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The role of lifestyle factors in childhood asthma

Syventävien opintojen kirjallinen työ

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Lääketieteellinen tiedekunta

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Asthma is a prevalent chronic respiratory illness affecting up to 5-10% of children worldwide. The prevalence and economic and social burden of asthma has been increasing for the past decades, especially in low- to middle-income countries. Asthma is characterized by inflammation and excessive bronchoconstriction of the airways, and it manifests with symptoms such as cough, wheezing, shortness of breath, chest tightness, and difficulty of exhaling. Childhood-onset asthma is commonly allergic based, and often accompanied by other allergic diseases such as atopic eczema, allergic rhinitis, and food allergy. While hereditary factors contribute to asthma onset, recent research has increasingly explored lifestyle, environmental, and dietary factors, and their effect on asthma incidence in children.

The aim was to review current data on the effect of lifestyle factors in childhood asthma.

A systematic search of the PubMed database was conducted to retrieve studies published within the last five years, with some high-quality older studies included. The focus was on maternal smoking during pregnancy, secondhand smoking, overweight, physical activity, parental stress, and negative life events. A total of 28 openly published articles in English were selected, focusing on childhood asthma, its incidence, and the aforementioned lifestyle factors.

Findings indicate that lifestyle factors play a significant role in the onset of childhood asthma. Childhood obesity correlates with an increased asthma risk, as does minimal physical activity. Maternal overweight or smoking during pregnancy may elevate a child's susceptibility to asthma. Elevated maternal stress levels before or during pregnancy have been linked to an increased odds of asthma in offspring.

The results suggest that fighting against childhood obesity and promoting physical activity may have protective effect on childhood asthma. In addition, by addressing the health and lifestyles habits of pregnant mothers may potentially reduce the incidence of childhood asthma. This includes sustaining normal weight, abstaining from tobacco smoking, avoiding exposure to secondhand smoke, and taking care of psychological health.

Keywords: asthma, lifestyle, tobacco, overweight, parental stress

TURUN YLIOPISTO
Lääketieteellinen tiedekunta

MYLLYNIEMI, MARI: Lasten astman ilmaantuvuuteen vaikuttavat elintapatekijät

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Astma on yleinen krooninen hengityselimistön sairaus, jota sairastaa jopa 5–10 % lapsista ympäri maailmaa. Astma on keuhkoputkien tulehdussairaus, johon liittyy keuhkoputkien liiallinen supistumisherkkyys. Astma voi puhjeta missä iässä tahansa, ja sen oireita ovat yskä, hengityksen vinkuna, hengenahdistus, painon tunne rintakehällä ja/tai uloshengitysvaikeus. Lapsuusiän astma liittyy usein myös muihin allergisiin sairauksiin: atooppiseen ihottumaan, ruoka-aineallergioihin ja allergiseen nuhaan. Perinnölliset tekijät vaikuttavat astman puhkeamiseen, mutta viime vuosina on lisääntyvästi tutkittu myös muita elintapa- ympäristö- ja ravintotekijöitä, jotka voivat vaikuttaa astman ilmaantuvuuteen.

Tämän opinnäytetyön tavoitteena oli perehtyä viimeaikaiseen kirjallisuuteen lasten astman ilmaantuvuuteen vaikuttavista elintapatekijöistä.

Tätä katsausta varten haettiin PubMed-tietokannasta aihepiirin tutkimuksia keskittyen viimeisen viiden vuoden aikana julkaistuihin artikkeleihin. Joitain laadukkaita vanhempia tutkimuksia on myös sisällytetty mukaan. Aihe rajattiin liikuntaan, ylipainoon, raskausajan tupakointiin, passiiviseen tupakointiin sekä vanhempien stressiin ja negatiivisiin elämäntapahtumiin. Aineistoon otettiin 28 englanninkielistä avoimesti julkaistua artikkelia. Artikkeleissa keskityttiin lasten astmaan, ilmaantuvuuteen ja edellä mainittuihin elämäntapatekijöihin.

Tutkimustulosten mukaan elämäntapatekijöillä on merkitystä lasten astman ilmaantuvuuteen. Lapsuuden ylipaino on yhteydessä lisääntyneeseen astmariskiin, samoin kuin vähäinen liikuntamäärä. Äidin ylipaino tai tupakointi raskauden aikana saattavat lisätä lapsen alttiutta astmalle. Myös passiivinen tupakointi tai isän tupakointi raskausaikana voivat lisätä astmariskiä. Lisäksi äidin korkea stressitaso raskautta ennen tai sen aikana on ollut yhteydessä lapsen kohonneeseen astmariskiin.

Tulokset viittaisivat siihen, että vähentämällä lasten ylipainoa ja lisäämällä liikuntaa voidaan pienentää lasten astmariskiä. Vaikuttamalla raskaana olevien naisten terveyteen ja elintapoihin voidaan mahdollisesti suojata lasta astmalta. Huomiota kannattaa kiinnittää tupakanpolton lopettamiseen, passiivisen tupakoinnin välttämiseen, painoon ja mielenterveyden tukemiseen.

