Doctoral School of Clinical Medicine
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Maternal age as an influencing factor of obstetrical and neonatal outcomes – retrospective studies in Southeastern Hungary

PhD Thesis

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List of scientific publications related to the subject of this thesis

I. **Karai A**, Gyurkovits Z, Nyári TA, Sári T, Németh G, Orvos H. Adverse perinatal outcome in teenage pregnancies: an analysis of a 5-year period in Southeastern Hungary. J MATERN FETAL NEONATAL MED 32(14):2376-2379. (2019). **IF: 1.737**.

II. **Karai A**, Orvos H, Paulik E, Pap É, Gyurkovits Z, Horváth E, Németh G, Sikovanyecz J. A nemi kromoszómákat érintő triszómiák in utero felismerésének gyakorisága a Szegedi Tudományegyetem Szülészeti és Nőgyógyászati Klinika beteganyagában 2003-2015 között. MAGYAR NŐORVOSOK LAPJA 83(2):90-94. (2020)

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IV. Polanek E, **Karai A**, Molnár R, Németh G, Orvos H, Balogh P, Paulik E. Association between sociodemographic, obstetric and lifestyle factors among Hungarian pregnant women – a cross sectional study. THE JOURNAL OF OBSTETRICS AND GYNAECOLOGY RESEARCH, 11 p. (2022). **IF: 1.697**

List of other publications

I. Boros Á, Raáb M, Károly É, **Karai A**, Kátai A, Bolba N, Pankovics P, Reuter G. A cluster of salivirus A1 (Picornaviridae) infections among newborn babies with acute gastroenteritis in a neonatal hospital unit in Hungary. ARCHIVES OF VIROLOGY 161:(6) pp. 1671-1677. (2016). IF: 2.058

II. Mosolygó T, Faludi I, Balogh EP, Szabó AM, **Karai A**, Kerekes F, Virók DP, Endrész V, Burián K. Expression of Chlamydia muridarum plasmid genes and immunogenicity of pGP3 and pGP4 in different mouse strains. INTERNATIONAL JOURNAL OF MEDICAL MICROBIOLOGY 304:(3-4) pp. 476-483. (2014). IF: 3.614

III. Balogh EP, Mosolygó T, Tiricz H, Szabó ÁM, **Karai A**, Kerekes F, Virók DP, Kondorosi É, Burián K. Anti-chlamydial effect of plant peptides. ACTA MICROBIOLOGICA ET IMMUNOLOGICA HUNGARICA 61:(2) pp. 229-239. (2014). IF: 0.778

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List of abbreviations

CI	confidence interval
DNA	deoxyribonucleic acid
EUROCAT	European Surveillance of Congenital Anomalies
FISH	fluorescence in situ hybridization
GDM	gestational diabetes mellitus
IQR	interquartile range
IUGR	intrauterine growth retardation
IVF-ET	in vitro fertilization-embryo transfer
LBW	low birth weight
MoM	multiple of the median
NICU	neonatal intensive care unit
NIPT	noninvasive prenatal tests
OR	odds ratio
PAPP-A	pregnancy- associated plasma protein-A
β-HCG	beta-human choriogonadotropin

1. Introduction

Promotion of healthy life start is an important priority all over the world. Health promoting or health damaging behaviour of mothers before conception and during pregnancy can influence the health status of their newborns, and their further life.

During the last decades the total number of births has been decreasing in Hungary, and today, the number of deliveries is around 90.000 per year. Parallel with this change, the age composition of pregnant women has been changed, the rate of advanced aged mothers (over 40 years) has increased [1-3].

In contrast the rate of preterm deliveries has not changed for years, it is around 8–9% despite efforts to decrease this number: extended system of health visitors, free prenatal care (insurance is not needed), antenatal steroid prophylaxis, use of surfactant, neonatal intensive care units (NICU).

