

Hazardous Environmental Exposure & Maternal Health

Capstone

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1. Abstract

Background

An estimated 12.6 million death globally were attributed to the environment in 2012, representing 26% of total deaths. Pregnant women represent a vulnerable group regarding their health and their unborn children.

Objectives

To investigate an association between environmental pollutants and maternal morbidities, and to develop policy recommendations.

Methods

For the literature review the data bases pubmed, cochrane and google scholar were searched. 18 studies and one meta-analysis were selected for the review.

Discussion

Associations between ambient and indoor air pollution as well as heavy metal exposure and gestational diabetes mellitus, hypertensive disorders and anemia in pregnancy could be presented. Especially women in low – and middle – income countries are affected.

The global public health threat from environmental pollution needs to be recognized and acted on; especially regarding vulnerable groups like pregnant women and children, who are the fundament of a future society.

2. Introduction

In recent years evidence for adverse health effects due to hazardous environmental pollutants became well established. An estimated 12.6 million death globally were attributed to the environment in 2012, representing 26% of total deaths (Prüss-Ustün et al., WHO, 2016). A recently published article by the Lancet (Landrigan et al., 2017) estimates 9 million premature deaths caused by pollution (16% of global deaths), three times more than from tuberculosis, AIDS and malaria combined and fifteen times more than from wars and any forms of violence together. The differences in numbers from the WHO and the Lancet can be explained by the definition of environment and pollution. Both estimated numbers show us the significance of the issue. The Lancet states:

"Pollution is the largest environmental cause of disease and premature death in the world today." (Landrigan et al., 2017)

The World Health Organization (WHO) estimates around 6.5 million premature deaths (11.6 % of all global deaths) worldwide caused by air pollution alone and states that indoor and outdoor air pollution is the source of heart disease, lung cancer, stroke and both chronic and acute respiratory diseases, including asthma (WHO, 2016). However, beside air pollution also exposure through water, soil, food, waste, agriculture and household hazards add to the global burden of disease (WHO, 2017).

Pregnant women, as well as the intrauterine fetus and born children, belong to a vulnerable group regarding health and especially environmental hazards. This paper focuses on environmental pollutants and the health effects on pregnant women. Not to neglect the fact that the health of newborns and children is highly related and dependent on the mother`s

health and also her exposure to environmental impacts during pregnancy and times of breastfeeding.

Why are pregnant women a vulnerable group for whom we should have higher concerns? Primarily, pregnant women give birth to the fundament of every society – the children. We need healthy pregnant women to give birth to healthy newborns and we need healthy children, as they are the future of every society. However, there are also physiological as well as behavioral reasons why they belong to vulnerable groups. Environmental exposures to specific food, chemical and biological agents, of a pregnant woman can have a negative impact on the fetus as well as on the health of the mother (Ondeck, 2009). The bio-chemical mechanism of adverse effects on the fetus or the mother`s health through environmental exposure, is not yet completely understand, researchers assume that it has to do with oxidative stress and inflammation induced by pollutants (Lavigne et al., 2016; Novack et al., 2016). Further on, pregnancy has an immense impact on physical processes and leads to endocrinal and cardiovascular changes, e.g. increased blood volume and oxygen consumption and altered blood pressure (Männistö et al., 2014). During these changes pathological processes can develop and lead to conditions such as gestational diabetes or pregnancy-induced hypertensive disease disorders. Associations between air pollution and pregnancy-related morbidities such as preeclampsia and gestational hypertension were found, both morbidities have health effects on the mother and the fetus (Landau & Novack et al., 2015; Novack et al., 2016; Lavigne et al., 2016;).

The idea for this paper was inspired by several articles published by a research group in the South of Israel, researching the environmental exposures of pregnant Bedouin women and adverse birth outcomes. After contacting the research group, the idea of a possible master`s

thesis was discussed on follow-up health data from the women and children, regarding possible health outcomes related to the measured exposures. This capstone-paper reviews and discusses the latest articles published on environmental exposure and maternal morbidities, e.g. gestational diabetes mellitus and pregnancy induced hypertensive disorders. The research on pregnant Bedouin women is presented in the chapter below.