Avainsanat: astma, elintavat, tupakka, ylipaino, vanhempien stressi

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Abbreviations

AD	atopic dermatitis
AE	atopic eczema
aHR	adjusted hazard ratio
aOR	adjusted odds ratio
aRR	adjusted risk ratio
BMI	body mass index
CI	control interval
GWG	gestational weight gain
HR	hazard ratio
MVPA	moderate-to-vigorous physical activity
OR	odds ratio
PR	prevalence ratio
PTSD	post-traumatic stress disorder
RR	risk ratio
RRR	relative risk ratio
SDP	smoking during pregnancy
SHS	secondhand smoke

1 Introduction

Asthma is a common chronic respiratory illness affecting people of all ages around the globe. In children, asthma is the most common chronic condition, affecting around 5-10% of children globally[1]. It's characterized by inflammation of the airways, increased mucus production and excessive bronchoconstriction. These cause cough and variable airflow limitation, resulting in shortness of breath and wheezing. Asthma brings a weighty burden to patients, families, and society worldwide and its rising costs to healthcare systems have been widely recognized. Asthma is often accompanied with other atopic diseases such as atopic eczema, food allergy, and allergic rhinitis. The typical progression of these allergic diseases is called the atopic march. Childhood asthma has gained considerable attention in recent years due to its escalating prevalence and its profound impact on the health and well-being of children worldwide. Growing number of research has been done trying to identify the different risks and factors contributing to prevalence and prevention of asthma.

While genetics certainly play a role in prevalence of asthma, emerging evidence suggests that lifestyle factors, including a wide range of environmental, behavioral, and dietary elements, exert a substantial influence on the development and exacerbation of childhood asthma. In this review of the literature, we focus on lifestyle factors' role and the risk of childhood asthma. Lifestyle factors in consideration will be parental tobacco smoking, secondhand smoke exposure, childhood and maternal overweight and obesity, childhood exercise, maternal stress during pregnancy and parental mental health.

Tobacco exposure, both prenatal and postnatal, has garnered attention as a significant risk factor for childhood asthma. Maternal smoking during pregnancy has been linked to intrauterine alterations that may predispose the developing fetus to respiratory problems later in life, including asthma. Additionally, exposure to secondhand smoke during early childhood has been associated with an increased risk of asthma and exacerbations in susceptible individuals. The harmful effects of tobacco smoke on the respiratory system are well-documented, making it a critical lifestyle factor to consider when addressing pediatric asthma risk.

Body mass index (BMI) is another influential lifestyle factor that has come under inspection in the context of childhood asthma. Childhood obesity is a growing concern globally, and its association with asthma has become increasingly apparent. Excess body weight can lead to inflammation and mechanical stress on the airways, contributing to the development and severity of asthma symptoms. Understanding the intricate relationship between BMI and asthma is crucial for designing effective prevention and management strategies for overweight and obese children with asthma.

Stress, both acute and chronic, has emerged as a psychosocial factor with the potential to modulate the risk of childhood asthma. Stress can trigger inflammatory responses and affect the immune system, which may increase the susceptibility to asthma development or exacerbation in children. Maternal psychological distress during pregnancy has been linked with higher rates of allergic diseases such as wheeze and asthma in offspring. Recognizing and addressing stress, depression, and other adverse life events as a lifestyle factor in pediatric asthma management underscores the importance of mental health in holistic asthma care.

Despite the extensive research conducted on childhood asthma, there are still certain aspects that we lack the understanding of. Especially the long-term effects of specific lifestyle factors on asthma

development and progression in children need further investigation. Different stress factors and their contribution to childhood asthma is something we do not fully understand yet. As the prevalence of childhood asthma continues to rise globally, the need for a holistic understanding of the lifestyle factors at play becomes increasingly urgent.

This review summarizes the effects of tobacco exposure, BMI, physical exercise, and stress as lifestyle factors that significantly influence the risk of childhood asthma. By exploring these factors in greater depth, we aim to provide a more nuanced understanding of the correlation between lifestyle and pediatric asthma, emphasizing the importance of adopting a holistic approach to both prevention and management. Through increased awareness and targeted interventions, we can better safeguard the respiratory health of the children, ultimately reducing the burden of childhood asthma on children, families, and healthcare systems alike.

2 Methods

For this review of the literature, a database search was performed in the spring of 2023. The search was performed in PubMed and limited to most recent open access studies, mostly onwards from 2016. A couple of older studies were included as well, if they provided quality research not found in more recent studies. The following search terms were used to find connections and effects between childhood asthma and tobacco, obesity, exercise and stress: ("tobacco*" OR “second-hand smok*” OR “smoking” OR "Tobacco"[Mesh]) AND ("prevent*" OR "risk*") AND ("child*" OR "Child"[Mesh]) AND ("asthma" OR "Asthma"[Mesh]); ("obesity*” OR “fatness*” OR “overweight*” OR “Obesity”[Mesh] OR “Pediatric Obesity”[Mesh]) AND ("prevent*" OR "risk*") AND ("child*" OR "Child"[Mesh]) AND ("asthma" OR "Asthma"[Mesh]); ("exercise*” OR “physical exercise*” OR “movement*” OR “activity*” OR “Exercise”[Mesh]) AND ("prevent*" OR "risk*") AND ("child*" OR "Child"[Mesh]) AND ("asthma" OR "Asthma"[Mesh]); ("stres*" OR ("Stress, Psychological"[Mesh]) OR "Stress Disorders, Traumatic, Acute"[Mesh]) OR "Financial Stress"[Mesh]) AND ("prevent*" OR "risk*") AND ("child*" OR "pediatric*"OR "Child"[Mesh]) AND ("asthma" OR "Asthma"[Mesh]). Studies that did not focus on asthma risk or prevention were ruled out. All studies focused on children or pregnant mothers and later their offspring. Statistical significance was determined by P-value < 0.05.

As part of this licentiate thesis, we also collected research data for FOPP-study (Fish Oil and Probiotics in pregnancy) at Turku University Hospital (TYKS) from 2020 to 2022. This included clinical work executing spirometry test to children of the age 5 or 6. These results will be used in further studies about childhood asthma risk and prevention.