Although the rate of preterm births runs like mentioned above, the rate of infant mortality has been decreasing year by year. The two main causes of infant's death are conditions that occurs in perinatal period (like prematurity) and congenital abnormalities.

Demography is globally changing, and it affects many of the non-modifiable factors of pregnancy outcome (e.g. maternal age).

Today, the importance of maternal age is increasing due to the demographical changes. The number of live births is decreasing, while maternal age is advancing. Health care providers have to be prepared to manage complications which are more common in advanced age such as gestational diabetes mellitus (GDM) and preeclampsia. The frequency of Caesarean section is also higher. Considering neonatal outcome there is higher rate of low birth weight, macrosomia, prematurity, intrauterine growth retardation, congenital malformations, neonatal intensive care admission and perinatal mortality.

It is also important to attend to teenage pregnancies and their perinatal outcome: higher rate of low birth weight, prematurity, intrauterine growth retardation, congenital malformations, neonatal intensive care admission and perinatal mortality.

It is a widely known fact that maternal age is one of the determining factors of many genetical aberrations. Therefore screening methods consider maternal age as an important variable. Several types of screening method are applied to determine chromosomal abnormalities: first trimester combined test (maternal age, nuchal thickness, maternal serum b-human chorionic gonadotrophin, pregnancy-associated plasma protein-A), free fetal deoxyribonucleic acid based tests, detailed ultrasound examination. If these screening

tests give rise to suspicion, an invasive procedure is needed like chorionvillus sampling or amniocentesis to get correct diagnosis. Autosomal aberrations are associated to maternal age, but in case of abnormalities of sex chromosome there is no correlation to maternal age. Furthermore, in case of abnormalities of sex chromosome these mentioned screening methods are less useful as in case of autosomal trisomies.

An adequate prenatal care can help to prevent maternal and perinatal complications and can decrease the number of neonates born with any kind of chromosomal aberration.

1.1. Changing pattern of fertility

Demography has been changing year by year worldwide. In developed countries the number of live births is decreasing, the life expectancy is increasing. Parallel with these tendencies the average maternal age is increasing (it is over 30 years of age when the first child is born) and among the 15–19 and 20–24 age group the age-specific fertility rate drops. In groups over 30, it's increasing [1].

In Hungary, the situation is the same. The total number of deliveries has been decreased in the last decades in Hungary. There were 148,673 live births in 1980, 97,597 in 2000, 90,335 in 2010 and only 89,193 live births in 2019 [2]. Although there is a decrease in the number of live births, the proportion of mothers over 40 years has increased, especially in the past ten years [2.6% (2354) in 2010 vs 5.3% (4757) in 2019] [3] similarly to the tendency in other developed countries. In 2018, the average maternal age at first child's birth was 28.8 years, and during the last decades, age specific fertility rate of women under 30 dropped by 30%, whereas in women over 30, it tripled [4]. Due to the demographic changes, the Hungarian population can be described as an ageing society; thus, childbearing is a key-question, and the new tendencies (delaying childbirth or having a baby over 40 years of age) do not point towards the growth of the population.

Over the last decades, several changes have been noticed. Contraceptives are more widespread, sexual provocation is more common through the media. All these factors have led to the increased number of teenage pregnancies throughout the world [5].

In Hungary the number of live births of young mothers (19 years old or younger) increased after World War II. In 1948 17,809 (9.3%) teenage mother gave birth (out of 191,907), and the proportion of this age group grew and grew in the following decades: in 1960 13.5% (19,641 out of 146,461), in 1970 15% (22,750 out of 151,819), in 1980 14.5% (21,522 out of 148,673) [6]. This tendency changed after the second millennium: in 2000

the rate of teenage mothers was 7.9% (7799 out of 97,597). The proportion of mothers at this age group has been nearly constant since 2005 [6.4% (6286 out of 97,496) in 2005, 5.8% (5296 out of 90,335) in 2010, 5.6% (5031 out of 89,193) in 2019] [3].

