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INTEGRATED STUDY MASTER'S THESIS

Caffeine Intake and Pregnancy Outcomes in Lithuania

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USED ABBREVIATIONS

- **11β-HSD2** – 11β-hydroxysteroid dehydrogenase type 2
- **A1Ars** – A1 adenosine receptors
- **ADORA2A** – adenosine A2A receptor
- **AMH** – Anti-Müllerian hormone
- **AOP** – apnea of prematurity
- **ASD** – Autism spectrum disorders
- **Areg** – amphiregulin
- **BMI** – body mass index
- **BP** – blood pressure
- **BPA** – bisphenol A
- **cAMP** – cyclic adenosine monophosphate
- **CNS** – central nervous system
- **COX2** – Cyclooxygenase-2
- **CVD** – cardiovascular disease
- **CYP1A2** – Cytochrome P450 1A2 enzyme
- **E2** – 17β-estradiol
- **E2Rα** – estrogen receptor alpha
- **GABA_A** – Gamma Aminobutyric Acid receptor type A
- **IGF-1** – insulin-like growth factor 1
- **IGF2** – insulin-like growth factor 2
- **IUGR** – intrauterine growth restriction
- **LH** – luteinizing hormone
- **Lif** – leukemia inhibitory factor
- **Ltf** – lactoferrin
- **Muc1** – mucin 1
- **PDEs** – phosphodiesterases
- **PIGF** – phosphatidylinositol glycan anchor biosynthesis class F
- **VEGF** – Vascular endothelial growth factor

SUMMARY

Epidemiological research has shown an association between maternal caffeine intake and adverse pregnancy outcomes, but the biological mechanisms behind these effects are still not well understood. Recent animal studies show adverse effects of caffeine during pregnancy in terms of oviduct contractility, uterine receptivity, embryo development, and placentation that together contribute to pregnancy complications. Notably, even under controlled laboratory conditions, individual animals display considerable variability in their responses to caffeine, pointing to a potential role for epigenetic regulation alongside genetic differences. Nevertheless, genetic variants influencing caffeine metabolism (such as CYP1A2 or ADORA2A polymorphisms) differ by region and ethnicity. That's why it would be beneficial to carry out similar studies in various settings and among different populations, including Lithuania. Participation in this study was voluntary and anonymous, and data was handled confidentially through online questionnaire. According to research results, there was no statistically significant effect of caffeine on pregnancy found. However, the extensive literature review and animal-model studies suggest that effect may be much less prominent, but still sufficient to even influence further generations.

Keywords: caffeine, pregnancy, birth weight, fetal development, gestational diabetes

SANTRAUKA

Epidemiologiniai tyrimai parodė ryšį tarp motinos vartojamo kofeino ir neigiamų nėštumo baigties rezultatų, tačiau šių poveikių biologiniai mechanizmai vis dar nėra iki galo išsiaiškinti. Naujausi tyrimai su gyvūnais rodo, kad kofeinas nėštumo metu daro neigiamą poveikį kiaušintakių kontraktiliškumui, gimdos receptyvumui, embriono vystymuisi ir placentos formavimuisi, o visa tai kartu prisideda prie nėštumo komplikacijų. Pažymėtina, kad net kontroliuojamomis laboratorinėmis sąlygomis atskiri gyvūnai labai skirtingai reaguoja į kofeiną, o tai rodo, kad greta genetinių skirtumų svarbų vaidmenį gali vaidinti ir epigenetiniai veiksniai. Vis dėlto, genetiniai variantai, darantys įtakos kofeino metabolizmui (tokie kaip CYP1A2 ar ADORA2A polimorfizmai), skiriasi priklausomai nuo regiono ir etninės priklausomybės. Taigi būtų naudinga atlikti panašius tyrimus įvairiose aplinkose ir tarp skirtingų populiacijų, įskaitant Lietuvą. Dalyvavimas šiame tyrime buvo savanoriškas ir anoniminis, o duomenys buvo tvarkomi konfidencialiai naudojant internetinę anketą. Remiantis tyrimo rezultatais, nebuvo nustatyta statistiškai reikšmingo kofeino poveikio nėštumui. Tačiau išsami literatūros apžvalga ir tyrimai su gyvūnais rodo, kad šis poveikis gali būti daug mažiau pastebimas, tačiau vis tiek pakankamas, kad paveiktų netgi vėlesnes kartas.

Raktiniai žodžiai: kofeinas, nėštumas, naujagimio svoris, vaisiaus vystymasis, nėščiųjų diabetas

INTRODUCTION

Coffee is much more than just a morning routine, it is a chemically complex drink, containing hundreds of biologically active compounds. While caffeine is its most famous ingredient, the roasting process of coffee beans actually creates new, beneficial for human health substances, such as chlorogenic acid quinides or quinolactones (1).

Needless to say, caffeine is one of the most consumed psychoactive substances globally, deeply integrated into global culture, daily life and commence. An estimated 80% of people worldwide consume 200 mg of caffeine every day, which is comparable to around three cups of espresso. North America and Europe typically have the highest per capita consumption rates (2). It has been recently estimated that more than 50 million cups of coffee are consumed daily worldwide, ranging from 5.4 to 11.4 kg/y per capita in several European countries, with the highest annual consumption registered in Finland, Norway and Denmark (11.4, 8.7 and 8.0 kg per capita, respectively) (3).

Moreover, drinks that contain caffeine, especially tea and coffee, have important social functions. While coffee is also consumed at home, it is frequently thought to have a strong social and aesthetic role, particularly when consumed outside the home, whereas tea frequently plays a key role in bringing family together (4). The consumption of coffee, in particular, has been linked to a "unique mystique associated with a wealthy, refined and intellectually evolved class" in some contexts, and energy drinks are also sometimes associated with social status and "fitting in" among adolescents. (5)

Main compounds of unprocessed coffee beans include carbohydrates (60.0%), reducing sugar (1.0%), sucrose (7.0%), pectin (2.0%), starch (10.0%), pentan (5.0%), hemicellulose (15.0%), whole cellulose (18.0%), lignin (2.0%), grease (13.0%), protein (N*6.25) (13.0%), ash content (oxide) (4.0%), tannic acid (13.0%), N-methylnicotinic acid (soluble) (1.0%), caffeine (soluble) (1.0~2.0%) (6).

Beyond its role as a stimulant, it has been estimated that caffeine may have an influence on human’s health. It is a subject of intense debate, showing both life-saving potential and significant risks. In neonatal care, for instance, caffeine is used with a major success for treating apnea in premature infants (AOP) and is now been established as one of neonatology's greatest success stories (7) (8). As well as it may cause harm – newer research suggests that high doses might increase the risk of cerebellar hemorrhage in preterm babies, especially with a high dose caffeine regime (9). Moreover, there’s a suggestion that high serum caffeine levels may trigger inflammatory responses in these same vulnerable patients (10).

The data regarding cancer is equally complex. Some evidence suggests that coffee might play a protective role against colon cancer. There's a theory that caffeine or some components of coffee act as antioxidants that protect against DNA damage and suppress tumor growth, although other studies show no correlation (11). There are also specific concerns for postmenopausal women, where heavy consumption (≥ 5 cups daily) has been linked to a higher risk of ovarian cancer (12).

Perhaps the most critical area of concern involves pregnancy. The important thing to remember in context of pregnancy is that caffeine freely crosses the placenta and reaches the fetus. Unlike adults, who process caffeine in 2 to 4 hours hours, a fetus lacks the necessary enzyme (CYP1A2) to break it down. In that way, it can stay in a fetus's system for up to 24 hours (13). This prolonged exposure is particularly concerning because it may interfere with heart development, potentially changing how cardiac genes are expressed or how the heart functions via adenosine receptors (14), (15).

While some literature suggests that keeping caffeine intake under 200 mg daily (about 1-2 standard cups of coffee) is relatively safe (16), several studies now link even low intakes, between 100 and 200 mg, to issues like higher risk of miscarriage (17), fetal growth restriction (18), low birth weight (19) (20) (21), and adverse outcomes in offspring in the future, including increased rates of overweight and obesity (22) (23), and even impaired cognitive development (24). Several animal studies show that such increased risk may be passed even to further generations (25) (26).

These findings raise the possibility that no truly "safe" threshold for caffeine consumption during pregnancy may exist. Interestingly, even under tightly controlled experimental conditions, individual animals show substantial variability in their responses to caffeine. This suggests that, beyond genetic differences, epigenetic regulation may also contribute to these phenotypic effects (27).

Genetic variants influencing caffeine metabolism (such as CYP1A2 or ADORA2A polymorphisms) differ by region and ethnicity and may likely contribute to the wide range of individual responses to caffeine (28) (29) (30) (31). For instance, certain A2A receptor polymorphisms are linked to differing levels of anxiety and sleep disturbances after caffeine consumption (32) (33) (34). Several cohort studies of pregnant women who regularly consumed caffeine have shown that those with higher CYP1A2 activity were more likely to experience spontaneous abortion and intrauterine growth restriction (35) (36). Additionally, specific CYP1A2 genotypes have been associated with a greater likelihood of reduced fetal birth size and recurrent pregnancy loss in mothers who consume caffeine (37) (38)

Taken together, these findings suggest that genetic differences in caffeine-metabolizing pathways significantly influence susceptibility to caffeine's effects, indicating that pregnancy outcomes depend not only on the amount of caffeine consumed but also on the individual's metabolic rate. That's why it would be beneficial to carry out similar studies in various settings and among different populations.

In such manner, **the aim** of the study was to perform a comprehensive literature review on this topic and evaluate caffeine consumption patterns and their potential health implications among pregnant and already delivered women in Lithuania, with particular emphasis on factors influencing consumption.

To achieve this aim, several **objectives** were established:

- to quantify daily caffeine intake among participants through provided questionnaire;
- to classify participants according to recommended caffeine intake thresholds (e.g., ≤200 mg and >200 mg per day);
- to identify the main sources contributing to caffeine consumption (e.g., coffee, tea, soft drinks, chocolate);
- to evaluate factors influencing caffeine consumption, including social and informational sources (e.g., literature, healthcare professionals' and family or friends' advice, social media);
- to examine potential associations between caffeine intake and selected lifestyle factors (in this research, alcohol consumption);
- to compare findings with existing literature regarding safe caffeine intake levels in the context of pregnancy, focusing on baby's weight and gestational diabetes.

Methods included literature search and cross-sectional study that was conducted using questionnaire-based data collection, available in several languages.

The study included **128 participants** (102 already delivered and 26 currently pregnant ladies) that were recruited on a voluntary basis as patients of Obstetrics department of Vilnius University Hospital Santaros Klinikos (Vilniaus universiteto ligoninė Santaros klinikos – VULSK) and online.

SEARCH STRATEGY AND SELECTION CRITERIA FOR LITERATURE REVIEW

In November 2024 – October 2025 literature search was performed in PubMed, PubMed Europe, Cochrane Library, and Google Scholar databases. Search terms were ("caffeine" OR "caffein" OR "theine" OR "coffee") AND ("pregnancy" OR "gestation" OR "maternal" OR "expectant") AND

("embryogenesis" OR "development" OR "fetal" OR "embryo") AND ("effects" OR "impact" OR "influence" OR "outcome"). Only articles in English, published from 2010 to 2025 were selected, with the focus on the last 5 years. References from relevant papers also were used.

LITERATURE REVIEW

Caffeine as a substance

Caffeine, also known as 1,3,7-trimethylxanthine or 1,3,7-trimethylpurine-2,6-dione ($C_8H_{10}N_4O_2$), is the most well-known of coffee compounds. It is considered as a xanthine alkaloid compound as it is a metabolite of nitrogen metabolism (39). Caffeine is an organic heterocyclic compound built with a purine base. Figure 1 displays its chemical structure (40).