3 Review of the literature

3.1 Tobacco

The many harmful effects of smoking tobacco and exposure to passive smoking are widely known. Maternal smoking during pregnancy and exposing a young child to tobacco smoke have been shown to increase the prevalence of wheeze and asthma in children in numerous studies. Continuous prenatal tobacco exposure prompts harmful developmental effects in fetus's lungs, thus diminishing lung function and increasing risk of non-atopic asthma[2]. Exposure to maternal smoking during pregnancy has been shown to cause persistent epigenetic modifications, particularly in enhancer regions regulating the activity of genes involved in airway inflammatory processes, thus contributing to the development of asthma symptoms among young children[3]. Maternal smoking exposes a fetus to many harmful chemicals including nicotine, which can restrict the blood flow in the placenta by elevating carboxyhemoglobin levels in the blood, and thus predispose the fetus for hypoxic stress[4]. Children who have smoking mothers are also more prone to lower respiratory illnesses and hospital admissions for respiratory infections[5].

Main characteristics of studies investigating the effects of tobacco smoking and passive smoking are summarized in Table 1. A recent systematic review in 2021 analyzed different health outcomes of smoking during pregnancy (SDP) and found SDP to increase the risk for asthma in the offspring (OR 1.9). Other negative health outcomes were sudden infant death syndrome, low birth weight, stillbirth and obesity.[6] An analysis from five European birth cohorts found increased but not statistically significant odds of prevalent asthma with any maternal smoking during pregnancy. Maternal smoking of ≥ 10 cigarettes/day during pregnancy was associated with persistent asthma (aOR 1.7). In this analysis secondhand smoke exposure during different periods of child's life (infancy, 1–2, 4–6, 8–10, or 14–16 y of age) was not associated with adolescent-onset asthma.[3]

In a Finnish birth cohort study the risk of asthma was highest among children who had two smoking parents (aOR 3.7) compared to those with non-smoking parents. Having one smoking parent also increased the risk (mother: aOR 1.7, father: aOR 2.9). This study also found paternal smoking cessation during pregnancy to be protective effect against asthma in offspring even if the mother continued smoking (aOR 0.3).[7]

A Mendelian randomization study showed maternal smoking around birth to be associated with increased risk of childhood asthma (OR 1.01)[8]. A large Japanese birth cohort study found similar results [9]. In another large Japanese birth cohort study, maternal smoking during pregnancy was significantly associated with an increased risk of asthma in the offspring dose-dependently (1–10 cigarettes per day: aOR 1.39; ≧ 11 cigarettes per day: aOR 1.57).[10]

A large Swedish population-based study showed again association between SDP and increased incidence of asthma as well as current asthma. The study took into consideration also the use of oral moist snuff during pregnancy. It found only a weak association between snuff use in pregnancy and asthma, no statistical significance.[11]

The only study not to find a significant association between parental smoking and offspring asthma was by Jung et al. This Korean study found dose-dependent association between paternal cotinine levels, the main metabolite of nicotine, and risk of childhood asthma. However, the study found no

significant association between parental cotinine-verified smoking group (non-smoker, passive or active smoker) and childhood asthma.[12]

A three-generation study found out that on the maternal side, grandmothers' smoking during pregnancy was associated with asthma with nasal allergies in their grandchildren (RRR 1.25). In the same study mothers' smoking during pregnancy as well as fathers' smoking before the age of 15 was associated with asthma without nasal allergies in their offspring (RRR 1.27; RRR 1.43).[13] A Norwegian study had similar findings. The grandmother's smoking when pregnant with the mother was positively associated with asthma in the grandchild at 36 months (aRR 1.15) and at 7 years (aRR 1.21). The association was positive independently regardless of the mother's smoking status when pregnant with the child.[14] A study from the Netherlands found grandmaternal smoking during pregnancy to be associated with higher asthma risk and lower lung function in male grandchildren. On the contrary, the study analyzed separately a children's group, and there maternal grandmother's smoking during pregnancy was associated with lower risk for asthma and childhood asthma.[15]

Exposure to secondhand smoke (SHS) is harmful for everyone, but especially for those who already suffer from respiratory illnesses. For children with asthma, SHS can increase the odds for asthma exacerbations and poor asthma control.[16] When it comes to maternal exposure to SHS during pregnancy, a Japanese birth cohort study found children to have a higher risk of asthma at 3 years of age if their mothers were frequently exposed to SHS during pregnancy compared to those who were seldom exposed to SHS (aOR 1.14)[9].

In a smaller Japanese study maternal SHS exposure at home and/or at work during pregnancy increased the risk of ever asthma and current asthma (aOR 2.41; aOR 4.82) among children whose mothers are never smokers. In the same study maternal active smoking before or during pregnancy was not associated with the risk of asthma in children.[17] In a Chinese study maternal smoking during the child's first year of life was strongly associated with childhood asthma (aOR 4.66)[18].

Exposure to SHS is found to be dose dependent. Daily maternal exposure to SHS in the second/third trimester was significantly associated with the development of asthma in the offspring compared with no SHS exposure (every day: aOR 1.26). Infants who were exposed to SHS at one month postpartum had no significantly increased risk for the development of asthma but an increased risk for wheeze.[10]