1.2. Pregnancy at teenage mothers

Over the last decades, remarkable changes have been noticed in family life and in sexual activity before marriage. Sexual provocation has increased through the media and contraceptives are easier available than before. All these factors have led to the increased number of teenage pregnancies throughout the world [5]. In the study by Orvos et al. in 1999 [7], most of the teenage mothers were single and almost one fifth of teenage mothers have never attended prenatal care (data were collected immediately after the political structure change). Nowadays changes have been noticed in the proportion of single mothers and of those who had a partner in life. Having a husband or a partner during pregnancy could mean appreciable support to the mother, and it can explain the high rate of attending prenatal care.

Teenage pregnancy and its effect on perinatal outcome have been brought into focus by a lot of studies. Many of them reported higher rate of low birth weight (LBW) [8-16,26,27,29], prematurity [8-18,26,27,28,29], intrauterine growth retardation (IUGR) [7,13,14], congenital malformations [9,19-22,26,], neonatal intensive care admission [10,23] and perinatal mortality [10,12,13,29] among these pregnancies. Marital status, low educational level, poverty, and lack of prenatal care are also risk factors of poor perinatal outcome among these young mothers [9,24,25,28]. On the other hand, there are some studies in the literature, which assert the contrary that young maternal age does not mean higher risks of adverse perinatal outcome [30,31].

1.3. Pregnancy at advanced maternal age

Advanced maternal age is traditionally described to be 35 years of age or over [32], whereas in recent years, new trends have suggested that it may be 40 years of age or over. In developed countries, the number of women who delay the first pregnancy or planning of another pregnancy is increasing. The reasons could be various, such as longer time spent in education, career plans first, later marriages or easier accessibility to modern contraceptive methods [33]. These women give birth to their first child in their 30s or 40s. Childbearing would be preferable in mid-twenties to early thirties, every social and health

care programme must prompt this age limit. Giving birth at a later age has more risks; therefore, it is highly important to support mothers over 40 during their pregnancy to deliver healthy babies.

Pregnancy at an advanced age and its effect on the perinatal outcome have been investigated by several studies. Many of them have reported that maternal complications, such as GDM and preeclampsia are frequent in older mothers [34-44,52-58]. The frequency of Caesarean section is also higher among them [36-40,42-46,52,53,56-58]. On the one hand, studies have found a higher rate of LBW [34,38,39,47,56,57], macrosomia [38,40,41,54,56,57], prematurity [36-40,45,47,48,53,54,57,58], IUGR [34,40,41,53,58], congenital malformations [34,49,52,53,56,58], neonatal intensive care admission [40,43,50,51,53,54,56], and perinatal mortality [34,35,54] in advanced age mothers and their babies. On the other hand, some studies have asserted the contrary, that is, advanced maternal age is not associated with higher risks of adverse perinatal outcome [59,60].

1.4. Congenital malformations

Maternal age is one of the determining factors of many genetical aberrations. Applying of screening methods is based on maternal age. Combined test (maternal age, nuchal thickness, maternal serum b-human chorionic gonadotrophin, pregnancy-associated plasma protein-A), free fetal deoxyribonucleic acid based tests, detailed ultrasound examination are used to determine chromosomal abnormalities. Suspicious cases need an invasive procedure like chorionvillus sampling or amniocentesis to get correct diagnosis.

Autosomal aberrations are associated with maternal age, but in case of abnormalities of sex chromosome there is no correlation with maternal age. The prenatal diagnosis of sex chromosome trisomies is not as efficient as of the autosomal trisomies because of the low sensitivity of the screening methods used in the investigated period and the various clinical appearance of sex chromosome trisomies.

Abnormalities of sex chromosome

The trisomies of sex chromosome are not so represented by literature as it is expected by right of their frequency [61]. The trisomies of sex chromosome are occurred by meiotic non-disjunction [61,62,63]. An extra chromosome causes different syndromes: triple X syndrome in females (extra X chromosome), Klinefelter syndrome in males (extra X chromosome) or Jacob syndrome (double Y syndrome) in males (extra Y chromosome).