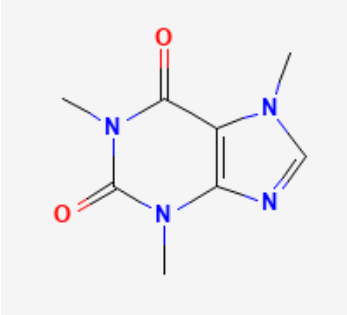

Figure 1. Caffeine chemical structure — National Center for Biotechnology Information (2026). PubChem Compound Summary for CID 2519, Caffeine

Beyond just coffee, this stimulant is a staple in tea, sodas and other beverages, as well as some medicines. It is present in green coffee beans at concentrations ranging from 0.5% to 2% of total chemical content. What makes it so effective is how quickly the human body processes it. After a drink, the gastrointestinal tract absorbs the caffeine almost immediately and sends it circulating through the entire system. Because of its chemical structure, it can easily cross the body's most restrictive filters, including the blood-brain barrier and the placenta. This is exactly why it is a major concern for fetal health during pregnancy.

Caffeine's pharmacokinetics

Caffeine has an oral bioavailability of nearly 100%, making oral administration the main route of delivery. For premature infants, this process is relatively quick. It generally takes between 30 minutes and two hours for the substance to reach its highest concentration in their bloodstream (known as peak plasma concentration Tmax).

While some substances bind heavily to blood proteins, in adults only about 10% to 36% of caffeine attaches to proteins like albumin, leaving the rest free to move through the body. (41) (42).

Furthermore, caffeine's lipophilic nature allows it to move effortlessly past the body's toughest defenses, including the blood-brain barrier and the placenta. No physiological barriers have been identified that

restrict its distribution, which is why it is so easily found in various body fluids, such as human breast milk and amniotic fluid (43).

Talking about distribution, even though caffeine does not accumulate in any specific tissues or organs, relatively high concentrations are found in the brain. This reflects caffeine's mechanism of action via binding to adenosine receptors, thar are mainly located within brain tissue. Animal studies indicate that approximately 80% of plasma caffeine can be detected in brain (44). Moreover, such pattern of distribution remains consistent across different ages but tends to be higher in women and individuals with obesity (45).

In adult population, only about 1% of caffeine is excreted unchanged, while approximately 80% is metabolized to 1,7-dimethylxanthine, 10% to 3,7-dimethylxanthine (theobromine), and 4% to 1,3-dimethylxanthine (theophylline). These metabolites are further broken down in the liver to monomethylxanthines and eventually to methyluric acids.

Even though the average half-life of caffeine in adults is around 5 hours, this number is rarely constant. There are several factors that can significantly alter its metabolism and duration. For example, nicotine acts as a metabolic accelerator: smokers often clear caffeine from their systems twice as fast as non-smokers. In contrast, in pregnant individuals, particularly during the third trimester, caffeine can stay active for up to 15 hours, so three times the usual duration. Newborns as well metabolize caffeine much more slowly. While in a full-term baby it might take eight hours to clear bloodstream from it, in a premature infant it could take up to 100 hours. This difference is largely due to their immature cytochrome P450 enzyme systems and underdeveloped demethylation pathways. By about 9 months of age, children typically exhibit caffeine elimination rates similar to adults. Moreover, individuals with impaired liver function or those taking cytochrome P450 inhibitors may have an extended caffeine half-life as a result of reduced enzymatic activity (46), (47).

Caffeine's pharmacodynamics

The primary mechanism of caffeine's action is its antagonism of adenosine receptors, particularly the A_1 and A_2 subtypes (46) (48) (49). A_1 receptors are generally associated with protective or homeostatic functions in tissues, whereas A_2 receptors play more regulatory roles. Because A_2 receptors are widely expressed in the CNS, they are largely responsible for the central effects observed with caffeine intake. The antagonism of the A2a receptor is particularly responsible for caffeine's wakefulness effects (50) (51).

Adenosine receptors are distributed throughout the body, not just within the central nervous system. They are G-protein–coupled receptors that influence cyclic adenosine monophosphate (cAMP) levels within tissues. Caffeine's second major mechanism involves inhibition of phosphodiesterases (PDEs)—specifically PDE1, PDE4, and PDE5—which are responsible for cAMP degradation (52). Additionally, caffeine can induce calcium release from intracellular stores and modulate GABA_A ionotropic receptors.

Taken together, these mechanisms produce effects broadly similar to those of β-adrenergic receptor agonists, which also elevate cAMP levels. However, caffeine's impact on the immune system is less straightforward and appears to be dose dependent. For example, Daly (2007) (53) found that at the low doses typically consumed by humans, caffeine's primary effects stem from adenosine receptor antagonism.

All four adenosine receptor subtypes (A_1, A_2A, A_2B, and A_3) regulate the production of cytokines and other immunoregulatory molecules, thereby contributing to anti-inflammatory effects.

Caffeine's impact on the cardiovascular system is defined by opposing biological mechanisms. On one hand, it strengthens the heart's contractions (a positive inotropic effect) by directly blocking A1 receptors in cardiac tissue. It also encourages the release of catecholamines, which further accelerates heart rate and contractility. At the vascular level, the body response is even more nuanced. Caffeine can lead to relaxation of vascular smooth muscle cells by direct antagonism adenosine receptors and stimulating the release of endothelial nitric oxide.

However, the vasodilatory effect is counterbalanced by increased sympathetic activity resulting from catecholamine release, as well as the positive inotropic and chronotropic actions on the heart, which together promote vasoconstriction. The interaction between these opposing mechanisms of dilation and constriction produces a highly individualized response that depends on factors such as caffeine dose, frequency of consumption, and the presence of comorbid conditions like diabetes or hypertension. In individuals who consume caffeine infrequently, systolic blood pressure may rise to 10 mm Hg. At the same time, habitual consumers usually develop a tolerance that prevents any significant acute change in BP (54).

Beyond the heart, caffeine significantly interferes with the role of adenosine in the brain. Adenosine is a fundamental regulator of diverse functions, including sleep, cognition, and pain perception. Its dysfunction is also linked to several serious neurological conditions, such as Alzheimer's (55),

Huntington's and Parkinson's diseases, as well as myasthenia gravis, epilepsy, depression, and schizophrenia (52). When caffeine is consumed consistently over time, the brain undergoes compensatory changes. It creates more A1 receptors for those being blocked, it is a process known as upregulation. Interestingly, this adaptation may offer neuroprotective benefits, particularly for patients recovering from issues like cerebral ischemia (56) (57).

At present, epidemiological research has noted that these physiological interactions may translate into long-term health benefits. Research by Ding et al. (2014) demonstrated that high-volume coffee consumption (up to six cups daily) was linked to a 33% reduction in the risk of developing type 2 diabetes. Furthermore, moderate intake appears to be beneficial for heart health. Current data indicates that drinking between three and five cups per day is associated with the lowest risk of cardiovascular disease (CVD) and overall mortality (Ming Ding, Ambika Satija et al.) Notably, even heavy coffee consumption does not appear to increase the risk of heart-related issues, suggesting a protective or at least neutral effect (58) (59). As well caffeine may have beneficial effects for population, affected by neurodegenerative disorders (60).

CAFFEINE EFFECTS ON REPRODUCTIVE HEALTH AND PREGNANCY

Caffeine's influence on reproductive health and pregnancy in general could be conditioned by a complex interplay of biological, environmental, and individual factors. For instance, while some studies suggest that high caffeine intake may be linked to reduced fertility, the evidence remains divided and findings are mixed (61) (62). The risks appear more pronounced during the early stages of gestation. A significant body of research indicates that even modest daily consumption, ranging from 100 to 200 mg, correlates with an increased likelihood of miscarriage or restricted fetal growth (63) (64) (65) (66). Some research suggests increased risks of gestational hypertension and preeclampsia, though evidence is inconsistent (67) (68).

According to literature, offsprings of mothers exposed to higher levels of caffeine may even have an impaired cognitive development (69), and higher risk of childhood overweight and obesity (70) (71). However, evidence linking caffeine intake to the data regarding congenital disabilities is notably inconsistent. This lack of clarity underscores a critical need for more robust, large-scale studies and more comprehensive research on the underlying biological pathways that determine how caffeine interacts with fetal development and congenital abnormalities.

Caffeine and fertility

Studies looking at caffeine use and female fertility have shown mixed results. Some studies found little connection between them (72) (73) (74) (75), while others reported that caffeine might lower fertility (76) (77) or even improve it (78).

Some caffeinated drinks might influence fertility for reasons unrelated to caffeine itself. It is vital to distinguish the effects of caffeine from other components found in popular beverages. For instance, the negative impact of soft drinks on fertility may be driven by metabolic stressors, such as insulin resistance and weight gain, or exposure to industrial contaminants like bisphenol A (BPA) found in can linings, rather than the caffeine itself (61).

The research results in field of caffeine related infertility problems are inconsistent. Early studies established a potential risk threshold at three cups of coffee per day (79), yet more recent, large-scale systematic reviews suggest a different conclusion. Following a protocol of an epidemiological systematic review of controlled clinical studies proposed by Huijuan Cao et al. in 2016 (80), an analysis found only low-quality evidence to support the idea that caffeine, regardless of the dose, significantly increases infertility risks (81). Furthermore, the type of beverage appears to play a role. Tea consumption, for example, has demonstrated a unique, non-linear association with reduced fecundability that differs from coffee or soda (62).

Recent animal model study by Abdelmissih S. et al. (82) has attempted to clarify these inconsistencies by looking at internal ovarian structures. In a study using mouse models, researchers observed that caffeine was associated with physical abnormalities, such as the development of cystic follicles and atretic oocytes. Interestingly, these structural changes occurred without a corresponding shift in systemic estrogen (E2) or Anti-Müllerian hormone (AMH) levels. This suggests that caffeine may not alter hormone production directly, but instead it interferes with how the body receives those signals. Specifically, the disruption might be caused by reduced sensitivity in estrogen receptors (E2Rα) within the ovary, even while the rest of the reproductive cycle appears to progress normally.

Another study by Ogunwole E. et al (83) using Wistar rats has provided detailed insights into how caffeine may damage reproductive tissues. Histological analysis showed dose-dependent structural changes in the ovaries, including congestion of connective tissues. Caffeine exposure led to sloughing of the plicae within the fallopian tube muscularis, degeneration of the uterine epithelial lining, and marked inflammation of myometrial stromal cells. Notably, those effects ppear to be long-lasting, persisting even after caffeine withdrawal. These physical changes are accompanied by hormonal shifts, specifically a

dose-dependent drop in estradiol levels and a reduction in luteinizing hormone (LH) following withdrawal.

The impact of caffeine is particularly evident when exposure occurs during the embryonic stage. Yadegari Dehnavi et al. found, that in female rodent offspring, high prenatal doses have been linked to a measurable decrease in both the weight and volume of the ovaries, alongside a reduced follicle count and a thinning of the zona pellucida (84). Male offspring are also susceptible to developmental interference. Research indicates that high maternal doses (e.g., 120 mg/kg/day) can lead to lower birth weights and impaired testosterone synthesis. At a molecular level, this exposure appears to disrupt testicular development by reducing Igf-1 gene expression and altering epigenetic markers, such as histone acetylation, adversely influencing development of gonads. Interestingly, the biological response is not linear. The lower dose (30 mg/kg/day) has been shown to actually increase the expression of certain steroid-producing enzymes (85).