Table 1. Tobacco smoking or passive smoking and the outcome of childhood asthma

REF	COUNTRY	N	AGE[1]	PREDICTOR	OUTCOME	DESIGN	EFFECT	FINDINGS
Thacher, 2018[3]	Sweden, Germany, The Netherlands	10 860	0-16	maternal smoking during pregnancy	early transient, persistent, and adolescent-onset asthma	birth cohort study	aOR 1.66, 95% CI 1.29–2.15	increased odds of persistent asthma with mothers smoking ⩾ 10 cigarettes/day during pregnancy SHS exposure was not associated with adolescent-onset asthma
Harju, 2016[7]	Finland	39 306	2-10	parental smoking and cessation during pregnancy	asthma in offspring	birth cohort study	aOR 3.7, 95 % Cl 3.2–4.4 aOR 0.35, 95% CI 0.3–0.4	increased risk of asthma if both parents smoked as well as if only one of the parents was a smoker paternal cessation of smoking during pregnancy decreased the risk of asthma regardless of maternal smoking
Ding, 2022[8]	Data from European origin population	361 194	0-16	maternal smoking around birth	childhood asthma	Mendelian randomization study	OR 1.0150, 95% CI 1.0018–1.0283	slightly increased risk of childhood asthma with maternal smoking around birth
Miyake, 2023[9]	Japan	75 411	3	maternal smoking status before and during pregnancy	bronchial asthma after the age of two	prospective birth cohort study	aOR 1.34, 95% CI 1.15–1.56 aOR 1.11, 95% CI 1.01–1.2	increased risk of bronchial asthma in children of mothers who sustained smoking during pregnancy, increased risk of asthma if the mother quit after finding out about the current pregnancy
Wada, 2021[10]	Japan	90 210	0-1	maternal smoking during pregnancy, prenatal and postnatal SHS exposure	wheeze or asthma in the offspring	birth cohort study	1-10 cigarettes/day: aOR 1.39, 95% CI 1.09–1.77 ⩾11 cigarettes/day: aOR 1.57, 95% CI 1.05–2.34 aOR 1.26, 95% CI 1.08–1.47	increased risk of wheeze/asthma in offspring with maternal smoking during pregnancy increased risk of wheeze/asthma in offspring with daily maternal exposure to secondhand smoke during pregnancy
Lundholm, 2020[11]	Sweden	788 508	0-8	smoking during pregnancy and snuff usage during pregnancy	incident asthma/ wheeze or current asthma	population based register study	smoking: aOR 1.22, 95% CI 1.17–1.28 snuff: aOR 1.06, 95% CI 0.96–1.18	increased risk of offspring asthma/wheeze with mothers smoking during pregnancy, weak association with maternal snuff usage during pregnancy and childhood asthma

Jung, 2021[12]	Korea	5 264	0-18	parental urinary cotinine levels	childhood asthma	population-based cross-sectional study	aOR 1.57, 95% CI 0.77–3.2	no significant association between the parental urinary cotinine-verified smoking group and childhood asthma group
Accordini, 2018[13]	Europe and Australia	8 758	age of grandchild-ren 0–51	grandmothers' smoking during pregnancy	childhood asthma with nasal allergies	population based cohort study	RRR 1.25, 95% CI 1.02–1.55	increased risk of asthma with nasal allergies in grandchildren whose grandmother smoked during pregnancy
Magnus, 2015[14]	Norway	53 169 + 25 394	3, 7	grandmothers' smoking during pregnancy	current asthma at 36 months and 7 years	mother and child cohort study	aRR 1.15, 95% CI 1.06–1.24 aRR 1.21, 95% CI 1.07–1.37	increased risk of offspring asthma (at 38 months and 7 years of age) if the grandmother was smoking when pregnant with the mother
Mahon, 2021[15]	The Netherlands	37 291	age of grandchild-ren 4-50	grandmaternal smoking	asthma and early childhood asthma in grandchildren	prospective longitudinal three generation cohort study	OR 1.38, 95% CI 1.06–1.79 OR 1.49, 95% CI 1.06–2.11	increased risk of asthma and early childhood asthma with maternal grandmaternal smoking during pregnancy in male grandchildren
Tanaka, 2020[17]	Japan	1 304	0-36 months	maternal smoking during pregnancy and maternal SHS exposure	ever asthma or current asthma	prospective prebirth cohort study	aOR 2.41, 95% CI 1.13–5.05 aOR 4.82, 95% CI 1.68–13.43	increased risk of ever asthma or current asthma in offspring with mothers who exposed to second-hand smoke during pregnancy maternal active smoking, either before pregnancy or during pregnancy, was not associated with the risk of ever asthma or current asthma
Ellie, 2021[18]	China	7 366	0-8	parental smoking	doctor diagnosed asthma	cross-Sectional study	aOR 4.66, 95% CI 1.99–10.92 aOR 4.16, 95% CI 1.88–9.20	increased risk of offspring asthma and current wheeze with maternal smoking during the child's first year of life

aOR = adjusted odds ratio, CI = control interval, SHS = secondhand smoke, OR = odds ratio, RRR = relative risk ratio, aRR = adjusted risk ratio
[1]Age is expressed in years.

3.2 Overweight, obesity, and exercise

Overweight and obesity are associated with many health problems both in children and in adults. Decreased lung function and increased risk for developing asthma are just two of them.

A large meta-analysis evaluated the relation between overweight or obesity and lung function both in children and in adults with and without asthma. This meta-analysis found obese children to have decreased lung function, more pronounced FEV1/FVC deficit (OR −2.4%) compared to those with normal weight and it was similar in subjects with (OR −1.5%) and without asthma (OR −1.6%).[19] Similar findings of decreased FEV1/FVC have been done in many other studies.[20,21] A meta-analysis from 2018 reviewed 16 case control studies and showed significant relationship between obesity or overweight and asthma. OR for asthma and overweight was 1.64 and OR for asthma and obesity was 1.92.[22]

A Taiwanese Mendelian randomization study found obesity to be associated with increased risk of developing asthma in 12-year-old children (OR 1.08) as well as increased risk for incident asthma (HR 1.28)[21]. An earlier Taiwanese study found overweight and obese girls with pre-asthmatic symptoms to have greater risk for asthma compared to normal weighed peers, but similar results were not found with boys.[20] Main characteristics of studies investigating the effects of overweight, obesity or exercise are summarized in Table 2.