2.1 Environmental exposures of pregnant Bedouin women in Israel

A group of researchers from the Ben Gurion University in cooperation with the Soroka University Medical Center, both located in Beer-Sheva in the south of Israel, published several papers about the environmental exposure of pregnant Bedouin-Arab women. Results of several studies with different sample sizes between 140 to 1'024 Bedouin women admitting for birth in the Soroka University Medical Center, were analyzed. The Bedouins in Israel are a low-socioeconomic minority in transition, in the south of Israel live around 200'000 Bedouins. An estimated 50 % live in traditional tribal settlements, residing in temporary shacks and tents surrounded by the geographical environment of the Negev desert. The low-socioeconomic status is – besides cultural, traditional and historical-political reasons - due to low educational level and high unemployment. The population is exposed to higher levels of environmental pollutants due to geographical as well as life-style reasons additionally the local industrial park poses another risk (Karakis et al., 2015). Landau et al. (2015) investigated about nitrogen dioxide (NO₂) or hazardous household exposure in association with congenital malformations and was able to show that minor malformations were associated with NO₂ exposure and major malformations with hazardous exposure in a household. Novack et al. (2016) analyzed the cell proliferation in umbilical blood cord samples in relation to ambient air pollution, a possible association was

shown, what would add to possible explanations about the bio-chemical mechanism of the pathological processes. And further, Karakis et al. (2015) studied an association between metal exposures and congenital malformations. In almost 30 % of the women metals were found in the urine, especially exposure to hazardous household was related to metals in urine. Aluminum exposure was associated with malformations and Arsenic exposure to preterm deliveries and lower birth weight. Interestingly, during the research a link to maternal pathologies was observed as well (Novack et al., 2016). Based on the findings of the research discussed in this chapter, for a possible follow-up of the data from the Bedouin women and their health, the literature was searched for possible association between environmental exposures and maternal pathologies.

3. Environmental Pollutants

Humans and every other living being is surrounded and influenced by the environment - nature and human made - they are living in, and have their own impact on the environment. With the industrialization and modernization in the last 200 to 500 years, the influence of humans on their surrounding environment changed enormously. The fast growing world population, the development of different industries and technologies, changed - and still changes - the environment and developed beside other effects in the today's known climate change. The Lancet discusses an increase of ambient air, soil and chemical pollution in the last 500 years (Landrigan et al., 2017). Beside the many benefits of modernization and industrialization for the humans, the side-effects of these change in the last 200 to 500 years, do not only have an - partly disastrous - impact on our surrounding environment, it also impacts the humans themselves, the physical as well as the emotional health.

The main environmental pollutants associated with adverse health outcomes are chemicals, biological agents or metals produced by transportation, industries, mechanized agriculture, mining, electricity generation, waste, geographical conditions (sand, dust), heating and cooking with biomass (Landrigan et al., 2017)

3.1 Environmental Pollutants and Maternal Health

Many studies researched the association between environmental pollutants and the adverse birth and or neonatal outcomes. Associations were found for preterm deliveries, small for gestational age (SGA) as well as low birth weight, others results showed associations with minor malformations (Lavigne et al., 2016; Karakis et al. 2015). However, the results are not always consistent. These literature review focuses on the effects on the mother`s health, less literature exists in this field. Most studies focused on two main groups of maternal pathologies, gestational diabetes mellitus and hypertensive disorders. The evidence is not always solid, however, several studies found an association or interesting results which are a fundament for further research and are worth considering. Furthermore the interaction between maternal morbidities and adverse neonatal outcomes, e.g. SGA, macrosomia or preterm birth needs to be considered. The bio-chemical mechanism, how environmental pollutants affect maternal health and can lead to pathologies stays unclear, several hypotheses exist and researchers assume oxidative stress and pro-inflammatory action caused by pollutants, also epigenetic mechanism are studied and discussed (Jedrychowski et al., 2012).