Triple X syndrome is a sex chromosome aneuploidy with 47,XXX karyotype. Out of the trisomies of sex chromosome this type of trisomy is the less prenatally diagnosed condition. This syndrome causes severe condition rarely and has a variety of physical and psychological features [63]. The patients are tall and fertile. Microcephaly, epicanthus and crooked pinky finger could be specific for the syndrome, learning disorder or renal involvement are rarely present. The incidence of triple X syndrome is one in 1,000 live born (1:900-1200) [61,64,65,66].

Klinefelter syndrome is defined by a 47,XXY karyotype. The incidence of it is 1:500-600 live born [66]. The classical phenotype is described by tall stature, infertility, gynecomastia, puberty disorder, sparse body hair and hypogonadism due to low serum testosterone. The patients have average intelligence, but mild mental retardation or behavioral disturbance may occur [62].

The patients suffering from Jacob syndrome (double Y syndrome) have 47,XYY karyotype. These males have tall stature, acne, learning and behavioral problems. The incidence of it is 1:1000 live born males [65,66]. Diagnosis of an XYY karyotype is commonly delayed (mean age at diagnosis is 17.1 years) and only 15% of patients are diagnosed with XYY syndrome out of all cases [64,67].

Detection rate of trisomies

None of these trisomies mentioned above can cause so severe phenotypic characteristics like Down syndrome which is an autosomal trisomy [61]. The clinical symptoms get worse as the number of sex chromosomes increases and improves due to mosaicism. The rate of in utero identification is higher in countries where prenatal screening is perfomed however the detection rate of trisomies of sex chromosomes is much lower than autosomal trisomies. According to data presented in the literature, 90% of cases with Patau or Edwards syndrome are prenatally diagnosed, the in utero identification rate of Down syndrome is over 75%, but only 20% of trisomies of sex chromosomes are recognized during pregnancy [68]. The difference lies in various clinical aspects of syndromes caused by trisomies of sex chromosome and sensitivity of applied screening methods. In case of trisomies of sex chromosome sensitivity of screening methods like ultrasound diagnostics, maternal serum markers [64,68] and free fetal deoxyribonucleic acid (DNA) based tests (noninvasive prenatal tests, NIPT) does not achieve the same level as in case of autosomal trisomies [69].

Fate of fetuses having any kind of trisomy

The trisomies of sex chromosomes are numerical abnormalities just like autosomal trisomies thus the Hungarian legislation consider them the same way. It means the pregnant woman can make her own decision about termination or having the baby if the trisomy is diagnosed before 24th week of pregnancy [70]. Informing the parents correctly and properly about the circumstances and potential outcomes is essential to decide responsibly. Early recognition of trisomies of sex chromosome are important to increase intervention for emerging developmental problems and apply hormonal substitution if it's necessary, potentially improving their quality of life [63,66].

1.5. Lifestyle factors among pregnant women

Foetal health can be affected by several lifestyle factors. Out of these the followings are the most important: diet, physical activity, smoking and alcohol consumption during pregnancy.

Diet of pregnant women

Adequate nutrition is important during pregnancy. It prevents GDM, hypertension, depression, preterm birth [71]. It can affect the development of cognitive, motor and socioemotional skills [72]. Most studies have examined the intake of micro- or macronutrients or foods (usually vitamin A and B12, folate, choline, iron, zinc, copper, selenium, iodine, omega-3 fatty acids, protein and fish) [73,74]. Some studies reported that unhealthy maternal diet during pregnancy was associated with lower intelligence scores [75], higher emotional-behavioral dysregulation [76], increased risk of externalizing problems [77] and hyperactivity-inattention symptoms [78] in the newborns. Mahmassani et al. found that a better-quality diet during pregnancy was associated with better visual spatial skills, better intelligence and executive function in the offspring [79].