The relationship between maternal pre-pregnancy body mass index (BMI), gestational weight gain (GWG) and risk of asthma in offspring has also been studied. Gestational weight gain is crucial for the health of both the mother and the developing fetus. Inadequate weight gain can lead to complications such as low birth weight and preterm birth, while excessive weight gain may increase the risk of gestational diabetes, hypertension, and complications during delivery. Optimal GWG depends on a woman's pre-pregnancy BMI. A study from U.S. found maternal pre-pregnancy overweight and obesity to be associated with offspring asthma (overweight OR 1.19; obesity OR 1.34). This association was shown to be stronger for non-allergic asthma than allergenic asthma, but the difference was not statistically significant. With regard to GWG, an association was suggested between gains of < 15 lb (6.8kg) and higher risk of offspring allergenic and non-allergenic asthma (OR 1.28).[23]

A large 2020 meta-analysis evaluated 22 observational studies and found similar association between maternal pre-pregnancy overweight (OR 1.13) and obesity (OR 1.41) with a risk of having childhood asthma. The risk of offspring asthma and wheeze was increased with very high GWG (aOR 1.24), moderate high GWG (aOR 1.12), and very low GWG (aOR 1.26) compared to mothers with normal GWG.[24] This supports the findings from earlier meta-analysis[25] and other recent studies[26–29].

When it comes to physical activity, being active as a child provides many health benefits. Avoiding overweight and obesity is one factor that decreases asthma risk, but physical activity alone has been suggested to be protective factor against asthma. However, exercise is a common trigger for bronchoconstriction in asthmatic children as airway inflammation decreases tolerance to exercise. A 2022 study found that increasing moderate-to-vigorous physical activity (MVPA) on asthma risk changes depending on the current MVPA level of the child. An increase of MVPA was associated with a lower asthma risk at lower levels (0–4 h/week) of MVPA. In contrast, for high-active children with ≥8 hours MVPA, the risk of asthma slightly increased for each additional 1 h/wk of MVPA (HR 1.005). In the same study BMI was positively associated with asthma risk (HR 1.042

for each kg/m^2).[30] A meta-analysis of 11 studies came to the same conclusion: low level of physical activity was associated with risk of new-onset asthma or wheezing.[31]

A study from United States found overweight/obesity to be associated with asthma in girls, but not in boys. High fitness status was associated with decreased asthma morbidity and emergency department visits in boys but not in girls.[32]

However, in urban residential areas, exercise predisposes children for air pollution and thus can attenuate the protective effect of physical activity. A study from New York City confirmed children who are physically active on a daily basis to have higher exposure to black carbon.[33] Black carbon results from incomplete burning of fossil fuels and has been associated with airway inflammation and asthma in earlier studies.[34]

Table 2 Overweight, obesity, or physical activity and the outcome of childhood asthma

REF	COUNTRY	N	AGE[1]	PREDICTOR	OUTCOME	DESIGN	EFFECT	FINDINGS
Chen, 2022[21]	Taiwan	7 069	12	BMI of children, obesity	physician diagnosed asthma	mendelian randomization study	OR 1.08, 95% CI 1.00–1.16	increased risk of asthma in obese children
Ho, 2011[20]	Taiwan	4 052	13–15	BMI of children, overweight and obesity	physician diagnosed asthma to a child with pre-asthmatic symptoms	prospective cohort study	OR 1.75, 95% CI 1.18–2.61	increased risk of asthma in obese girls with pre-asthmatic symptoms no association with obese boys
Azizpour, 2018[22]	North America, Peru, Brazil, Europe, Middle East	8 397	2.2–18	BMI of children, overweight and obesity	physician diagnosed asthma	meta-analysis	OR 1.64, 95% CI 1.13–2.38 OR 1.92, 95% CI 1.39–2.65	increased risk of asthma in overweight or obese children
Dumas, 2016[23]	United States	12 963	9–14	maternal pre-pregnancy BMI (overweight and obesity) and GWG	physician diagnosed allergic and non-allergic asthma during childhood or adolescence	longitudinal study	OR 1.19, 95% CI 1.03–1.38 OR 1.34, 95% CI 1.08–1.68 OR 1.28, 95% CI 0.98–1.66	increased risk of offspring asthma with maternal pre-pregnancy overweight and obesity suggested higher risk with GWG of <6.8 kg and offspring asthma
Ekström, 2015[27]	Sweden	3 294	1–16	maternal BMI around week 10 in pregnancy	offspring asthma, rhinitis, eczema, and sensitization	birth cohort study	per 5kg/m^2 increase aOR 1.23, 95% CI 1.07–1.40	increased risk of prevalent asthma with higher maternal BMI no effect on other outcomes
Harpsøe, 2013[28]	Denmark	38 874	0–7	pre-pregnancy BMI and GWG	offspring asthma, wheezing, atopic eczema, and hay fever	birth cohort study	aOR 1.54, 95% CI 1.34–1.76 aOR 1.97, 95% CI 1.38–2.83	increased risk of offspring asthma and wheezing with obese mothers GWG ≥ 25 kg was associated with current severe asthma no effect on AE or hay fever
Polinski, 2017[29]	United States	6 450	0–4	pre-pregnancy BMI	childhood asthma	birth cohort study	aOR 1.25, 95% CI 0.99–1.59 aOR 1.63, 95% CI 1.26–2.12	increased risk of offspring asthma with overweight and obese mothers