In general, while these animal studies consistently demonstrate that caffeine can act as a reproductive toxin by altering tissue structure and gene expression, these findings must be interpreted with caution. The controlled environment of a laboratory often involves doses that exceed typical human consumption. Consequently, while the experimental data points toward significant potential risks, the evidence from human clinical trials remains largely inconclusive and subject to debate.

Caffeine and Embryo Transport

Embryonic implantation marks the critical gateway for establishing a successful pregnancy, and is perhaps the most vulnerable stage, accounting for nearly 75% of all pregnancy losses (86).

One of the main factor of these losses is the retention of embryos within the oviduct. If transport is delayed even slightly, the embryo may arrive in the uterus after the "window of uterine receptivity" has already closed, making successful implantation impossible (87) (88) (89). The movement of an embryo through the fallopian tube relies on two distinct biological forces: synchronization of ciliary beating in the ampula and rhythmic muscular contractions and relaxations of the myosalpinx in the isthmus (90). These muscular movements are orchestrated by specialized "pacemaker" cells known as interstitial cells of Cajal (91) (92) (93).

Interestingly, in vitro exposure to caffeine eliminated slow-wave pacemaker activity in the oviduct, which in turn suppressed the rhythmic contractions of the myosalpinx through a cAMP-dependent mechanism (94). These findings indicate that caffeine can interfere with myosalpinx contractility and impact the

transport of embryos, potentially leading to its entrapment in the isthmus. Additionally, caffeine's role as an adenosine receptor antagonist further complicates this process. Adenosine is a critical regulator of spontaneous contractions in the human fallopian tube, at the same time caffeine's interference alters plasma adenosine levels in a dose-dependent manner (95) (96). By blocking these receptors, caffeine disrupts the natural peristaltic patterns required for on-time delivery of the embryo to the uterus.

Beyond physical transport issues, the embryo quality itself may also be affected because of caffeine exposure. Qian, J et al. carried out an experimental in vivo study on mice (97). They found out that high levels of caffeine have been shown to directly degrade embryo quality: in vivo models suggest that caffeine exposure during the cleavage stage induces asymmetric cell division and significant cellular fragmentation, resulting in poor implantation potential and reduced pregnancy success.

Caffeine also appears to "de-synchronize" the uterus by altering the genetic signaling required for receptivity. The establishment of a receptive environment is tightly controlled by steroid hormones and specific signaling molecules. Qian, J et al. identified several key genetic targets that are dysregulated by caffeine consumption. In pro-inflammatory and signaling genes, COX2 expression had an abnormal (ectopic) expression in epithelium of uterine lumen, at the same time combined with reduction in subepithelial stroma. Genes, responsive to estrogen, such as leukemia inhibitory factor (Lif), mucin 1 (Muc1), showed remarkable dysregulation even at moderate caffeine doses, and lactoferrin (Ltf) was altered in high doses. Progesterone-responsive genes, including amphiregulin (Areg), have been also suppressed. These findings indicate that caffeine interferes with how the uterine lining responds to essential pregnancy hormones. Together, these findings suggest that caffeine interferes with the uterine epithelium's responsiveness to steroid hormones, potentially leading to impaired uterine receptivity.

Taken together, these observations suggest that both moderate and high intakes of caffeine act as a dual threat to early pregnancy. By simultaneously altering oviductal peristalsis and impairing the molecular receptivity of the uterus, caffeine creates an environment where embryos are either physically delayed or biochemically rejected. At higher concentrations, the direct disruption of embryonic development leads to more severe outcomes, including miscarriage, smaller litter sizes, and reduced birth weights.

Caffeine and Placentation

Understanding how caffeine affects the developing placenta is important, because perturbations in placental structure or function can contribute to adverse pregnancy outcomes such as intrauterine growth restriction (IUGR), low birth weight, or preeclampsia.

Research suggests that caffeine consumption during the middle and later stages of gestation can significantly compromise placental health. In rodent models, this exposure has been linked to a reduction in total placental weight and a breakdown of its internal architecture. It may be achieved potentially through chronic over-activation of renin–angiotensin system in both placenta and mother, as well as trigger of p53-dependent apoptosis specifically within trophoblast cells, which are essential for maintaining the placental barrier (98). Beyond structural damage, caffeine acts as a powerful disruptor of blood flow within the reproductive system. Study done by Kimmel CA et al. reported that even a single caffeine dose administered during critical developmental windows has been shown to sharply decrease the volume of blood reaching the ovaries, uterus, and decidua (99), indicating that caffeine-induced vasoconstriction in the uteroplacental circulation may alter the placenta's critical function to deliver nutrients to the developing embryo. Consequently, the resulting nutritional deficit may be a primary cause of the growth restrictions observed in caffeine-exposed pregnancies.

In humans, caffeine also stimulates the release of catecholamines into the maternal circulation (63). Elevated catecholamines can induce uteroplacental vasoconstriction, reducing blood flow within the intervillous space (100). Diminished uteroplacental perfusion compromises the passage of crucial components to fetus, and such reductions in placental blood circulation are strongly associated with impaired fetal growth (101).

According to literature, a critical molecular factor in fetal development is the enzyme 11β-hydroxysteroid dehydrogenase type 2 (11β-HSD2). In humans, a reduction in the activity of this enzyme, encoded by the HSD11B2 gene, is a well-established marker for fetal growth restriction (102).

Recent research into the biological mechanisms of caffeine suggests that its effects are primarily mediated through adenosine receptors. Specifically, caffeine and its metabolite, paraxanthine, appear to target the adenosine A2B receptor. Activation of this pathway leads to a decrease in intracellular cAMP levels which in turn suppresses the expression and activity of 11β-HSD2 within placental trophoblasts (103) (104). This relationship was further confirmed by using forskolin, an activator of adenyl cyclase. When researchers introduced forskolin to stimulate cAMP production, the inhibitory effects of caffeine were reversed. These findings categorize11β-HSD2as a primary molecular target through which caffeine can compromise fetal growth, highlighting the previously unrecognized role of A2B receptor signaling in placental health (104).

Supporting this, studies in pregnant women have documented that consuming just two cups of coffee during the third trimester can trigger a sharp rise in maternal adrenaline. This hormonal spike is

associated with an approximately 25% drop in the blood flow reaching the intervillous spaces of the placenta (105). Collectively, these findings indicate that caffeine exposure during middle and later gestation stages may substantially affect both embryonic and placental development, providing a potential explanation for the IUGR observed among human pregnancies with significant caffeine intake (106).

Another experimental study suggests that caffeine exposure may alter angiogenesis in the chick yolk sac and chorioallantoic membranes by reducing cell proliferation, increasing apoptosis, and downregulating key pro-angiogenic genes (such as VEGF, PlGF, IGF2) while altering expression of angiopoietins (107). Interestingly, there's a suggestion that caffeine exposure may be linked to immune dysfunction in animal models, which could also impact placental development or function (108).

Caffeine and fetal development

IUGR. Evidence regarding the harmfulness of prenatal caffeine exposure to the human fetus during development remains inconsistent. Multiple studies have demonstrated that caffeine can influence fetal development through several biochemical and physiological mechanisms. One proposed mechanism is caffeine-induced elevation of intracellular cyclic AMP (109), resulting from phosphodiesterase inhibition. Increased cAMP levels may disrupt normal cellular development processes and have been associated with fetal asphyxia (65).

Cardiac function. Adenosine, whose receptors are blocked by caffeine, plays a critical role in regulating tissue oxygen delivery and utilization. The regulatory role of adenosine is crucial for protecting the fetal heart from low-oxygen environments (hypoxia). Because caffeine blocks A1 adenosine receptors (A1ARs), it essentially damages this biological shield. During development, these receptors are the primary controllers of heart rate, at the same time, by inhibiting them, caffeine disrupts the cardiac natural response to hypoxic stress (65) (110).

Research in mouse models suggests these early disruptions lead to permanent structural damage. Caffeine exposure during early mouse gestation results in reduced embryonic myocardial mass that eventually manifests in adulthood as concentric cardiac hypertrophy. It is characterized by increased ventricular mass and decreased pumping efficiency (111) (112).

At the molecular level, this reprogramming is driven by extensive changes in gene expression. In another animal study done by Fang X et al., researchers identified hundreds of transcripts and exons involved in cardiac structure and DNA methylation that are altered by caffeine exposure. There were findings that

primary embryonic cardiomyocytes of mice had markedly altered not only structural genes of the heart, but also hormone-related genes, key cardiac transcription factors, and several microRNAs after prenatal caffeine exposure. Essentially, caffeine leads to a state of global DNA hypomethylation in embryonic heart cells, meaning the epigenetic blueprint for cardiovascular health is modified before birth (113).

Liver. Research involving rodent models has established a clear link between prenatal caffeine exposure and both structural and functional abnormalities in the liver. A primary mechanism behind these changes is the elevation of maternal glucocorticoid levels, which fundamentally alters the liver's developmental trajectory. For instance, this hormonal increase triggers the over-expression of genes related to glucocorticoid function, such as GR/C/EBPα. Simultaneously, it suppresses the IGF-1 signaling pathway, specifically IGF1/IGF1R/Akt2, leading to a reduction in fetal IGF-1 levels. These combined effects contribute to significant developmental dysfunction in the fetal liver and are associated with catch-up growth patterns in offspring affected by intrauterine growth restriction (114).

Noticeably, the metabolic consequences of prenatal caffeine exposure (PCE) appear to manifest differently based on the sex of the offspring, though both lead toward a higher risk of chronic disease. In females, caffeine-induced glucocorticoids enhance histone modifications and upregulate key lipogenic factors, including sterol regulatory element binding protein 1c and fatty acid synthetase. The result is a sustained increase in the synthesis of hepatic triglycerides that persist into adulthood, creating a lifelong susceptibility to non-alcoholic fatty liver disease (NAFLD) (115). In males, the pathway to liver dysfunction is slightly different, characterized by elevated corticosterone levels and a breakdown in cellular maintenance processes. Specifically, PCE leads to impaired autophagic flux and the inhibition of β-oxidation, which leads to impaired ability to break down fats. All those factors contribute to an abnormal accumulation of lipids within the liver, eventually leading to the development of NAFLD later in life (116).

Musculosceletal system. The impact of maternal caffeine consumption on the fetal skeleton is characterized by several distinct developmental disruptions. One major concern is the interference with H-type blood vessel formation, which is essential for healthy bone growth. This occurs because caffeine triggers the suppression of Connective Tissue Growth Factor (CTGF), leading to long bone dysplasia (117).

Additionally, caffeine appears to "weaken" bones during developmental stages. According to literature, high levels of maternal glucocorticoids, combined with the hypomethylation of the angiotensin-converting enzyme (ACE) gene, can lead to altered bone growth and a higher risk of osteopenia in later

life. At a molecular level, the disruption of the GR/HDAC11 (glucocorticoid receptor/histone deacetylase 11) signaling pathway reduces the expression of 11β-HSD2 (11β-hydroxysteroid dehydrogenase type 2) and alters histone acetylation H3K9ac (histone H3 at lysine 9). These changes weaken the bone matrix and significantly increase the individual's future vulnerability to osteoporosis (117).

Joint health is also compromised through multiple generations. Reduced H3K9 acetylation can interfere with TGF-β signaling, resulting in long-term articular defects. Furthermore, caffeine alters the relationship between glucocorticoids, IGF1, and the glucose transporter GLUT1. This imbalance leads to the degradation of the cartilage matrix and the buildup of advanced glycation end-products (AGEs), which collectively elevate the risk of developing osteoarthritis (118).