Physical activity

Regular physical activity during pregnancy has a lot of advantages. It reduces the incidence of hypertensive disorders, GDM, excessive gestational weight gain, fetal macrosomia, lumbopelvic pain, anxiety and prenatal depression. Pregnancy exercise did not influence maternal or perinatal adverse outcomes (for example rate of Caesarean-section or instrumental delivery) [80]. Walking, stationary cycling, swimming, a variety of aerobic are safe activities during pregnancy [81,82,83]. Of course, pregnant women's

previous fitness level should be considered before recommending exercise and healthcare providers must inform these women of contraindications (for instance ruptured membranes, premature labor, incompetent cervix, uncontrolled hypertension or diabetes mellitus, vaginal bleeding) [82].

Smoking

Maternal smoking during pregnancy is associated with many negative outcomes, such as preterm birth, infant mortality or delayed intrauterine development and can lead to newborns with reduced birth weight, birth length, and head and chest circumference; it reduces delivery gestational age; and lowers the first-minute Apgar score [84].

The study of Yang et al. found that maternal smoking before or during pregnancy (even at a low intensity, 1–5 cigarettes per day) significantly increased the risk of congenital anomalies (congenital diaphragmatic hernia, gastroschisis, limb reduction defect, cleft lip with or without cleft palate, cleft palate alone, and hypospadias). Women who smoked before pregnancy and quitted during each trimester of pregnancy still had higher risk of congenital anomalies than women who did not smoke before and throughout pregnancy. The study recommends that smoking cessation interventions should be implemented before pregnancy [85].

Alcohol consumption

Alcohol consumption during pregnancy is associated with a variety of fetal malformations, including cognitive deficits, behavioral abnormalities and growth disorders [86]. Pregnant women should avoid alcohol consumption completely during pregnancy. However, many women still drink alcohol during pregnancy. In Rockliffe's systematic review and meta-synthesis some women who used alcohol during pregnancy believed that cessation may harm their baby in some way or they had good test results confirming a healthy baby and it supported them to continue to drink alcohol. Enviroment is also important. If drinking alcohol is a social norm, a pregnant woman who stops drinking could feel isolated, so she may choose to drink alcohol because she wants to keep her relationships [87].

Women's knowledge of healthy lifestyle is an important factor to have healthy babies. Health care professionals must give adequate, consistent information to each pregnant women considering the individual differences.

2. Aims

The aims of this thesis are the followings:

- To determine if teenage pregnancy is associated with adverse perinatal outcome with particular regard to congenital malformations.
- To determine the association between advanced maternal age and various adverse maternal and neonatal outcomes.
- To investigate the cases with in-utero-diagnosed trisomies of sex chromosome, and to determine the frequency of prenatal identification and outcome of these pregnancies.
- To determine the association between demographic factors and lifestyle factors in pregnant women.

3. Materials and methods

We delivered two types of studies to characterize the role of mothers' age in the outcome of pregnancy. On the one hand, hospital documentation based data collection was done to study the association between the maternal age and the obstetrical and perinatal outcomes. All data were registered anonymously. The study protocol was approved by the Regional and Institutional Human Medical Biological Research Ethics Committee of the University of Szeged, Hungary (No: 4046).

On the other hand, a self-administered questionnaire and health documentation based study was done to analyze the lifestyle of pregnant women in various age-groups. The participation was voluntary, and a written informed consent was obtained from each participant of the study. The study protocol was approved by the Regional and Institutional Human Medical Biological Research Ethics Committee of the University of Szeged, Hungary (No: 3328).

3.1 Design and subjects

Study of teenage mothers

A retrospective analysis was done on teenage mothers (under 20 years of age) with more than 24 complete weeks of gestation, who delivered between 1 January 2010 and 31 December 2014 at the Department of Obstetrics and Gynecology, University of Szeged (study group). We compared the data of teenage mothers with the data of all mothers who delivered in Hungary during the study period (control group) [6]. Our department is a regional healthcare center, which means that high-risk pregnancies are transferred from the Southeastern part of Hungary to here (it means three counties out of 19, around 1,250,000 people out of nearly 10 million).