4. Maternal pathologies

The majority of pregnant women are healthy and pregnancy is not a state of disease. However, there are pregnancy related pathologies like gestational diabetes mellitus or hypertensive disorders. Many physical functions are affected and changed through pregnancy, for example the endocrine system, the blood volume and blood pressure (Page et al., 2015)

4.1 Gestational Diabetes Mellitus

Gestational diabetes mellitus (GDM) is defined by the WHO as "*a carbohydrate intolerance resulting in hyperglycemia of variable severity with onset or first recognition during pregnancy*" (WHO, 2013). The prevalence of GDM is globally increasing and the reasons are most likely multifactorial, environmental factors are part of the discussion. The prevalence and incidence in the literature is estimated and discussed around 4-14% worldwide (Shapiro et al., 2015; Peng et al., 2015). The established time to test for GDM is between the 24th to 28th weeks of gestation. Associations between increased plasma glucose level and adverse fetal and maternal outcomes are well established. Adverse outcomes include macrosomia, large for gestational age (LGA), shoulder dystocia and preeclampsia (WHO, 2013). GDM can have long-term health effects, 2 in 3 women with GDM develop diabetes type 2 later in life (Malmqvist et al., 2013).

4.2 Hypertensive Disorders in Pregnancy

The group of hypertensive disorders of pregnancy includes gestational hypertension, chronic hypertension, preeclampsia and eclampsia. Estimated around 10% of pregnant

women are globally affected. The main symptom for hypertensive disorders is high blood pressure (hypertension) and an additional proteinuria (high levels of protein in urine) leads to the diagnosis of preeclampsia, which again can lead to the severe form of an eclampsia (seizures). Preeclampsia and eclampsia especially can have a damaging impact on the mother's and child's health. However, until today the pathogenesis is not completely understood. Explanations include disturbance in placentation in the beginning of pregnancy, followed by generalized inflammation and endothelial damage. Obesity, diabetes and chronic hypertension are some of the risk factors (WHO, 2011). Pregnancy induced hypertensive disorders have been associated with increased risk for chronic hypertension, endothelial dysfunctions and renal disease later in life (Farzan et al., 2015).

5. Literature Search

The literature search was performed on the database pubmed, cochrane and google scholar. Most articles were published between the years 2014-2017, except two articles from the year 2012 and 2013.

Keywords for exposure included: air pollution, environmental pollutants, environmental hazards, environmental exposure, indoor air pollution, persistent organic pollutants, heavy metals (biomarkers), aluminum, lead, arsenic exposure, nitrogen dioxide.

Keywords for the outcomes: Maternal health, environmental health, maternal (co-) morbidities, pregnant women, health effects pregnancy, hypertensive disorders, pregnancy-induced hypertension, hypertensive disorders of pregnancy, gestational diabetes mellitus, hypertensive disorders, preeclampsia, preeclampsia eclampsia, postpartum depression, depression pregnancy, thyroid pregnancy, thyroid hormones pregnancy.

18 studies and one meta-analysis were selected and are discussed in the chapters followed below:

6. Air Pollution

Air pollution is defined by two main groups: Ambient air pollution (AAP) and indoor (household) air pollution (IAP). The World Health Organization states that today air pollution is the biggest environmental risk factor. AAP can have many different sources, ranging from transportation, industries as well as geographical conditions such as dust and sand. AAP is measured mainly by the levels of nitrogen dioxide (NO₂), carbon monoxide (CO), sulfur dioxides (SO₂), ozone (O₃) and particulate matter (PM₁₀ and PM_{2.5}). Particulate matter itself is mostly composed by a mixture of solid and liquid particulates of organic and inorganic substances, composed mainly from sulfates, nitrites, ammonia, sodium chloride, ammonia, black carbon, mineral dust and water. All air pollutants are associated with increased morbidity and mortality (WHO, 2016). Indoor pollution is mainly caused by cooking and heating with biomass on an open fire and second hand smoking. An estimated 3 billion people are still relying on solid fuels to cook and heat, like wood, animal dung, charcoal, coal and crop wastes. IAP is measured mostly by the levels of particulate matter (PM_{2.5}) and carbon monoxide (CO) (WHO, 2014).