Neurological function. The central nervous system is equally sensitive to prenatal caffeine exposure, which can induce both oxidative stress and genetic damage within the brain. In animal models, these stressors alter the expression of survival-related proteins like BAX (BCL2-associated X protein) and Bcl-2 (B-cell lymphoma 2) in the hippocampus. Such molecular shifts result in observable behavioral changes, including significant memory deficits, anxiety, and symptoms resembling clinical depression (118). Caffeine also appears to influence how the brain handles electrical excitability. While many exposed rodents show an increased susceptibility to generalized seizures, some specific groups exhibit a delay in seizure onset. Researchers believe these differing reactions are likely due to c-Fos (cellular oncogene Fos) mediated pathways, which may offer a localized neuroprotective response against the stimulatory effects of caffeine (119).

Effects on pregnancy and birth outcomes

An important note should be taken that often it is difficult to make a proper conclusion because of the changes in patterns of caffeine consumption during pregnancy. Pregnant ladies tend to lessen caffeine intake and that's why less adverse events are reported (120). According to Chen L. et al. study, approximately 97% of mothers consumed the stimulant primarily through soda. The average intake was recorded at approximately 130 mg daily. While most women successfully lower or eliminate caffeine once they learn they are pregnant, certain demographic factors influence these habits. For instance, unintended pregnancies and younger maternal age are statistically linked to higher consumption levels. Furthermore, there is a clear correlation between heavy caffeine intake (exceeding 300 mg per day) and other lifestyle factors, such as cigarette or alcohol use (121).

Caffeine consumption and maternal pregnancy complications

A substantial amount of research explored how caffeine influences maternal metabolic function and its relationship with the development of gestational diabetes mellitus (GDM), as well as conditions such as preeclampsia, gestational hypertension (GH), and pregnancy-related anemia.

Gestational diabetes mellitus. The relationship between caffeine and Gestational Diabetes Mellitus (GDM) appears to depend heavily on the source of the beverage. Data from Kukkonen et al. suggest that moderate coffee consumption during the first trimester does not raise GDM risk and may even offer a slight protective effect. However, a higher intake of cola was linked to an increased risk. It is the finding that researchers believe is likely driven by sugar content and metabolic impact rather than the caffeine itself (122). Interestingly, the timing of consumption during pregnancy may also play a role. While intake during the 10–13-week window shows no significant link to GDM, moderate consumption (up to 100 mg/day) between weeks 16 and 22 was associated with a 47% reduction in GDM risk compared to total abstinence (123). Even when measuring direct plasma levels of caffeine and its metabolite, paraxanthine, no significant link to impaired glucose tolerance was identified, suggesting that moderate amounts do not disrupt maternal insulin sensitivity (123).

Gestational hypertension/preeclampsia. Extensive evidence suggests that caffeine does not play a major role in the development of gestational hypertension (GH) or preeclampsia. A large-scale meta-analysis, done by Chen, B. et al. and involving over 114,000 pregnant women concluded that there is no significant statistical association between caffeine exposure and these hypertensive complications (67). These findings were also supported by cohort study done by Hinkle, S. N, et al., that evaluated both self-reported caffeine intake and objective plasma concentrations of paraxanthine. Neither of those parameters showed a meaningful link to elevated blood pressure during pregnancy (123). Interestingly, consumption of caffeinated beverages between 16 and 22 weeks of gestation was associated with modest improvements in fasting cardiometabolic markers.

Anemia during pregnancy. While caffeine appears relatively neutral regarding blood pressure and glucose, it has a more direct negative impact on maternal iron levels. Research indicates that even infrequent consumption of caffeinated drinks can double the risk of developing anemia during pregnancy (124). This association is likely attributable to the way caffeine interferes with the digestive system's ability to process non-heme iron. By inhibiting iron absorption in the gastrointestinal tract, caffeine reduces the total amount of iron available to the mother, which can facilitate the onset of pregnancy-related anemia (125).

Adverse pregnancy and labor outcomes

Recurrent pregnancy loss. The question of whether caffeine consumption directly causes pregnancy loss remains a subject of intense debate in epidemiological research. Some data suggests that high-volume intake before conception (specifically four or more servings per day) is linked to an increased risk of spontaneous abortion, particularly between the eighth and nineteenth weeks of gestation (126).

However, the data is not always clear. David A Savitz et al. have found no significant relationship between caffeine intake and total miscarriage risk across multiple stages of pregnancy (127). On another hand, the results of prospective cohort population-based study suggest that the risk associated with high caffeine doses exists. Furthermore, the risk appears to be driven by caffeine as a molecule rather than other compounds in coffee, as similar patterns of loss were observed among those consuming caffeine from non-coffee sources, according to The Weng X. et al., although the results are based on small population sample (eight ladies, two of whom experienced a pregnancy loss), who consumed more than 200mg of caffeine daily. (63) (128).

These concerns extend into later stages of pregnancy as well. There is emerging evidence that elevated caffeine intake correlates with a higher likelihood of late-term miscarriage and stillbirth. While the precise strength of this association is still being debated, some research indicates that caffeine may be an independent risk factor for unexplained recurrent miscarriage, even when accounting for variables like maternal age and tobacco use (129) (130).

Preterm Birth. This association has been investigated for over 30 years with inconsistent results. Some studies report positive or inverse associations, while most suggest no clear association (131). This lack of association is supported by high-level clinical evidence. For example, a randomized, double-blind, controlled trial compared women who switched to decaffeinated coffee with those who maintained their usual high-caffeine intake. The results showed no meaningful difference in the average length of gestation between the two groups (132).

Despite these broad findings, new molecular research is adding complexity to the discussion. A recent case-control study utilized plasma analysis to examine hundreds (more than 800) of molecular features and found that caffeine levels were significantly higher in women who experienced preterm birth compared to those who delivered at term. This suggests that while general population trends may not show a clear link, specific individual metabolic responses to caffeine might still play a role in the risk of preterm birth (133).

Offspring outcomes

Epigenetic effects. As caffeine's chemical structure closely resembles adenine and guanine, which are the components of DNA, there is a theoretical possibility that it may be mistakenly incorporated into DNA during replication (63). This potential intercalation could contribute to chromosomal abnormalities and influence fetal growth. The research done in 2023 by Schellhas, L. et al. found specific changes in DNA methylation (DNAm) in umbilical cord blood, associated with coffee and soda consumption during pregnancy. However, the current evidence is not yet strong enough to confirm that typical maternal intake levels permanently alter a child's epigenetic profile at birth, mainly due to low level of caffeine consumption in studied participants (134).

Growth and development. The impact of caffeine on physical growth appears to follow a clear dose-response pattern. A dose-response meta-analysis of cohort studies made by Soltani, S. et al in 2023 concluded that for every additional 100 mg of caffeine consumed daily, there is a measurable increase in the risk of lower birth weight (LBW) (135). Remarkably, even intake levels below the standard 200 mg (above 50 mg) limit have been linked to infants being born small-for-gestational-age (SGA). These growth restrictions are not limited to weight, but also to shorter body length, smaller limb circumferences and reduced skinfold measurements (138) (139). On the other hand, another study reported inconsistent findings, with some associations between maternal coffee intake and higher birth weight (140).

Neurodevelopment. The relationship between caffeine and congenital issues like neural tube defects (NTDs) remains complex. The study by Schmidt R. et al. noted a positive association between caffeine and spina bifida and encephalocele, though results vary significantly across different racial and ethnic groups and do not show a consistent dose-response relationship (142).

According to previous research, high maternal caffeine intake (exceeding 300 mg daily) may be associated with early developmental delays. In a prospective study an interesting observation was made. At six months of age, these delays often manifest in communication, personal-social behavior, fine motor and problem-solving skills, while gross motor skill delays become more evident by the twelve-month age (136).

Research into the long-term neurodevelopmental effects of prenatal caffeine exposure has shown varying results depending on the specific condition being studied. For instance, the Adolescent Brain Cognitive Development (ABCD) study with 9157 participants found that prenatal exposure may alter the structure of white matter in the brain. Children aged nine to ten who were exposed to caffeine in utero showed

higher scores for psychopathology, including conduct disorders and oppositional defiant behavior (143) (137).

Furthermore, the evidence regarding Attention-Deficit/Hyperactivity Disorder (ADHD) is largely negative. Multiple comprehensive analyses by Haan et al. established no evidence linking maternal caffeine intake to ADHD symptoms in their children (138) (139).

In contrast, the relationship between caffeine and Autism Spectrum Disorder (ASD) presents a more complex picture. Some findings of meta-analysis by Patti M. A. et al. suggest that caffeine intake during gestation may act as a potential marker for increased susceptibility to ASD-related behaviors in early childhood. These behaviors are often measured using the Social Responsiveness Scale (SRS), a tool where elevated scores indicate a higher prevalence of traits associated with the autism spectrum. Data from longitudinal cohorts, such as the EARLI (Early Autism Risk Longitudinal Investigation) study, have noted a positive correlation between self-reported caffeine intake during pregnancy and higher SRS-T-scores in offspring between the ages of 3-8. Interestingly, this association appears to be influenced by maternal physiology. Evidence from the HOME (Health Outcomes and Measures) study indicates that a higher pre-pregnancy Body Mass Index (BMI) may intensify this relationship, suggesting that metabolic factors could play a mediating role in how caffeine influences neurodevelopmental traits (140).

Oncological influence. Recent epidemiological investigations have raised concerns regarding the potential link between maternal caffeine consumption and specific pediatric malignancies. Data from the research done by Hu Z et al. in 2024 indicates that prenatal exposure to caffeinated beverages, coffee in particular, correlates with an elevated risk of childhood brain tumors (CBTs), with a notable emphasis on the development of gliomas (141).

Beyond the central nervous system, similar trends have been observed in hematological cancers. According to Karalexi M. A. et al., high maternal coffee intake demonstrates a positive association with the incidence of childhood acute myeloid leukemia (AML). Their findings showed that this risk may be dependent on the beverage source. Coffee correlated with higher AML risk, whereas tea consumption showed no such relationship. Tea intake was inversely associated with hyperdiploidy, while no other cytogenetic abnormalities showed meaningful associations with either beverage (142).

Hu Z et al. also noted that the biological mechanisms linking maternal intake of caffeinated beverages to childhood neoplasms, CBTs, remain unclear. Both coffee and tea contain caffeine, and caffeine-related compounds are known to inhibit DNA topoisomerase II (topo II), an enzyme essential for proper DNA

replication and cell division. Inhibition of topo II can lead to chromosomal abnormalities and translocations, which are hypothesized to contribute to the development of certain infant tumors (141).

Obesity risk. Research on the metabolic effects of prenatal caffeine exposure suggests that higher maternal caffeine consumption is positively correlated with an increased BMI and a higher risk of pediatric obesity. Notably, the type of beverage may influence this risk, with some evidence suggesting that coffee has a more pronounced impact on childhood adiposity than tea (143).

Large-scale epidemiological data highlights a clear dose-response relationship in this area. In Li D. K. et al. study, in-utero exposure has been linked to a nearly twofold (87%) increase in the risk of childhood obesity compared to offspring with no exposure. This observation appears to follow a linear trend, where one-unit increase ($\log_{10}$ scale) in maternal intake corresponded to a 23% increase in the offspring's obesity risk. Interestingly, this association is often more stable in cases of persistent obesity rather than for intermittent elevations in BMI, and the effects seem to be more pronounced in girls than in boys (144).

Beyond general weight gain, prenatal caffeine exposure may influence specific fat distribution. In another study, children whose mothers consumed at least 180 mg/day of caffeine higher percentages of total body fat and increased accumulation of liver fat by the age of ten (145).