Study of advanced maternal age

A retrospective case-control study was performed among women who delivered between January 1, 2015 and December 31, 2017 at the Department of Obstetrics and Gynecology, University of Szeged, Hungary.

During the 3-year study period, 7799 births were recorded at the Department of Obstetrics and Gynaecology. All women aged 40 years or over (4.8% of total births) were involved into the analysis as cases (n=378); out of these, 374 were singleton gestations (four twin gestations were excluded from the analysis). The controls (n=378) were selected

from women aged 25–29 years (14.8% of total births) who delivered during the same period, the controls were selected according to the number of previous deliveries; in case of more than one option a random selection was applied; twin gestations were excluded, too.

Study of sex chromosome trisomy

We analyzed the data of deliveries and abortions at the Department of Obstetrics and Gynecology, University of Szeged between 2003 and 2015. During these 13 years of time 31287 deliveries and 14990 terminations were performed at the Department of Obstetrics and Gynecology, University of Szeged. Out of these terminations, 481 (3.2%) were based on medical indication including fetal numerical chromosomal aberration in 140 (0.9%) cases. Out of these 140 cases six were trisomies of sex chromosome (three Klinefelter syndrome, three triple X syndrome). There were other six prenatally diagnosed cases, which resulted in delivery according to mothers' choice. Out of the six newborns two have Klinefelter syndrome, two have Jacob syndrome, and two have triple X syndrome.

Study of lifestyle factors

A cross-sectional, questionnaire-based study was performed among women delivering in the Department of Obstetrics and Gynecology, University of Szeged in 2014–2015. Altogether 1669 women were included into the study, who filled the questionnaire one or two days after delivery. Multiple pregnancies were excluded from the present analysis. Finally, due to multiple pregnancies (n=49) and missing data, 1548 mothers were involved into the final analysis.

3.2 Investigated parameters

Study of teenage mothers

The following parameters were analyzed: demographic data of the mothers (maternal age, marital status, smoking during pregnancy, attending prenatal care, number of previous gestations and deliveries), maternal complications (GDM, preeclampsia, threatened preterm delivery), neonatal data (prematurity, mode of delivery, mean birth weight, IUGR, congenital malformation, Apgar score at 5 min, umbilical cord blood pH, admission to NICU).

Gestational age was established by the last menstrual period, first-trimester ultrasonography or the examination of newborn. Preterm delivery was considered before

37 complete gestational weeks, IUGR means birthweight below the 10th percentile for gestational age according to sex. Prenatal care was adequate when the first visit was registered below 16 weeks of gestation or at least four check-ups were done during pregnancy.

Study of advanced age mothers

The data collected from the medical records comprised mothers' age, marital status (single, married, and in partnership), smoking habits, and the following obstetrical data: number of previous pregnancies (primigravida vs. multigravida), in vitro fertilization-embryo transfer (IVF-ET), attending prenatal care (it was considered adequate when the first visit was registered before 16 weeks of gestation or at least four check-ups were attended during pregnancy), registered maternal complications (GDM or preeclampsia during actual pregnancy), threatened preterm delivery, weeks of gestation, and mode of delivery. Neonatal data included birth weight and length, congenital malformations, Apgar score at 5-minute, umbilical cord blood pH, and admission to NICU.

The variables of maternal outcome for statistical analysis were diagnosis of GDM, diagnosis of preeclampsia, threatened preterm delivery, and mode of delivery (Caesarean section vs. vaginal delivery). The variables of neonatal outcome for statistical analysis were preterm birth (birth before 37 completed gestational weeks), low birth weight (below 2500 g), macrosomia (birth weight of 4000 g and over), congenital malformations (detected by prenatal genetic sampling or during routine screening: ultrasound examinations during pregnancy or physical examination of the newborn), umbilical cord blood pH <7.1, and admission to NICU.