6.1 Ambient Air Pollution and Hypertensive Disorders

2014 a systematic review and meta-analysis was published by Pedersen et al. (2014) analyzing the association between ambient air pollution and pregnancy-induced hypertensive disorders. A total of 17 articles including over 1'000'000 pregnancies were analyzed. The results suggest evidence for a correlation between ambient air pollution

exposure and pregnancy-induced hypertensive disorders, although a significant heterogeneity between the articles exists.

The results of Savitz et al. (2015) do not support an association between ambient air pollution and hypertensive disorders in pregnancy. In their large sample size study in New York they examined hospital discharge diagnosis from 268`601 births and estimates of PM_{2.5} and NO₂ exposure levels according the maternal residual address. In unadjusted analysis, they found a positive association between exposure and risk of gestational hypertension. After adjustment, especially for the confounder 'delivery hospital', no evidence was established. The authors explained the confounder 'delivery hospital' with "institutional-level differences in disease coding and diagnosis".

A research group in Denmark (Pedersen et al., 2017) studied the impact of road traffic pollution on preeclampsia and pregnancy-induced hypertensive disorders. Data from 72'745 singleton pregnancies were collected by general practitioners inclusive computer-assisted telephone interviews with follow-up interviews. Exposure was calculated with the residential address and the estimation of the AirGIS dispersion model. Interestingly in this study, the impact of road traffic was measured by estimated NO₂ concentration as well as the noise exposure. Pedersen et al. found an association between NO₂ exposure and road traffic noise with preeclampsia and gestational hypertension.

Another study by Jendrossek et al. (2017) in Germany did not find significant results regarding residential air pollution, traffic, greenness and maternal hypertension. In this comparison of two populations (n=3063), only in one residential area an association with PM_{2.5} and maternal hypertension was found. The research group also looked at the factor

'greenness' by expecting a positive effect on hypertensive disease due to a green environment, based on results of another study mentioned in the article, however in this study no significant effects were found. Compared were two populations (n=3063).

Männistö et al. (2014) showed with their results a direct impact of acute air pollution exposure on the blood pressure at the hospital admission of pregnant women for delivery. The exposures of NO_x, SO₂ and CO were associated with increased blood pressure among normotensive (normal blood pressure) women and had the same or even stronger effect on pregnant women with gestational hypertension or preeclampsia.

In a study with a large cohort of around 100'000 women, Olsson et al. (2015) studied the possible association between traffic air pollution (NO_x) and adverse pregnancy outcomes. The results provided a strong association between traffic pollution and hypertensive disorders after adjusting to confounders. The association was even stronger than the connection to preterm deliveries and small for gestational age (SGA) outcomes.

An earlier study conducted 2012 (Jedrychowski et al.) is worth mentioning in this review, since the authors used a different method to measure the exposure. Jedrychowski et al. measured air pollution exposure (PM) with personal air monitoring over a 48 hours period among 431 pregnant women and found a significant correlation between exposure to air pollution and hypertensive effects. Additionally the environmental tobacco smoke as a confounder was measured.

6.2 Ambient Air Pollution and Gestational Diabetes Mellitus

Hu et al. (2015) studied a population of 410`267 women in Florida, USA, regarding their air pollution exposure during pregnancy and the risk of GDM. Their results suggest an association between PM_{2.5} and Ozone exposure and the development of GDM. Hu et al. found differences in the strengths of odd ratios regarding the measurement in different trimesters of pregnancy or the whole length of the pregnancy.

Another study published one year later (Fleisch et al. 2016) in Massachusetts, USA, regarding an association between PM_{2.5} exposure and GDM in 159`373 women found no significant evidence for a general relation. However, for women in the youngest age stratum – below 20 years – an increased exposure in the second trimester was associated with GDM.

In an earlier study in the year 2013, Malmqvist et al. investigated the association between low level NO_x exposure and two pregnancy complications, GDM as well as preeclampsia in 81`110 singleton pregnancies in Sweden. The odd ratios for both complications increased significantly with a higher pollution exposure.