Findings from a large Norwegian prospective cohort study (with a total of over 50,000 participating mother-child pairs) similarly indicated that even minimal caffeine consumption during pregnancy was associated with accelerated growth during infancy and a higher likelihood of being overweight during the preschool years. This suggests that the "programming" effects of caffeine can influence a child's weight development from birth through at least the first eight years of life (22).

However, it is important to note that literature is not entirely unanimous. Some research has observed a contrasting effect, where exposure to caffeine and its metabolite, paraxanthine, was instead linked to reductions in both height and weight during early childhood (146). These inconsistencies highlight the need for a deeper understanding of how individual metabolic variations may influence the way a fetus responds to caffeine.

Future fertility. The consequences of prenatal caffeine exposure may even extend into the reproductive lifespan of the next generation. Research by Eubanks et al. on the long-term reproductive health of adult females who were exposed to caffeine in utero suggests a potential compromise in their baseline fertility. Specifically, these individuals demonstrate a significantly higher probability of presenting with Anti-

Müllerian hormone (AMH) concentrations below the clinical threshold of 1.0 ng/mL. Because AMH serves as a primary biomarker for assessing a woman's remaining ovarian reserve, essentially the size of her resting follicle pool, these suppressed levels strongly suggest that maternal caffeine intake could inadvertently diminish the future reproductive capacity of female offspring (147).

USED METHODS AND DATA COLLECTION FROM THE PATIENTS

While researching this topic, data collection was performed from December 2024 until February 2026 in department of Obstetrics and Pregnancy pathology unit of Vilnius university hospital Santaros Klinikos in Vilnius. The patients were asked to fill an online questionnaire created in Google Forms, consisting of 35 questions for delivered ladies and 32 questions for currently pregnant women. All those questions were split into 3 parts: about their gynecological anamnesis, average daily caffeine consumption and potential caffeine tolerance or addiction (annex 1) The questionnaire was available in Lithuanian, English, Ukrainian and Russian languages. The number of responses eligible for further evaluation was 105 for delivered and 23 for currently pregnant ladies.

Main hypotheses for research include H0 (There is no association between maternal caffeine intake and fetal/birth weight after adjusting for gestational age) and H1 (There is an association between maternal caffeine intake and fetal/birth weight after adjusting for gestational age). Also, for GD factor H0 (There is no difference in caffeine intake between women with and without gestational diabetes) and H1 (There is a difference in caffeine intake between women with and without gestational diabetes). To see if there is higher prevalence of increased caffeine intake in ladies with higher alcohol intake, the hypotheses H0 (there is no association between alcohol intake and caffeine intake) and H1 (there is an association between alcohol intake and caffeine intake) were established. It would be also interesting and important to evaluate the influence of caffeine with adjusted smoking status mothers, however in this study all patients reported no evidence of smoking during pregnancy.

For evaluation of daily caffeine intake, the values presented in work of Jensen, Tina Kold et al. (148) was used. According to them, each ladies' daily caffeine intake was estimated based on standard serving assumptions. A cup was defined as 150 mL, with caffeine contents assigned as follows: 117 mg per cup of coffee, 70 mg per cup of tea, 5 mg per cup of chocolate beverages, 70 mg per 0.5 L of cola or diet soft drinks, and 7 mg per 50 g chocolate bar. Also, ‘‘weekly intake of cola’’ was calculated as the sum of reported drinks of cola and diet soft drinks (assuming diet soft drinks to be cola).

Data collected from the online questionnaires were compiled and organized using Microsoft Excel (Microsoft Corporation, USA). Statistical analysis was performed using R 4.3.3 and Rcmdr (R Foundation for Statistical Computing, Vienna, Austria). Descriptive statistics were used to summarize the patients' information. Data distribution was assessed prior to analysis, and appropriate statistical tests and correlation analyses were applied, and results were reported with 95% confidence intervals (95% CI) and p-values. A p-value < 0.05 was considered statistically significant.

Research results and discussion

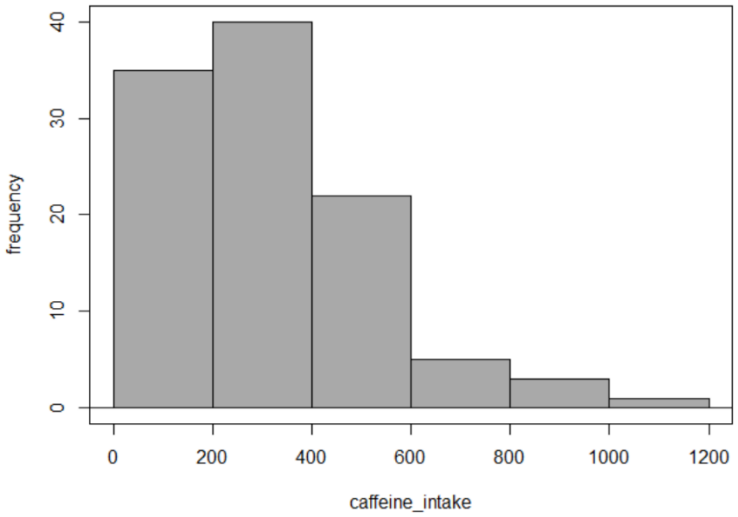

Figure 2. Caffeine intake (mg) data distribution in delivered ladies

The first step before main statistical analysis was to check the normality of caffeine intake data distribution. For this Rcmdr was used (graphs -> Histogram) (fig. 2). We can clearly see that data distributed non-normally, although in Shapiro-Wilk test p-value < 0.05 (0.000005733), so for further analysis Mann–Whitney will be used.

Interestingly, it can be noted that majority (67,2%, n = 86) of pregnant and delivered ladies, who filled the questionnaire, tended to drink more caffeine than is recommended by American College of Obstetricians and Gynecologists (200 mg) (fig.3). Among them, mean values were 271.5 mg/day for currently pregnant ladies (Q1-Q3: 194 – 334); 323 mg/day for already delivered (Q1-Q3: 187 – 421) and 315.0 mg of

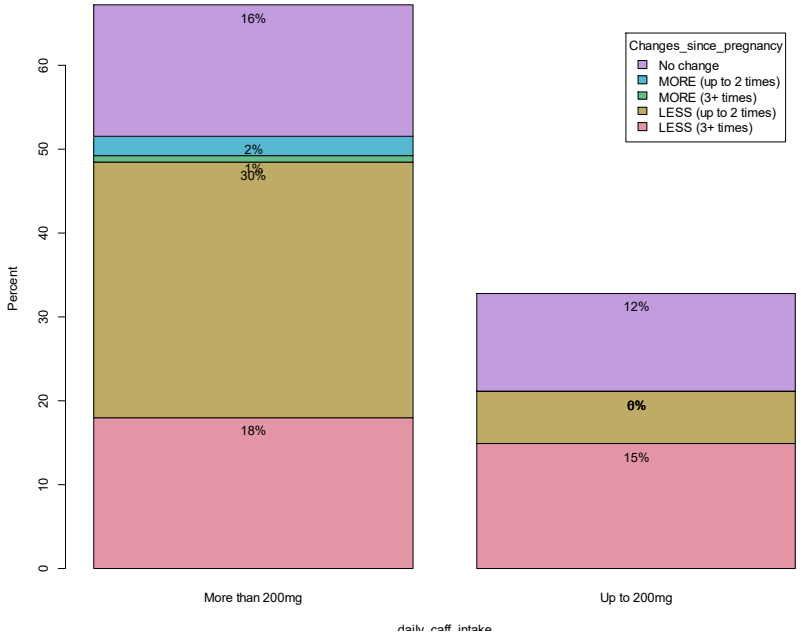

Figure 3. Daily caffeine intake and changes in it since pregnancy

caffeine per day for combined group (Q1-Q3: 188.2 – 411.8), with maximum reported value of 1193.0 mg per day.

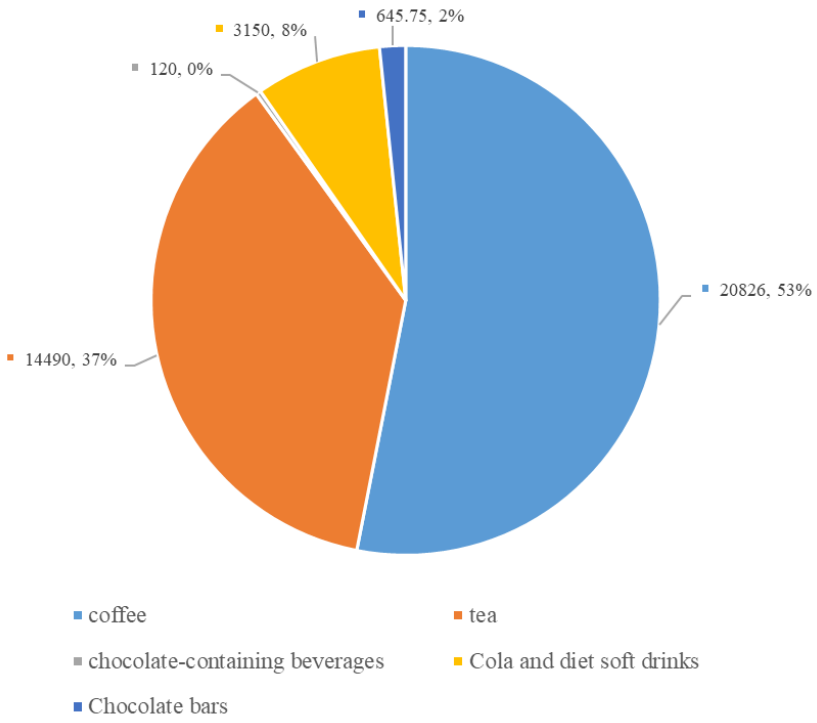

Figure 4. Main sources of caffeine among participants

The next chart shows the main sources of caffeine intake among pregnant women (fig. 4). Among participants, most caffeine comes from coffee, which makes up over half of the total intake (20826 mg, 53%). Tea is the second main source at 37% and 14490mg. Other sources contribute much less, with cola and diet soft drinks accounting for 8% and 3150mg, and chocolate bars only 2% and 645,75mg. Chocolate-containing drinks contribute almost none (120mg of general intake).

Most (72%) of ladies replied that they have changed their habits regarding caffeine-containing products intake during pregnancy. Among those who lowered caffeine intake (69%), 96% reported that they were drinking less caffeine since they found out about their pregnancy, with 50% lessening their caffeine intake up to 2 times and 46% for more than 3 times. Some of participants stated that their daily caffeine amount they ingest was increased – 2% reported 2 times higher caffeine intake and 1% even 3 times higher (fig. 5).

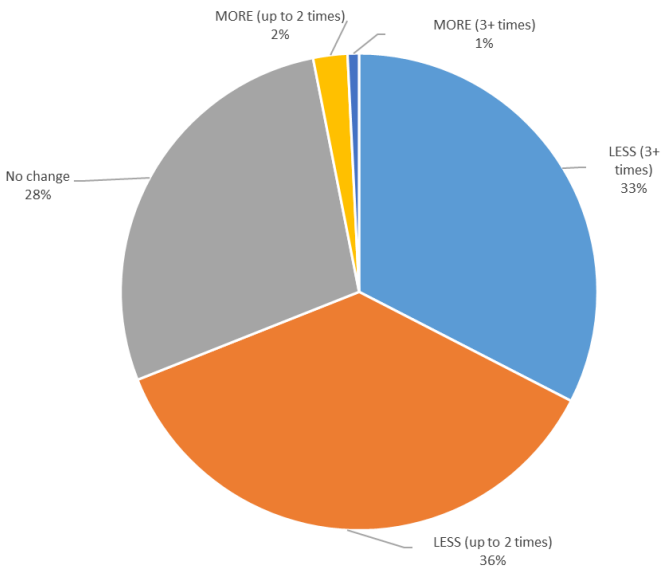

Figure 5. Changes in caffeine intake

Women were also asked about the reason why their caffeine intake was changed. Here, a bar chart based on mean values (proportions) was used to present sources of influence on lady's decisions, as multiple responses were allowed. Literature on the internet was the most commonly reported source (33.6%), followed by doctor's advice (19.5%). Social media (9.4%) and family/friends (6.3%) were less frequently reported, while other sources were negligible (0.8%) (fig. 6).