Srugo, 2021[26]	Canada	248 017	0–7	pre-pregnancy BMI and GWG	anaphylaxis, asthma, dermatitis, and rhinitis in children	population based cohort study	aHR 1.08, 95% CI 1.05–1.11	increased hazards of offspring asthma with obese mothers no associations with GWG and any allergic outcome
Lu, 2022[30]	United States	542 486	2–17	moderate to vigorous physical activity	physician diagnosed asthma or wheeze and at least 2 prescriptions of specific asthma medication	retrospective cohort study	HR 0.981, 95% CI 0.97–0.99 HR 1.005, 95% CI 1.002–1.009	an increase of MVPA was associated with a lower asthma risk at lower levels (0–4 h/week) of MVPA high-active children with ≥8 hours MVPA had an increased risk of asthma for each additional 1 h/wk. of MVPA
Lu, 2016[32]	United States	4 828	12–16	child's BMI and cardiorespiratory fitness test on treadmill	history of asthma and current asthma	cross-sectional comparative study	aOR 1.64, 95% CI 1.16–2.31 aOR 1.77, 95% CI 1.15–2.72 aOR 0.43, 95% CI 0.24–0.76	increased odds of history of asthma and current asthma in girls with overweight or obesity lower odds of asthma-related ED visits and wheezing related to exercise in boys with high fitness level

BMI = body mass index, OR = odds ratio, CI = control interval, GWG = gestational weight gain, aOR = adjusted odds ratio, AE = atopic eczema, aHR = adjusted hazard ratio, MVPA = moderate-to-vigorous physical activity, HR = hazard ratio, ED = emergency department
[1]Age is expressed in years.

3.3 Stress and parental mental health

During pregnancy, a fetus is vulnerable to many maternal influences, which can greatly affect the health and wellbeing of the child later in life. Growing research evidence has been linking maternal psychological stress during pregnancy with childhood asthma and other allergic diseases in the offspring. Potential mechanisms linking maternal stress and offspring asthma are disrupted stress-response and high cortisol levels in pregnant women. Disturbances of the hypothalamic-pituitary-adrenal axis has been studied the most, but also different brain neurotransmitter changes may alter the immune function and predispose a child to developing asthma.[35] High stress can alter the cytokine balance of the fetus and flavor Type 2 immune response.[36] Maternal stress may also directly lead to premature birth, which produces its own health risk to the child, including higher risk of developing asthma.[37]

Parental mental disorders have many adverse effects on a child's life. Besides psychiatric and neurodevelopmental problems, these children have an increased risk of injuries, asthma, malnutrition and diarrhea according to a large meta-analysis.[38] A meta-analysis of 9 studies examined mother's prenatal mental disorders (anxiety and/or depression) mental health service use, prenatal distress and negative life events and the risk of childhood asthma or atopic dermatitis in the offspring. The study found prenatal depression to influence childhood asthma compared to mothers without depression whereas no significant association was found for childhood atopic dermatitis.[39]

A recent FinnBrain birth cohort study examined mothers' chronic psychological distress (depressive and anxiety symptoms) during pregnancy and the risk of childhood wheeze and eczema by the age of 24 months. It found mother-experienced psychological distress symptoms that are chronically elevated across pregnancy to be associated with offspring wheezing and eczema at the age of 24 months. Risk of wheezing ever was elevated with maternal consistently high depressive symptoms (aOR 2.74) or moderate and increasing anxiety symptoms (aOR 1.9). Similarly, wheezing without eczema was associated with consistently high depressive (aOR 3.60) and moderate and increasing anxiety symptoms (aOR 2.43).[40]

A Taiwanese longitudinal study found patients with post-traumatic stress disorder to have increased risk of asthma (no separation between different asthma types) after adjusting for demographic data and related comorbidities. This study looked at patients of all ages, but the association was strongest with young patients under 20 years of age (HR = 4.01).[41]

A large Canadian population based cohort study found children whose mothers used mental health services during pregnancy to have higher odds of developing asthma (OR = 1.16).[42] Another study found prenatal stress from bereavement to be weakly associated with asthma events in children aged 0-3 (HR 1.04), but not with older children. However, an association was observed in children whose mothers lost a child (HR 1.34).[43]

Two large Danish cohort studies from 2019 and 2020 found no statistically significant association between maternal prenatal exposure to negative life events and increased risk of any childhood asthma. In the earlier study maternal low job control was associated with increased risk of all three asthma phenotypes (early-onset transient asthma, early-onset persistent asthma and late-onset asthma) among mothers with low job demands. The later study found higher levels of psychological job demands and psychosocial work stressors not to be associated with childhood asthma.[44,45]

Two studies examined maternal stress and childhood wheeze with young children at 12 or 48 months of age. Smejda et al[46] found association between prenatal exposure to maternal stress measured by life events as stress factors and wheezing in children, whereas a Mexican study found girls to be more vulnerable to maternal postnatal stress than boys when it comes to risk of wheeze.[47]

Table 3 Stress or parental mental health and the outcome of childhood asthma

REF	COUNTRY	N	AGE[1]	PREDICTOR	OUTCOME	DESIGN	EFFECT	FINDINGS
Puosi, 2022[40]	Finland	1 305	0-2	maternal distress, depressive and anxiety symptoms during pregnancy	wheezing or eczema	Birth cohort study	aOR 2.74, 95% CI 1.37–5.50 aOR 1.94, 95% CI 1.06–3.54	increased risk of wheezing in offspring with maternal consistently high depressive symptoms as well as with moderate depressive symptoms and increasing anxiety symptoms
Hung, 2019[41]	Taiwan	5 518	< 20	prevalence of asthma with patients diagnosed with PTSD	asthma	longitudinal study	HR 4.01, 95% CI 1.69–9.51	patients with PTSD had an increased risk of asthma
Liu, 2015[43]	Denmark	750 058	0-15	mothers suffering bereavement 1 year prior to or during pregnancy	childhood asthma	cohort study	HR 1.03, 95% CI 1.00–1.06	prenatal stress following maternal bereavement was associated with a marginally increased risk of asthma events in children
Pape, 2020[44]	Denmark	75 156	3-10	maternal stress both in private life and at work	childhood asthma	birth cohort study	no association	no support to an elevated risk of childhood asthma related to exposure to stress during pregnancy
Rosa, 2016[47]	Mexico	417	2	maternal negative life events in pregnancy and postnatally	childhood wheeze	prospective birth cohort study	RR 1.12, 95% CI 1.00–1.26 RR 1.21, 95% CI, 1.08–1.35	higher maternal psychosocial stress during pregnancy and postnatally was associated with increased risk of wheeze
Smejda, 2018[46]	Poland	370	1	maternal psychological stress during pregnancy	AD, food allergy, wheezing and recurrent respiratory tract infections	prospective cohort study	OR 1.09, 95% CI 1.01–1.2	maternal stress during pregnancy increased the risk of wheezing in children
Liu, 2019[45]	Denmark	547 533	6	negative life events and job stressors	childhood asthma	population based cohort study	PR 1.02, 95% CI 0.99–1.06 PR 1.17, 95% CI 1.11–1.23	maternal exposure to negative life events prenatally was not significantly associated with offspring asthma among mothers with low job demands, low job control was associated with increased risk for asthma