6.3. Indoor Air Pollution and Hypertensive Disorders

Research on indoor air pollution is carried out mainly in developing countries due to the fact, that the majority of the people in low income countries still cook and heat with open fire or unsafe ovens. Burning of biomass like wood or coals extracts many pollutants such as carbon monoxide and PM_{2.5}, especially if plastic is added. Regarding the world population, it is estimated that still around 3 billion households rely on biomass-based cooking and heating (Quinn et al., 2016). Pregnancy-related morbidities in developing

countries often have a higher implication on the woman's and child's health and contribute to higher mortality rates.

The Ghana Randomized Air Pollution and Health Study introduced a cook-stove intervention for 817 pregnant women and their newborns in 2016 (Quinn et al., 2016). The results showed a significant positive association between CO exposure and the diastolic blood pressure. Interestingly for the measurement of exposure, women received a 72-h body-monitor in this study. Not included in this cross-sectional study was the observation of maternal outcomes later in pregnancy, like hypertension or preeclampsia.

A study published 2015 by Agrawal and Yamamoto studied data from 39'657 women in India who had a live birth in the previous 5 years, regarding an association between indoor air pollution and symptoms of preeclampsia and eclampsia. The results showed that women, who live in households where biomass or solid fuels are used for cooking or heating, have two times higher odds of reporting symptoms of preeclampsia or eclampsia. Beside the significance and importance of the results, a limitation of the research is the self-reported symptoms of preeclampsia and eclampsia, since the diagnosis of these severe gestational disorder has strict indications, e.g. proteinuria and hypertension.

Wylie et al. (2015) studied the difference between pregnant women cooking with wood compared to women using gas for cooking and the association with maternal hypertension in East India. The cross-sectional survey of 1'369 pregnant women required the information about living and environmental standards from an interview with the women. The data regarding hypertension disorders were measured with a postpartum blood pressure measurement. Women cooking with wood were one third less likely to have a

postpartum hypertension, although the difference did not reach statistical significance. Possible explanations for these interesting results were explained by the authors of the studies with a possible connection to the found evidence in other studies that smoking reduces the risk for preeclampsia. Two limitations of the study are worth mentioning: First, the time of blood pressure measurement could be questioned as meaningful, since the blood pressure can decrease after delivery. Second, the exposure information was obtained by interview but no monitoring measurement of the exposure was included in the study.

Alexander et al. (2017) conducted a randomized controlled trial in Nigeria to show a possible effect of the introduction of ethanol cook-stoves to reduce blood pressure in pregnant women. Traditional cooking with biomass fuel, in Nigeria with firewood or kerosene, is assumed to have a hypertensive effect. 162 pregnant women were assigned to ethanol cook-stoves and other 162 women to the control-group. A significant reduction of the diastolic blood pressure was observed. The blood pressure was measured 6 times during pregnancy.

6.4 Indoor Air Pollution and Anemia in pregnant women

One cross-sectional study was found in the literature research regarding indoor biomass air pollution and an association with anemia (Page et al., 2015). The definition of anemia is low levels of hemoglobin; the main contributor for this condition is an iron deficiency. Anemia can result in fatigue and low productivity and can affect cognitive and motor development. In pregnancy it is associated with low birth weight, and increased risk for maternal and neonatal morbidities (WHO, 2015). The study measured data from 12'781 women in a rural

area in India and found significant associations between biomass fuel smoke pollution and mild to severe anemia in pregnant women. Anemia in pregnancy can have further consequences on the health of the women and the newborn, e.g. higher risk of mortality due to ante- or postpartum hemorrhage or sepsis. The studied cohort's prevalence of anemia was 90.5%. The study results showed a higher relative risk for anemia in pregnancy for women using biomass fuel (wood, straw, dung and crop residues) compared to women using clean fuel (electricity, liquefied petroleum gas, natural gas and biogas).