Study of sex chromosome trisomy

The following parameters were examined: frequency of pregnancy termination, medical indications of termination (the rate of numerical chromosome abnormalities based on fetal karyotyping and out of these the rate of sex chromosomal trisomies) at the Department of Obstetrics and Gynecology, University of Szeged between 2003 and 2015. Simultaneously all of the sex chromosome trisomies diagnosed by prenatal cytogenetic methods (amniocentesis, chorionvillus sampling) and the outcome of these pregnancies were investigated at the Department of Medical Genetics, University of Szeged between 2003 and 2015.

Study of lifestyle factors

The self-administered questionnaire contained general, sociodemographic, lifestyle, conception, previous and current pregnancy related questions. Health documentation comprised mothers' health characteristics during pregnancy, and right after delivery; data about delivery type and complications; and health characteristics of the newborn.

Lifestyle-related questions included diet, physical activity, smoking and alcohol consumption. Dietary habits of mothers were measured by the frequency of vegetable, fruit, fish, fast food, salty snack, sweets, and soft drink consumption. Physical activity was evaluated by a question asking whether the mother was regularly physically active or not during current pregnancy, without any specification of the movement type. Smoking status was divided into two subgroups: smokers and non-smokers (never smokers and ex-smokers). Alcohol consumption was divided into 'no alcohol consumption' and 'alcohol consumption during pregnancy' groups.

Maternal diet, physical activity, smoking and alcohol consumption during pregnancy were expressed in diet, physical activity, alcohol consumption and smoking scores. Dietary score included vegetable, fruit, fish, fast food, salty snack, sweets and soft drink consumption. Physical activity score included physical activity during pregnancy and attendance at special pregnancy exercise classes. Smoking and alcohol consumption were categorized as "yes" or "no". The given points of each field could be seen in Table 9. The components of "healthy lifestyle" were defined according to the following: minimum 10 points in diet field were considered "healthy diet"; minimum 2 points in physical activity field as "regular physical activity"; and 3–3 points in smoking and alcohol consumption fields were considered as "non-smoking" and "no alcohol consumption".

3.3 Statistical analyses

Study of teenage mothers

The binomial test was applied to compare proportions of the anomalies observed in Szeged to the Hungarian national rates. Furthermore, Student's t-test was applied to compare the average birth weight between the two groups. The trends in incidence of teenage deliveries were investigated using Poisson's regression. All statistical analyses were carried out using STATA (StataCorp, College Station, TX, USA) 9.0 statistical software, $p<0.05$ was considered to be statistically significant.

Study of advanced maternal age

Simple descriptive statistics were used to describe the overall characteristics of the sample. Chi-squared test, Mann-Whitney U test, and Fischer's Exact test were used to examine the differences between the case group and the control group. Simple and multiple logistic regression analyses were used to assess the contribution of maternal age (older vs younger age-group) to various maternal and neonatal outcomes. Adjustment was performed for marital status, smoking status, primigravity, IVF-ET, and attendance to prenatal care.

The determinations of the logistic regression models were based on the Hosmer–Lemeshow goodness of fit tests for each dependent variable [88]. Statistical significance was defined at $p<0.05$. Odds ratios (OR), adjusted odds ratios (AOR) and 95% confidence intervals (CI) were calculated for each variable. All statistical analyses were performed with the IBM SPSS Statistics 24.0 version.

Study of sex chromosome trisomy

No special tests were used by statistical software.

Study of lifestyle factors

Characteristics of study population were evaluated by descriptive statistics. The association between the separate components of healthy lifestyle (diet, physical activity etc.) and sociodemographic characteristics were analysed with chi-square test. The level of statistical significance was set at $p<0.05$. Statistical analysis was performed by using IBM SPSS Statistics 26.0 program.

