014	Children (6-13 years) residing near a petrochemical complex of central Taiwan	Liver function	Children with the highest concentration of TDGA living near this petrochemical complex had significantly increased subclinically abnormal aspartate aminotransferase	Wang et al. (2019b)