7. Heavy Metals

Heavy metals occur naturally and today they are widely used in industry, medicine, agriculture, and technology. Concerns and evidence about their effects on the health and environment are increasing in the last decades. Arsenic, cadmium, chromium, lead and mercury are considered as high risk metals regarding health because of their high degree of systematic toxicity. Exposure to heavy metals can have carcinogenic and toxic effects, what can lead to damages in organs and nerves as well as behavioral symptoms as well as cancer (Tchounwou et al., 2012). Cadmium, lead and mercury are also part of air pollution (WHO, 2007).

7.1 Metals and Hypertensive Disorders in Pregnancy

In a prospective cohort study in the United States, Farzan et al. (2015) found an association between arsenic exposure in well water and increase in blood pressure (BP) in pregnant women. Data from 514 pregnant regarding exposure (urine, toenail and water sample) and

outcome (BP) were collected and analyzed. In the cohort of the study more than 10% of household wells exceed the arsenic maximum contaminant level (10ug/L).

In a case-control study conducted by Moyene et al. (2016) in the Democratic Republic of Congo an association between metal exposure and preeclampsia was found. 24-hours urine-samples were analyzed in 88 cases with preeclampsia and 88 controls. High levels of metals were found in the cohort but even higher levels in the women with preeclampsia. Especially the level of lead was significantly increased.

7.2 Metals and Gestational Diabetes Mellitus

A study based on the data of the Maternal-Infant Research on Environmental Chemicals (MIREC) study in Canada found an association between arsenic exposure and GDM and impaired glucose tolerance (IGT). 1'274 women in pregnancy were included and metals were measured in the first trimester blood samples and GDM and IGT according the general guidelines (Shapiro et al. 2015).

The results of the nested case-control study from Peng et al. (2015) support the findings from Shapiro et al. (2015). 137 cases with GDM compared to 190 women in the control group were studied out of 1'359 pregnant women in a hospital in China. Arsenic, mercury, lead, cadmium, and chromium levels were measured in the meconium of the newborns of both groups. A high prevalence of GDM of 12.2% in the cohort of 1'359 women was detected. After adjustment, arsenic, cadmium and chromium were positively associated with GDM and especially arsenic had a high odds ratio.

8. Discussion and policy recommendations

In the last decades a growing body of evidence and awareness developed regarding the possible damaging health effects of environmental pollutants (Prüss-Ustün et al., WHO, 2016; Landrigan et al., 2017). Although the numbers speak for themselves, a lack of awareness exists and even health professionals as well as public health professionals fail to see the connection between the epidemic of non-communicable diseases and pollution. The health effects due to pollution are underestimated in the calculation of the global burden of disease (Landrigan et al., 2017). Pregnant women belong to a vulnerable group who deserve special attention because of the health of the unborn fetus they are carrying as well as their own health which can have long-term effects through the combination of physiological and pathological changes in pregnancy in itself and environmental exposures.

The literature discussed in this review shows evidence of an association of different hazardous environment exposures, like air pollution and heavy metal, and maternal morbidities. However, the literature is not always consistent and few studies did not find an association. For example the literature discussed regarding ambient air pollution and maternal pathologies: Two (Savitz et al, 2015; Jendrossek et al., 2017) of the six studies discussed in the chapter 6.1 challenge the hypothesis of an association between AAP and hypertensive disorders in pregnancy. However, the meta-analysis (Pedersen et al., 2014) as well as the four other studies discussed present supporting results. It is important to look at different factors like sample size, method of measurement of exposure as well as the definition of the covariates used for adjustments. Regarding hypertensive disorders the definition of outcomes is a further challenge; countries as well as institutions use different definitions and guidelines for the classification of the disorders, also regarding the severity