aOR = adjusted odds ratio, CI = confidence interval, PTSD = post-traumatic stress disorder, HR = hazard ratio, RR = risk ratio, AD = atopic dermatitis, OR = odds ratio, PR = prevalence ratio

[1]Age is expressed in years.

4 Discussion

This literature review assessed the impact of lifestyle factors regarding to the risk of developing childhood asthma. The main findings of this literature review are 1) maternal smoking during pregnancy and exposure to tobacco smoke in childhood increase the prevalence of wheeze and asthma in children. 2) Childhood overweight and obesity decrease lung function and increase the risk for childhood asthma. Maternal pre-pregnancy obesity predisposes a child to higher asthma risk as well as high gestational weight gain. 3) Physical activity can reduce the risk of asthma in children whose activity level is low to begin with. 4) Maternal psychological stress and parental mental health disorders can impact childhood asthma risk, underscoring the importance of addressing maternal well-being during pregnancy.

Tobacco smoking has been understood to be harmful to both adults and children in numerous ways. The studies in this literature review support these assumptions. This review of literature included total 12 studies examining correlation between tobacco and childhood asthma (Table 1). Smoking during pregnancy increased the odds of childhood asthma in all six studies examining this aspect. The association between maternal smoking and childhood asthma involves intricate mechanisms, including in utero exposure to harmful substances, epigenetic modifications, immune system modulation, and disruptions in prenatal lung development. A Mendelian randomization study found only slightly increased risk for asthma, whereas the other studies found stronger evidence. Methodological differences and variations in smoking exposure assessments may contribute to this discrepancy. The findings from these studies suggest that tobacco smoke exposure during pregnancy primarily increases the risk of early-childhood asthma whereas high exposure may increase the risk of persistent asthma. The risk of childhood asthma seems to be dose-dependent: higher the number of cigarettes smoked by the mother, higher the risk of asthma in their offspring.

A Korean cross-sectional study[12] was the only study to use parental cotinine-verified smoking status in their analysis. Other studies relied on self-reported smoking status. Cotinine-verified smoking status might be assumed to be more accurate than self-reported smoking status, as people tend to diminish their bad habits. However, this Korean study found no significant association between the parental smoking group and childhood asthma group. These contradictory findings can be caused by different measurements of SHS exposure, different adjusted confounders used in statistical analyses, differences in time to diagnosis, and difficulty in distinguishing between the effects of exposure to SHS by paternal and maternal smoking.

Parental smoking cessation before or during pregnancy was shown to decrease the risk of asthma in offspring. Strongly encouraging parents to quit smoking is important when trying to minimize the burden of asthma disease. Despite the better knowledge, there are still mothers and fathers who smoke during the pregnancy of their child. Tobacco is highly addictive and individuals have trouble quitting it even if they wanted to. Having more professional support with smoking cessation could be helpful to parents-to-be who are unable to quit smoking by themselves. These smoking cessation programs would increase the health of the parents as well as decrease the risk of childhood asthma in their offspring.

Only one Swedish research paper[11] studied the use of oral moist snuff during pregnancy and its correlation to childhood asthma. Interestingly this study found only weak association between snuff usage during pregnancy and childhood asthma, no statistical significance. Snuff usage is growing popularity especially in Nordic countries and therefore it is important to investigate more on the effects that it may have with fetus development and risk of inflammatory illnesses.

Three cohort studies examined multi-generational effects of tobacco smoking by studying the effects of grandmaternal smoking during pregnancy and grandchildren's risk of asthma. All three studies found grandmothers' smoking during pregnancy to increase the odds of childhood asthma in grandchildren. Smoking during pregnancy has long lasting effects on generations to come which increases the importance of abstaining from cigarette smoking during pregnancy.

Overweight and obesity are associated with numerous adverse health outcomes. Containing normal body weight has been hypothesized to reduce the prevalence of many respiratory illnesses since obesity decreases lung function (decreased FEV1/FVC ratio). This review covered 11 papers studying the relation between overweight/obesity and childhood asthma and four papers studying physical activity and childhood asthma (Table 2).

Three studies focused on the relation between body mass index of children and physician diagnosed asthma. These studies showed asthma risk increasing with the rising of body mass index. Children with obesity had higher OR for risk of asthma compared to children with overweight. However overweight children are in greater risk for asthma compared to their normal weighted peers. The relationship between obesity and asthma is not completely clear, but several hypotheses have been suggested, for example, different immune system responses or predisposing factors with birth weight, energy usage and nutrition.[22]

Five cohort studies examined the association between maternal pre-pregnancy BMI and gestational weight gain. All these studies found mothers' overweight or obesity to increase the risk of asthma in their offspring. Trying to maintain normal body mass index is not only beneficial for the individual, but also to their possible offspring later in life. However, weight management is extremely complex and maintaining normal body weight can be challenging despite the awareness of the health risks associated with being overweight.