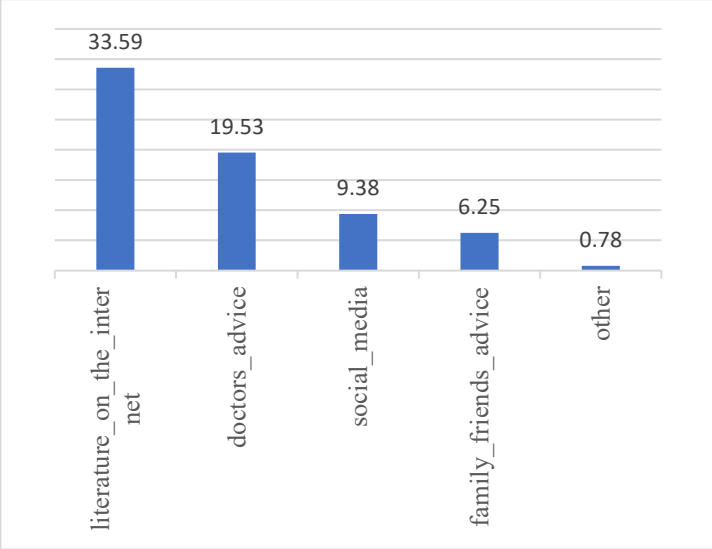

Figure 6. Influence on caffeine intake

For the analysis of ***correlations between caffeine intake and baby's weight*** the data from already delivered ladies was used (n = 106). Multiple linear regression analysis showed that maternal caffeine intake was not significantly associated with birth weight after adjustment for gestational age. For each additional 1 mg of maternal caffeine intake, birth weight is estimated to change by 0.12 g, with a 95% confidence interval ranging from −0.29 g to 0.53 g, after adjusting for gestational age. (β = 0.12 g per 1 mg, 95% CI = −0.289 to 0.534, p = 0.556). For graphical image, the "Component+residual plots" graph was performed (fig. 7). It shows the relationship between birth weight and caffeine intake after removing the influence of gestational age. Blue dashed line shows the linear regression effect from the model (β = 0.12 g per mg, p = 0.556), so the linear relationship is essentially flat. Pink smooth line is LOESS smoother (Locally Estimated Scatterplot Smoothing), that is non-parametric trend that shows actual pattern of data. In here we can see slight fluctuations at low caffeine values (0-400 mg), but an increase at very high values (700-1200 mg), however there are only few observations above 600-800 mg, so that upward trend is not reliable. In conclusion, the plot showed no clear linear association and substantial scatter of residuals, supporting the

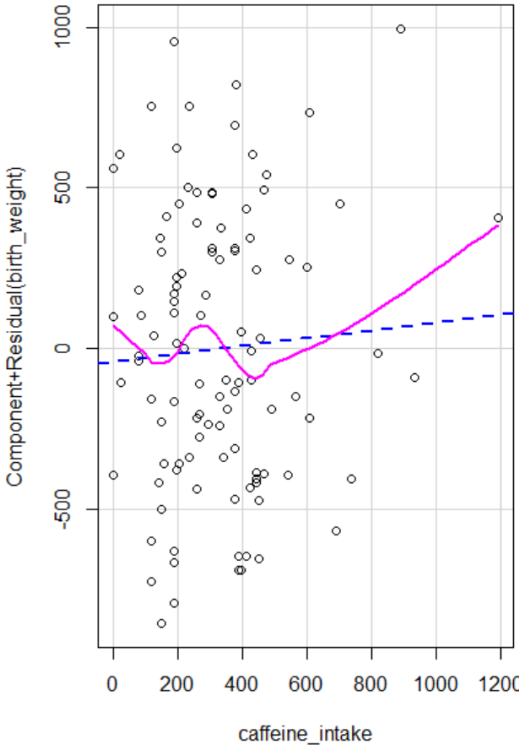

Figure 7. Component+residual plots graph for correlation between caffeine intake and baby's weight

regression analysis that maternal caffeine intake was not significantly associated with birth weight, this visually confirms the statistical result of p = 0.556.

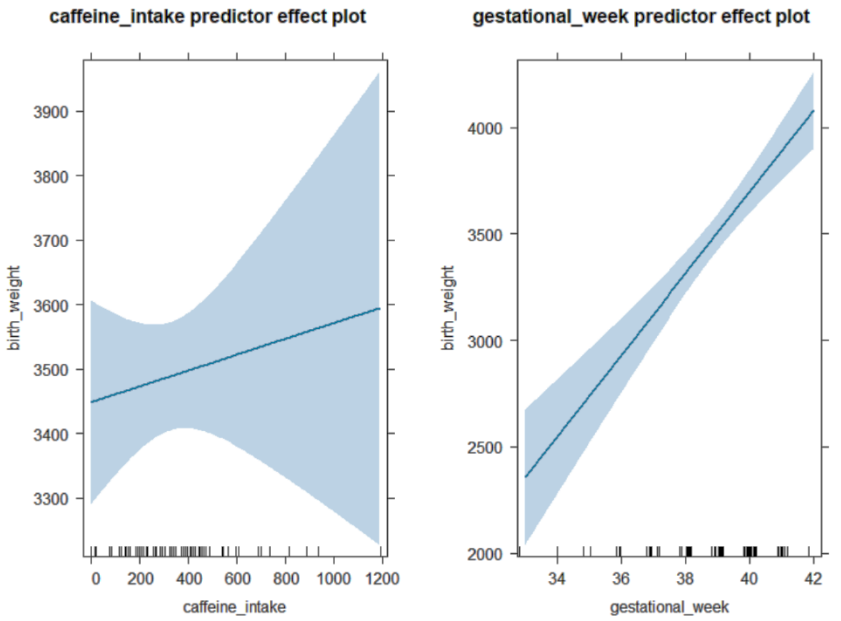

Figure 8. Predictor effect plot for effect of caffeine adjusted to gestational age on baby's weight

Another graph showing adjusted relationship between caffeine and birth weight is the Predictor effect plot (fig. 8). Each plot visualizes the effect of one predictor after adjusting for the other. Blue line is predicted birth weight from the regression model, while blue shaded area is a 95% confidence interval. On the caffeine effect plot (on the left) the line increases only slightly, and the confidence interval is very wide. So, this graph clearly shows the strong gestational age effect, that is biologically reasonable, and the lack of statistically significant caffeine effect.

A post-hoc power analysis was performed using G*Power for the multiple linear regression model. Red curve shows the distribution if the null hypothesis is true. Blue curve shows the distribution if the effect exists. Green vertical line shows critical F value, α – probability of false positive, and β – probability of false negative results. With a total sample size of 106 participants, two predictors, and α = 0.05, the model had a statistical power greater than 0.99 to detect the observed effect size ($f^2 = 0.525$) (fig. 9).

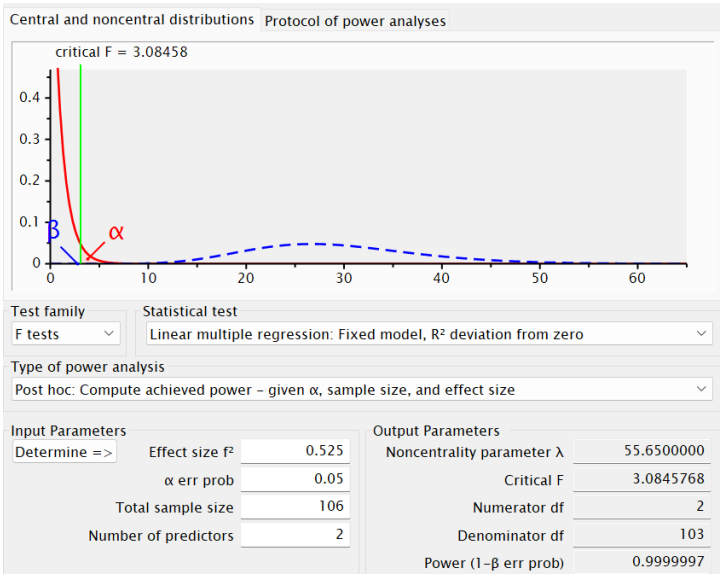

Figure 9. Post-hoc power calculation

To conclude, according to the data that was obtained, there is no statistically significant caffeine effect on baby's weight after adjusting for gestational age (β = 12 g per 100 mg, 95% CI = -0.289 to 0.534, p = 0.556).

Next step was to determine whether there is a ***correlation between acquiring gestational diabetes (GD) and maternal caffeine intake***. As the data has non-normal distribution, the Mann-Whitney test was used to compare medians of caffeine consumption between patients with and without GD. There were 94 patients without diagnosed with GD and 36 patients with GD. In conclusion, Caffeine intake did not differ significantly between pregnant patients with and without gestational diabetes. The Hodges-Lehmann estimate of the median difference was -40 mg (95% CI: 109.99997 to 29.99997mg, Mann–Whitney U (Wilcoxon rank sum test) = 1506.5, p = 0.336). Median (IQR) intake was 304 mg (192–446) in the GD group and 275 mg (188–397) in the non-GD group.

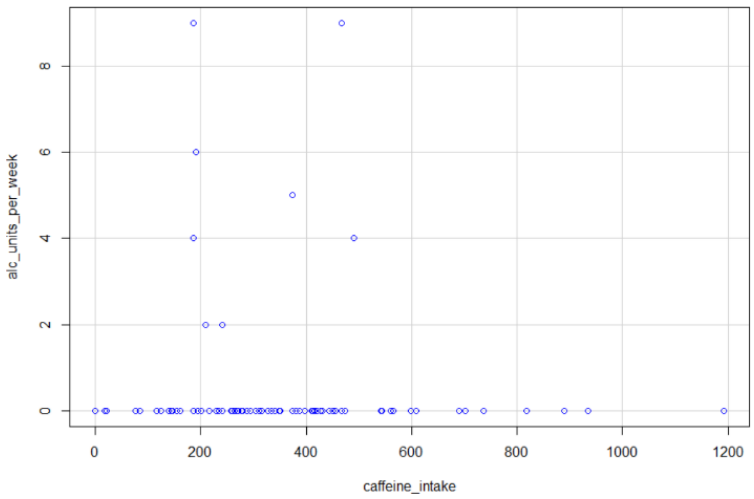

Figure 10. Scatterplot for alcohol weekly intake (units) vs daily caffeine intake (mg)

To see if there was an ***association between higher alcohol and caffeine intake together***, as some studies suggest such observation (121), the scatterplot graph was performed (fig 10). In Lithuanian groups There was no correlation between alcohol intake and caffeine intake (Spearman's ρ = −0.012, p = 0.890), indicating no association between the two variables in this sample.