and the time of onset. To measure the exposure to air pollution is a challenge itself, since the measurements are mostly based on the residential address and pollution estimations with the help of satellite programs or monitoring stations estimations. Olsson et al. (2015) states: "*The approaches to estimate pregnant women's exposures to air pollutants have been very different and are changing over time towards a finer spatial resolution in air pollution exposure data.*" Most studies are conducted with large sample sizes, only Jedrychowski (2012) measured the exposure with personal air monitoring and found evidence for a significant correlation. The main reason why only few studies with personal monitoring exist will be the financial aspect. It would be worth considering studying smaller samples and use personal monitors to reduce unclear confounders like commuting, work place and isolation of homes (Olsson et al., 2015). Often no information exists about the mobility of a person, the commuting and the workplace, how much time the person spends at home or outside and if air conditioning is used. All these questions, to the knowledge of the author, are an unanswered challenge in the research done until today. It is to be expected that studies conducted in various regions of the world with different living and resource conditions as well as cultural and gender differences (e.g. how much time spends the woman or men in and around the house) will result in a large variety of exposure levels.

The measurement of metals is simpler due to urine and blood samples also the meconium sample is an interesting way to measure metal exposure. Most studies conducted interviews with the women or used their medical files for the information to adjust for confounders, like smoking and obesity; however, few studies were missing this data.

In this paper the exposures were categorized in ambient air pollution, indoor air pollution and metals, although a distinction is not always that simple in reality. Heavy metal exposure can be part of air pollution (WHO, 2007).

Looking at the different exposure leads us also to another essential point in the discussion of environmental pollution – the differences between resource-strong and low – or middle income countries (LMIC) are intriguing as the differences between studies conducted in Western Europe and North America versus Asia and Africa showed. Almost 90% of death related to air pollution, occur in low- and middle-income countries, with nearly 2 out of 3 in South-East Asia and Western Pacific regions (WHO, 2016). The majority of the population in LMICs is still using biomass-fuel for cooking and heating, their living conditions make it often difficult to differentiate between ambient/outdoor and indoor pollution. Especially the research with Bedouin women, discussed in the introduction, are an interesting example how ambient and indoor pollution as well as pollution through hazardous household equipment can be hard to distinguish due to living (shacks, tents), social (women stay at home most of the time) and geographical (desert, dust and wind) conditions. Further on, high income countries are shifting their polluting productions to LMIC due to less regulations and lower salaries and taxes (Landrigan et al., 2017).

Most studies focused on two pregnancy-related morbidity-groups, e.g. gestational diabetes mellitus and hypertensive disorders. The possible long-term consequences should not be underestimated. High correlations between GDM and Type 2 Diabetes in the future are well established as well as hypertensive disorders in pregnancy and higher risks for cardiovascular problems later in life (Malmqvist et al., 2013; Farzan et al. 2015). The increasing numbers of diabetic disease globally has multifactorial reasons but the role of

environmental factor should be taken into consideration. This paper discusses only a small part of the problem, further associations with different maternal morbidities and especially also postpartum morbidities could be interesting, e.g. (postpartum) depression, infections and hemorrhage.

Two main international agreements are important to mention in this discussion: The Sustainable Development Goals (SDGs) from the United Nations Development Programme and the international Paris agreement on Climate Change from the United Nations Framework Convention:

The Sustainable Development Goals were developed based on the Millennium Development Goals (MDGs) in the year 2015, when the MDGS came to the end of their terms (WHO, 2015). Interestingly many of the 17 goals of the SDGs are related to the subject of this paper. Clean water and sanitation (number 6), affordable and clean energy (number 7), responsible consumption and production (number 12) and climate action (number 13) are just some points directly related to environmental protection, climate change and health. But many of the other goals are part of this discussion, for example: no poverty (number 1), good health and well-being (number 3), quality education (number 4) and gender equality (number 5) (UNDP, 2015). As discussed before, the majority of affected people are living in poor countries, to reduce poverty means more possibility to reduce environmental pollutant exposure and therefore to increase the health of a population. On the other hand, to reduce environmental pollution means to reduce poverty. A healthy population means working people, what can reduce poverty. Education creates awareness and to be aware of the problem is needed to make people change their life-styles and policy-makers to create solutions. Last but not least, this discussion is also about gender issues. Focusing on

pregnant women, as mentioned before a vulnerable group, means to talk about a group of the society which per se has still in many parts of the world less rights and opportunities compared to men. Also regarding environmental exposures, many women cannot protect themselves due to living conditions, social norms and lack of education. Especially indoor pollution due to cooking and heating with an open fire poses a high risk.