Three of these studies also looked the role of gestational weight gain with the risk of offspring asthma. A meta-analysis[24] found increased risk for childhood asthma with mothers who had both very high GWG and moderate high GWG. The same study found also very low GWG to increase the risk of asthma in offspring. A large Danish birth cohort study found GWG $\geqslant$ 25kg to increase the risk of offspring asthma. However, GWG had no effect on offspring atopic eczema or hay fever. A study from United States found only a suggested higher risk with GWG less than 15lb and offspring asthma. Whereas a Canadian study found no associations with GWG and any allergic outcome. These differences in the results might be explained by various methods used to categorize GWG or information and selection biases of the data.

Regular physical activity in children offers numerous health benefits, and it has been suggested to play a protective role against asthma. However, the relationship between physical activity and asthma risk is complex and influenced by various factors. The lack of standardized, validated approaches to measure physical activity can contribute to mixed results. In this review three studies were evaluating the correlation between physical activity and risk of childhood asthma. Recent research shows that higher level of physical activity was associated with a lower asthma risk for children with lower initial activity levels.[30]

Childhood physical activity and exercise is often linked to environmental factors as well. In urban areas, exercise can expose children to air pollution, potentially counteracting the protective effects of physical activity. Physically active children in polluted areas may have higher exposure to

pollutants like nitrogen dioxide and black carbon, which are associated with airway inflammation and asthma.

The relationship between maternal psychological stress and parental mental health and the risk of childhood asthma is a topic of growing research interest, investigating on maternal well-being during pregnancy and the long-term health outcomes of their offspring. Potential mechanisms linking maternal stress and offspring asthma are disrupted stress-response and high cortisol levels in pregnant women. High stress can alter cytokine balance of the fetus and flavor Type 2 immune response. Maternal stress can also lead to premature birth, and therefore increase the risk of developing asthma. This review of literature evaluated seven studies investigating various parental stress scenarios and the risk of asthma and atopic diseases in the offspring (Table 3).

Beyond maternal stress, parental mental health disorders have also been associated with an increased risk of childhood asthma and various other health issues. A comprehensive meta-analysis[38] identified a range of adverse effects on children's lives due to parental mental disorders, including psychiatric and neurodevelopmental problems, injuries, malnutrition, diarrhea, and asthma. This suggests that the mental health of both parents can have a substantial impact on the well-being of their children.

Comparing the different studies on parental mental health and risk of childhood asthma poses challenges due to the diverse approaches in measuring parental stress and mental health challenges during pregnancy. Studies employ different methodologies, including various stress scenarios and measurement tools. The absence of a standardized framework for evaluating maternal stress, coupled with variations in cultural and individual factors influencing stress responses, complicates attempts to draw cohesive conclusions across studies.

The FinnBrain birth cohort study[40] found mother-experienced psychological distress symptoms during pregnancy to be associated with increased risk of offspring wheezing, highlighting the influence of prenatal psychological morbidity exposure on immune system of the fetus.
A meta-analysis[39] found that prenatal depression significantly increased the risk of childhood asthma, emphasizing the importance of addressing maternal mental health during pregnancy.
Similarly, a Taiwanese longitudinal study[41] observed an increased risk of asthma among young patients under 20 years old with post-traumatic stress disorder, however the pathophysiology between PTSD and asthma risk remained unknown.

Results from published studies on the association between prenatal exposure to negative life events and childhood asthma are inconsistent. Whereas some studies found full support for increased risk of asthma after maternal exposure to negative life events, two big Danish cohort studies from 2019 and 2020 did not find statistically significant associations between maternal prenatal exposure to negative life events and an increased risk of childhood asthma, except in cases where maternal job control and demands were considered.

The collective evidence reinforces the importance of holistic maternal care that considers mental health as an integral component of prenatal well-being. Routine mental health assessments during pregnancy, particularly focusing on depressive and anxiety symptoms, may aid in identifying at-risk individuals and facilitating timely interventions. There is still a lot of uncertainty when it comes to mental health, stress, and childhood asthma risk. Further research is needed to unravel the intricacies of this relationship and inform targeted interventions and prevention strategies.

5 Summary

This review underscores the significance of addressing lifestyle factors, maternal well-being, and parental mental health to reduce the risk of childhood asthma. These findings provide valuable insights for healthcare professionals and individuals to develop targeted interventions and prevention strategies that promote better respiratory health and overall well-being in children. Further research is needed to unravel the complexities of these relationships and to reduce the burden of childhood asthma.

Tobacco smoking increases the risk of childhood asthma in several scenarios. Numerous studies have shown maternal smoking during pregnancy to be harmful for the offspring. Paternal smoking also plays role in children's asthma risk and the effects of smoking history can be seen even in the grandchildren of tobacco smoking mothers. Predisposing a child to secondhand tobacco smoke early in life increases the risk of childhood asthma. It's critical to highlight the importance of smoking cessation for both parents before and during pregnancy as well as minimize childhood exposure to tobacco.

Childhood overweight and obesity not only reduce lung function but also elevate the risk of childhood asthma. Maternal pre-pregnancy obesity and high gestational weight gain further contribute to this risk, highlighting the need for maintaining a healthy weight pre-pregnancy and beyond. Physical activity is beneficial in reducing the risk of asthma, particularly in children with low activity levels. Public measures trying to prevent rising obesity epidemic can help decrease the burden of asthmatic diseases in also generations to come.

The findings from these studies underscore the complex relationship between maternal stress, parental mental health, and childhood asthma. While there is compelling evidence to suggest a link between these factors, the precise mechanisms and outcomes remain a subject of ongoing research. Recognizing the importance of maternal well-being during pregnancy and addressing parental mental health issues may play a crucial role in reducing the risk of childhood asthma and improving the overall health and well-being of children.

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