For a ***potential caffeine addiction***, a self-made Likert-scale questionnaire was created (annex 1). This decision can be explained by the motive to shorten the time participants should spend to fill the form. Even though official questionnaire like Caffeine Expectancy Questionnaire (CaffEQ) by Huntley, E. D. & Juliano, L. M. (2012) does exist, it requires more time to fill as it's composed of 47 items in standard version and of 20 in shorter one. The questionnaire used

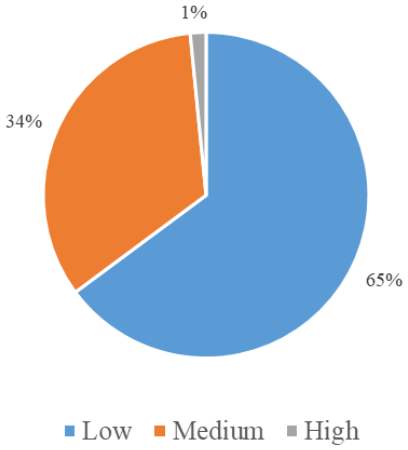

Figure 11. Caffeine addiction risk among participants

in this study is composed of only 6 short questions with grading system from 1 to 5 (with maximum general score 6–30). One question ("I can skip drinking caffeine for one day or more") was scored in reverse manner. Participants were categorized into low (6-13), moderate (14-22), and high (23-30) levels of addiction risk based on predefined score ranges. Analysis of their responses indicated that 65% of participants were at low risk, 34% at moderate risk, and 1% at high risk.

CONCLUSIONS AND PRACTICAL RECOMMENDATIONS

This study showed that high caffeine consumption is quite common among women, and although many participants reported reducing their intake, a considerable proportion still consumed more caffeine than the recommended levels (200 mg per day).

Most participants stated that the internet and healthcare professionals are their main sources of information regarding caffeine, suggesting that both informal and professional guidance play an important role in influencing behavior.

The results did not show strong or obvious associations between caffeine intake and baby's weight and gestational diabetes in this sample. However, this does not necessarily mean that caffeine has no effect. According to existing literature and animal studies, caffeine may have subtle or long-term effects particularly during pregnancy, that are not easily detectable in short-term or observational studies like this one.

These findings support the idea that even if immediate or visible effects are not observed, there may still be underlying biological impacts. This helps explain why the commonly recommended threshold of 200-300 mg per day continues to be used in guidelines, as a precautionary measure to minimize potential risks.

STUDY LIMITATIONS

The main limitation of this research is that all data is based on self-reported answers and observations of the patients. As a result, it is difficult to ensure complete accuracy, since patients may be subjective in their responses or may unintentionally omit or forget certain details. Also, the sample power analysis result evaluated in this study was sufficient, however, data collection was performed via online survey, which may have influenced participant responses and introduced potential biases.

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135. Maternal caffeine consumption during pregnancy and risk of low birth weight: a dose-response meta-analysis of cohort studies. ***Soltani, Sanaz et al.*** *2, s.l. : Critical reviews in food science and nutrition, 2023, Vol. 63, pp. 224-233.*

136. Association between maternal caffeine intake during pregnancy and child development at 6 and 12 months: The Japan Environment and Children's Study. ***Nishihara, Shinkichi et al.*** *s.l. : Early human development, 2022, Vol. 171. 105607.*

137. Prenatal caffeine exposure: association with neurodevelopmental outcomes in 9- to 11-year-old children. ***Zhang, Rui et al.*** *5, s.l. : Journal of child psychology and psychiatry, and allied disciplines, 2022, Vol. 63, pp. 563-578.*

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139. Prenatal smoking, alcohol and caffeine exposure and offspring externalizing disorders: a systematic review and meta-analysis. ***Haan, Elis et al.*** *10, Abingdon, England : Addiction, 2022, Vol. 117, pp. 2602-2613.*

140. Association between self-reported caffeine intake during pregnancy and social responsiveness scores in childhood: The EARLI and HOME studies. ***Patti, Marisa A et al.*** *1, s.l. : PloS one, 2021, Vol. 16. e0245079.*

141. Maternal smoking, consumption of alcohol, and caffeinated beverages during pregnancy and the risk of childhood brain tumors: a meta-analysis of observational studies. ***Hu, Zihao et al.*** *1, s.l. : BMC public health, Vol. 24, p. 1238.*

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152. Maternal caffeine intake during pregnancy and the risk of delivering a small for gestational age baby: Kuopio Birth Cohort. ***Kukkonen, Anni et al.*** *1, s.l. : Archives of gynecology and obstetrics, 2024, Vol. 310, pp. 359-368.*

153. Mendelian randomization study of maternal coffee consumption and its influence on birthweight, stillbirth, miscarriage, gestational age and pre-term birth. ***Brito Nunes, Caroline et al.*** *1, s.l. : International journal of epidemiology, 2023, Vol. 52, pp. 165-177.*

154. Maternal caffeine consumption and risk of neural tube defects. ***Schmidt, Rebecca J et al.*** *11, s.l. : Birth defects research. Part A, Clinical and molecular teratology, 2009, Vol. 85, pp. 879-89.*

155. Caffeine exposure in utero is associated with structural brain alterations and deleterious neurocognitive outcomes in 9-10 year old children. ***Christensen, Zachary P et al.*** *s.l. : Neuropharmacology, 2021, Vol. 186. 108479.*

ANNEXES

Annex 1

Kofeino poveikis nėštumo metu

Šis klausimynas skirtas jau **šiuo metu nėščioms moterims.**

Pirmiausia dėkojame visoms dalyvėms už dalyvavimą mūsų tyrime. Jūs labai padedate!

Tai konfidencialus tyrimas, skirtas kofeino vartojimo ir nėštumo baigties sąsajoms tirti. Visi atsakymai yra visiškai anonimiški, tačiau prašome jūsų būti sąžiningomis.

Pildant šį klausimyną svarbu žinoti **kūdikio svorį (apskaičiuotą ultragarsu), savo ir kūdikio sveikatos būklę bei suvartojamo kofeino kiekį.**

Šį klausimyną sudaro 3 pagrindinės dalys, skirtos duomenims apie:
1. Nėštumo anamnezė - tai ilgiausia dalis, kitos 2 yra daug trumpesnės. Jūsų bus klausiama apie nėštumą;
2. Kofeino vartojimą;
3. Galimą priklausomybę nuo kofeino.

Šiam klausimynui užpildyti prireiks **iki 25 minučių.**

Section 1 of 3

1. Patvirtinkite, kad norite dalyvauti šiame tyrime.
    - Sutinku

2. Kiek jums metų? (Parašykite skaičių, pvz., 34) _____

3. Ar nėštumo metu turėjote kokių nors lėtinių sveikatos problemų (nesusijusių su nėštumu)? Jei taip, nurodykite.
    - Ne
    - Kita: _____

4. Ar pastojote natūraliai, ar pagalbinio apvaisinimo būdu (IVF ir kt.)?
    - Natūraliai
    - Pagalbinis apvaisinimo procedūros - su sava kiaušialąste
    - Pagalbinis apvaisinimo procedūros - su donoro kiaušialąste

5. Ar nėštumo metu vartojote kokių nors vaistų? Jei taip, nurodykite, kokius.
    - Negėriau jokių vaistų
    - Kita: _____

6. Ar nėštumo metu sirgote ūmiomis infekcijomis? ***Jei taip***, nurodykite, kokiomis.
    - Nesirgau jokia infekcine liga

- Kita: _____

7. Ar prieš tai turėjote persileidimų? ***Jei taip***, kiek kartų?
   - Ne
   - 1
   - 2
   - 3
   - Kita: _____

8. Nurodykite nėštumų skaičių:
   - 1 - tai mano pirmasis nėštumas
   - 2
   - 3
   - 4
   - Kita: _____

9. Ar esate gimdžiusi? Kelintas būtų Jums šis gimdymas?
   - 0 - tai mano pirmasis gimdymas
   - 1
   - 2
   - 3
   - 4
   - Kita: _____

10. Ar laukiatės vieno vaikelio ar dvynių?
    - 1
    - 2
    - 3
    - 4
    - Kita: _____

11. Kelinta dabar yra jūsų nėštumo savaitė? (Parašykite skaičių, pvz., 38) _____

12. Kurią nėštumo savaitę paskutinį kartą jums buvo atliktas ultragarsinis tyrimas? _____

13. Koks kūdikio (-ių) svoris (g) apskaičiuotas ultragarsu? _____

14. Ar nėštumo metu jums buvo diagnozuoti su nėštumu susiję sutrikimai (pvz., preeklampsija, nėščiųjų diabetas, nėščiųjų cholestazė, retrochorioninė hematoma, oligohidramnionas ir kt.). Jei taip, nurodykite.
    - Neštumo metu nebuvo komlikacijų
    - Kita: _____

15. Ar Jums buvo diagnozuota vaisiaus raidos ydų? (pvz., širdies pertvaros defektai, vaisiaus augimo sulėtėjimas, gastroschizė, galūnių anomalijos)? Jei taip, nurodykite kūdikio būklę
    - o Ne
    - o Kita: _____

16. Ar dabar rūkote? Jei taip, pasirinkite variantą „kita“ ir nurodykite, kiek vidutiniškai cigarečių surūkote.
    - o Ne
    - o Kita: _____

17. Ar rūkėte iki nėštumo metu (taip pat ir nėštumo pradžioje)? ***Jei taip***, pasirinkite variantą „kita“ ir nurodykite, kiek vidutiniškai rūkėte per dieną.
    - o Aš nerūkau
    - o Kita: _____

18. Ar nėštumo metu (taip pat ir nėštumo pradžioje) vartojote alkoholio? Jei taip, pasirinkite variantą „kita“ ir nurodykite, kiek vidutiniškai išgerdavote per savaitę.
    - o Nevartojau jokio alkoholio
    - o Kita: _____

19. Ar nėštumo metu (įskaitant ankstyvąjį nėštumą) vartojote kokių nors psichoaktyviųjų medžiagų? Jei taip, pasirinkite „kita“ ir nurodykite, kokias ir kaip dažnai.
    - o Nevartojau jokio psichoaktyviųjų medžiagų
    - o Kita: _____

Section 2 of 3

20. Ar nuo tada, **kai sužinojote, kad esate nėščia**, pasikeitė jūsų suvartojamo kofeino kiekis, lyginant su tuo, kuris buvo prieš pastojant?
    - o Ne
    - o Taip, suvartojau ŠIEK TIEK DAUGIAU kofeino turinčių produktų (iki 2 kartų daugiau)
    - o Taip, suvartojau DAUG DAUGIAU kofeino turinčių produktų (3 ir daugiau kartų daugiau)
    - o Taip, suvartojau ŠIEK TIEK MAŽIAU kofeino turinčių produktų (iki 2 kartų mažiau)
    - o Taip, suvartojau DAUG MAŽIAU kofeino turinčių produktų (daugiau nei 3 kartus mažiau)

21. Kas turėjo įtakos jūsų suvartojamos kavos kiekiui, jei jį pakeitėte? Pažymėkite visus tinkamus variantus arba pridėkite savo:
    - ☐ Gydytojo patarimai
    - ☐ Literatūra internete
    - ☐ Draugo ar giminaičio patarimas
    - ☐ Socialinė žiniasklaida

□ Kita: _____

22. Kiek puodelių **kavos** kasdien išgėrėte per pastarąją savaitę?
- 0
- 1
- 2
- 3
- 4
- 5+ (jei įmanoma, nurodykite tikslų skaičių parinktyje „Kita“)
- Kita: _____

23. Kiek puodelių **arbatos** kasdien išgėrėte per pastarąją savaitę?
- 0
- 1
- 2
- 3
- 4
- 5+ (jei įmanoma, nurodykite tikslų skaičių parinktyje „Kita“)
- Kita: _____

24. Kiek puodelių **šokolado turinčių gėrimų** kasdien suvartojote per pastarąją savaitę?
- 0
- 1
- 2
- 3
- 4
- 5+ (jei įmanoma, nurodykite tikslų skaičių parinktyje „Kita“)
- Kita: _____