The international Paris agreement from the United Nations Framework Convention on Climate Change made every member commit to reduce greenhouse gases like PM₁₀, NO₂ and O₃, a big step in reducing pollutant exposures. In the Paris climate change conference, 2015, the health threat of air pollution was addressed as a global public health problem. A report regarding climate change and the impact on human health states:

"The socioeconomic cost of health problems caused by climate change is considerable, and certain groups are more highly impacted by climate-sensitive diseases and other health impacts. These groups can include children, the elderly, people infected with the human immunodeficiency virus, migrants, indigenous peoples, people living in poverty, and women (in particular pregnant women)." (United Nations, FCCC, 2017)

Environmental pollution also has an economic impact, it is expensive. An estimated 4.6 trillion USD welfare losses are attributed to pollution yearly, 6.2 % of the global economic output (Landrigan et al., 2017). Landrigan et al. (2017) stated in the Lancet:

"The claim that pollution control stifles economic growth and that poor countries must pass through a phase of pollution and disease on the road to prosperity has repeatedly been proven to be untrue."

From the presented and discussed associations and evidence from the health effects of environmental pollutants on maternal health the following recommendations to policy-makers, educators and public health professionals are suggested:

- Increase the national and international efforts and collaborations to reduce pollution
- Change laws and increase regulations on motor vehicle and polluting industries (e.g. coal or chemical industries). For example, increased taxes on cars and fuel
- Invest in public transportation, bike lanes, walkability (away from busy roads) and relocate infrastructure of roads
- Support start-ups, new innovations and the clean-tech industry for new ideas
- Support research on environmental pollution and health, monitoring of pollution
- Funding of new jobs through creation of sustainable cities, green technologies
- Educate the public through different media but especially in all school levels
- Educate health professionals, e.g. doctors, nurses, midwives
- Educate women in the reproductive age, educate pregnant women and parents
- Know-how, resource and technology support from high-income countries and the United Nations to low – and middle income countries to improve the infrastructure, introduce and implement regulations regarding transportations, industries and household equipment (e.g. gas-stove)

Opposition is expected from the motor vehicle industry itself as well as the other polluting industries such as coal-industry, since they are making a financial profit out of their businesses. Further opposition will rise from some politicians and the government itself, since they often earn from these industries, the government in form of taxes. Further on the relocation or reconstruction of streets and infrastructure is very expensive and the construction of new train or tramlines is time- and cost-intense. However, one could argue that this would create new jobs, because an important aspect to discuss is the group of employees who will protest against losing their jobs in specific industries. The role of the state and the international organizations is to offer alternatives and to produce new jobs in renewable energy for example. In many countries around the world, politicians as well as the public will argue that other topics have higher priority such as security and religion. However, the international research conducted about environmental pollution and people's health as well as the SDGs and the Paris agreement prove enough facts to make the world countries a step forward and start to eliminate the public health hazard from environmental pollution. As the World Health Organization states:

"The results of the study reinforce the public health principle that creating and maintaining healthy environments should be a priority of primary prevention. A change in perception to view the environment as an essential element of health protection, while adequately preserving it, would greatly benefit people's health. Coordinating and acting across sectors will be necessary, as many different sectors play a crucial role (e.g. energy, industry/manufacturing, water and sanitation, agriculture, housing, transport) in determining environmental risks and conditions." (Prüss-Ustün et al., WHO, 2016)

The health of pregnant women, unborn fetuses and children is essentially important for the future of our societies. Children are the future and we need healthy pregnant women to have healthy children who can work in future –hopefully more sustainable - economies.

The good news is that it is possible to reduce pollution; many high-income countries could prove this in the last decades and could show that prevention of pollution can be highly cost-effective. Many high-income countries and some middle-income countries changed laws and introduced regulations; today they present better air and water quality (Landrigan et al., 2017). It is time to look at pollution as a global problem and to act on it.

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