25. Kiek **kolos ir dietinių gaiviųjų gėrimų** kasdien suvartojote per pastarąją savaitę?
- 0
- 0,5 L
- 1 L
- 1,5 L
- 2 L
  2,5+ L (jei įmanoma, nurodykite tikslų skaičių parinktyje „Kita“)
- Kita: _____

26. Kiek **šokolado plytelių (50 g)** kasdien suvalgote per pastarąją savaitę?
- 0
- 1
- 2
- 3
- 4
- 5+ (jei įmanoma, nurodykite tikslų skaičių parinktyje „Kita“)

- Kita: _____

Section 3 of 3

Šis skyrius skirtas asmens priklausomybei nuo kofeino įvertinti.
Pasirinkite labiausiai jums tinkantį variantą nuo 1 iki 5, susijusį su pateiktais teiginiais, kai:

1. Visiškai nesutinku
2. Nesutinku
3. Neutralus
4. Sutinku
5. Visiškai sutinku

27. Kasdien negaliu funkcionuoti be kofeino.
    1_____2_____3_____4_____5

28. Vieną ar daugiau dienų galiu negerti kofeino.
    1_____2_____3_____4_____5

29. Man reikia kofeino, kad galėčiau išgyventi dieną (darbas, laikas su šeima, sporto salė).
    1_____2_____3_____4_____5

30. Nerimauju dėl suvartojamo kofeino kiekio.
    1_____2_____3_____4_____5

31. Nerimauju dėl per didelio kofeino kiekio vartojimo pasekmių sveikatai.
    1_____2_____3_____4_____5

32. Mano tolerancija kofeinui padidėjo nuo tada, kai pradėjau gerti kofeiną.
    1_____2_____3_____4_____5

Kofeino poveikis nėštumo metu

Šis klausimynas skirtas jau **gimdžiusioms moterims.**

Pirmiausia dėkojame visoms dalyvėms už dalyvavimą mūsų tyrime. Jūs labai padedate!

Tai konfidencialus tyrimas, skirtas kofeino vartojimo ir nėštumo baigties sąsajoms tirti. Visi atsakymai yra visiškai anonimiški, tačiau prašome jūsų būti sąžiningomis.

Pildant šį klausimyną svarbu žinoti **Jūsų kūdikio svorį po gimdymo, Jūsų ir kūdikio sveikatos būklę bei kofeino vartojimą**.

Šį klausimyną sudaro 3 pagrindinės dalys, skirtos duomenims apie:
1. Nėštumo anamnezė - tai ilgiausia dalis, kitos 2 yra daug trumpesnės. Jūsų bus klausiama apie nėštumą;
2. Kofeino vartojimą;
3. Galimą priklausomybę nuo kofeino.

Šiam klausimynui užpildyti prireiks **iki 25 minučių.**

1. Patvirtinkite, kad norite dalyvauti šiame tyrime.
    - Sutinku

2. Kiek jums buvo metų, kai gimdėte? (Parašykite skaičių, pvz., 34) _____

3. Ar nėštumo metu turėjote kokių nors lėtinių sveikatos problemų (nesusijusių su nėštumu)? Jei taip, nurodykite.
    - Ne
    - Kita: _____

4. Ar pastojote natūraliai, ar pagalbinio apvaisinimo būdu (IVF ir kt.)?
    - Natūraliai
    - Pagalbinis apvaisinimo procedūros - su sava kiaušialąste
    - Pagalbinis apvaisinimo procedūros - su donoro kiaušialąste

5. Ar nėštumo metu vartojote kokių nors vaistų? Jei taip, nurodykite, kokius.
    - Negėriau jokių vaistų
    - Kita: _____

6. Ar nėštumo metu sirgote ūmiomis infekcijomis? ***Jei taip***, nurodykite, kokiomis.
    - Nesirgau jokia infekcine liga
    - Kita: _____

7. Ar prieš tai turėjote persileidimų? ***Jei taip***, kiek kartų?
    - Ne
    - 1
    - 2
    - 3

- Kita: _____

8. Nurodykite nėštumų skaičių:
   - 1 - tai mano pirmasis nėštumas
   - 2
   - 3
   - 4
   - Kita: _____

9. Ar esate gimdžiusi? Kelintas būtų Jums šis gimdymas?
   - 1 - tai mano pirmasis gimdymas
   - 2
   - 3
   - 4
   - Kita: _____

10. Ar turėjote daugiavaisį, ar vienvaisį nėštumą? Nurodykite vaisių skaičių:
    - 1
    - 2
    - 3
    - 4
    - Kita: _____

11. Ar gimdėte vaginaliniu, ar cezario pjūvio būdu?
    - Vaginaliniu būdu
    - Cezario pjūvio būdu

12. Kelinta buvo nėštumo savaitė, kai gimdėte? (Parašykite skaičių, pvz., 38) _____

13. Koks buvo kūdikio(-ių) svoris (g)? _____

14. Kiek buvo balų Apgar skalę?
    - 7-10
    - 4-6
    - 0-3
    - Nežinau/neprisimenu

15. Ar nėštumo metu jums buvo diagnozuoti su nėštumu susiję sutrikimai (pvz., preeklampsija, nėščiųjų diabetas, nėščiųjų cholestazė, retrochorioninė hematoma, oligohidramnionas ir kt.). Jei taip, nurodykite.
    - Neštumo metu nebuvo komlikacijų
    - Kita: _____

16. Ar Jums buvo diagnozuota komplikacijų gimdymo metu (pvz., pečių distocija, gimdymo disfunkcija, mekonijaus aspiracija, vaisiaus hipoksija, vaisiaus kvėpavimo nepakankamumas, gimdymo trauma ir t. t.). Jei taip, nurodykite.
    - o Ne, man buvo visiškai nesudėtingas gimdymas
    - o Kita: _____

17. Ar jūsų kūdikiui buvo diagnozuoti kokie nors įgimti defektai, anomalijos ar sindromai (pvz., širdies pertvaros defektai, Falloto tetralogija, įgimtos inkstų ligos, neurologiniai sutrikimai)? Jei taip, nurodykite.kūdikio būklę.
    - o Ne
    - o Kita: _____

18. Ar dabar rūkote? Jei taip, pasirinkite variantą „kita“ ir nurodykite, kiek vidutiniškai cigarečių surūkote.
    - o Ne
    - o Kita: _____

19. Ar rūkėte iki nėštumo metu (taip pat ir nėštumo pradžioje)? ***Jei taip***, pasirinkite variantą „kita“ ir nurodykite, kiek vidutiniškai rūkėte per dieną.
    - o Aš nerūkau
    - o Kita: _____

20. Ar nėštumo metu (taip pat ir nėštumo pradžioje) vartojote alkoholio? Jei taip, pasirinkite variantą „kita“ ir nurodykite, kiek vidutiniškai išgerdavote per savaitę.
    - o Nevartojau jokio alkoholio
    - o Kita: _____

21. Ar nėštumo metu (įskaitant ankstyvąjį nėštumą) vartojote kokių nors psichoaktyviųjų medžiagų? Jei taip, pasirinkite „kita“ ir nurodykite, kokias ir kaip dažnai.
    - o Nevartojau jokio psichoaktyviųjų medžiagų
    - o Kita: _____

Section 2 of 3

22. Ar nuo tada, **kai sužinojote, kad esate nėščia**, pasikeitė jūsų suvartojamo kofeino kiekis, lyginant su tuo, kuris buvo prieš pastojant?
    - o Ne
    - o Taip, suvartojau ŠIEK TIEK DAUGIAU kofeino turinčių produktų (iki 2 kartų daugiau)
    - o Taip, suvartojau DAUG DAUGIAU kofeino turinčių produktų (3 ir daugiau kartų daugiau)
    - o Taip, suvartojau ŠIEK TIEK MAŽIAU kofeino turinčių produktų (iki 2 kartų mažiau)
    - o Taip, suvartojau DAUG MAŽIAU kofeino turinčių produktų (daugiau nei 3 kartus mažiau)

23. Ar pasikeitė kofeino kiekis, kurį vartojate **po gimdymo**, palyginti su tuo, kurį vartojote prieš nėštumą?
    - o Ne
    - o Taip, suvartojau ŠIEK TIEK DAUGIAU kofeino turinčių produktų (iki 2 kartų daugiau)
    - o Taip, suvartojau DAUG DAUGIAU kofeino turinčių produktų (3 ir daugiau kartų daugiau)
    - o Taip, suvartojau ŠIEK TIEK MAŽIAU kofeino turinčių produktų (iki 2 kartų mažiau)
    - o Taip, suvartojau DAUG MAŽIAU kofeino turinčių produktų (daugiau nei 3 kartus mažiau)

24. Kas turėjo įtakos jūsų suvartojamos kavos kiekiui, jei jį pakeitėte? Pažymėkite visus tinkamus variantus arba pridėkite savo:
    - ☐ Gydytojo patarimai
    - ☐ Literatūra internete
    - ☐ Draugo ar giminaičio patarimas
    - ☐ Socialinė žiniasklaida
    - ☐ Kita: _____

25. Kiek puodelių **kavos** kasdien išgėrėte per pastarąją savaitę?
    - o 0
    - o 1
    - o 2
    - o 3
    - o 4
    - o 5+ (jei įmanoma, nurodykite tikslų skaičių parinktyje „Kita“)
    - o Kita: _____

26. Kiek puodelių **arbatos** kasdien išgėrėte per pastarąją savaitę?
    - o 0
    - o 1
    - o 2
    - o 3
    - o 4
    - o 5+ (jei įmanoma, nurodykite tikslų skaičių parinktyje „Kita“)
    - o Kita: _____

27. Kiek puodelių **šokolado turinčių gėrimų** kasdien suvartojote per pastarąją savaitę?
    - o 0
    - o 1
    - o 2
    - o 3
    - o 4
    - o 5+ (jei įmanoma, nurodykite tikslų skaičių parinktyje „Kita“)
    - o Kita: _____

28. Kiek **kolos ir dietinių gaiviųjų gėrimų** kasdien suvartojote per pastarąją savaitę?
    - 0
    - 0,5 L
    - 1 L
    - 1,5 L
    - 2 L
      2,5+ L (jei įmanoma, nurodykite tikslų skaičių parinktyje „Kita“)
    - Kita: _____

29. Kiek **šokolado plytelių (50 g)** kasdien suvalgote per pastarąją savaitę?
    - 0
    - 1
    - 2
    - 3
    - 4
    - 5+ (jei įmanoma, nurodykite tikslų skaičių parinktyje „Kita“)
    - Kita: _____

Section 3 of 3

Šis skyrius skirtas asmens priklausomybei nuo kofeino įvertinti.
Pasirinkite labiausiai jums tinkantį variantą nuo 1 iki 5, susijusį su pateiktais teiginiais, kai:

6. Visiškai nesutinku
7. Nesutinku
8. Neutralus
9. Sutinku
10. Visiškai sutinku

30. Kasdien negaliu funkcionuoti be kofeino.
1_____2_____3_____4_____5

31. Vieną ar daugiau dienų galiu negerti kofeino.
1_____2_____3_____4_____5

32. Man reikia kofeino, kad galėčiau išgyventi dieną (darbas, laikas su šeima, sporto salė).
1_____2_____3_____4_____5

33. Nerimauju dėl suvartojamo kofeino kiekio.
1_____2_____3_____4_____5

34. Nerimauju dėl per didelio kofeino kiekio vartojimo pasekmių sveikatai.
1_____2_____3_____4_____5

35. Mano tolerancija kofeinui padidėjo nuo tada, kai pradėjau gerti kofeiną.
1_____2_____3_____4_____5