4. Results

4.1 Study of teenage mothers

Table 1 shows the main characteristics of teenage mothers. During the 5-year study period, 12,845 births were recorded at the Department. The total number of teenage pregnancies was 274 (2.1%). Out of these, 273 were singleton gestations and one was twin pregnancy.

Table 1 Characteristics of teenage mothers (N=274)

Characteristics	**n**	**%**
Maternal age		
<14 years	1	0.4
14 years	6	2.4
15 years	6	2.4
16 years	28	11.0
17 years	47	16.9
18 years	72	25.9
19 years	114	41.0
Marital status		
Single	119	43.4
In partnership	123	44.9
Married	32	11.7
Smoking during pregnancy		
Yes	66	24.0
No	208	76.0
Attending prenatal care		
Regularly	259	94.5
Irregularly	8	3.0
Never	7	2.5
Number of previous gestations		
0	184	67.2
1	65	23.7
2 or more	25	9.1
Number of previous deliveries		
0	235	85.8
1	32	11.7
2 or more	7	2.5

In Hungary, the total number of births was 448,852, out of these 27,777 (6.18%) were teenage pregnancies.

Most of them in the study group (41.0%) were 19 years old and only one was under 14 years (Table 1). Among teenages the rate of marriage was 11.7%, but the number of single mothers and number of mothers who lived in partnership was nearly the same. A total of 66 mothers (24.0%) reported smoking during pregnancy, 94.5% of them attended prenatal care regularly, but seven mothers (2.5%) never attended. 90 mothers (32.8%) had history of previous gestation(s) and 14.2% of the mothers had at least one previous delivery (Table1).

The rate of maternal complications during pregnancy is demonstrated in Table 2. GDM was significantly lower among teenage mothers than in the control group. Preeclampsia was more common in teenage mothers, than in the control, but there was no significant difference.

Table 2 Maternal complications during pregnancy (N=274)

Complications	**Teenage mothers**		**Control[a]**	**P-value**
	n	%	%	
Gestational diabetes	5	1.8	6.3	<0.001
Preeclampsia	21	7.6	6.0	0.250
Threatened preterm delivery	22	8.0	8.0	1.000

[a] National data

Table 3 summarizes the data of the perinatal outcome in the control and in the study group. The rate of premature deliveries was worse in the study group (10.2%) than the national rate (8.9%), but it was not significant. Frequency of spontaneous vaginal delivery and Caesarean section were similar in the two groups (66.5 vs. 65.2 and 33.5 vs. 34.8%). IUGR occurred a little bit more often in the teenage group. Significant difference was found in mean birth weight, in rate of congenital malformations, and in admission to NICU.

Table 3 Perinatal outcome of newborns (N=275)

	Teenage mothers		Control[b]	P-value
Premature	28	10.2 %	8.86%	0.450
Mode of delivery				
Vaginal delivery	183	66.5%	65.2%	
Caesarean section	92	33.5%	34.8%	0.660
Mean birth weight (g)	3110.2±564.03		3247	<0.001
IUGR	26	9.4%	8.0%	0.370
Congenital malformation	22	8.0%	5.0%	0.036
Apgar score at 5 min <7	4	1.5%	data not available	
Umbilical cord blood pH <7.2[a]	51	18.5%	data not available	
Newborn transferred to NICU	34	12.4%	8.0%	0.014

[a]Measurement was not performed in all cases (14). [b]National data.
IUGR: intrauterine growth retardation; NICU: neonatal intensive care unit

Table 4 shows the types of congenital malformations registered in the study group. 22 babies from the 275 newborns of teenage mothers had congenital malformations (8.0%), three of them had multiple malformations.

Table 4 The incidence of various fetal malformations.

Defects	Incidence	
Neural tube defects/hydrocephalus	2	0.8%
Heart defects	2	0.8%
Single umbilical artery	1	0.4%
Abdominal wall defect (gastroschisis)	1	0.4%
Urogenital defects	7	2.8%
Musculoskeletal defects	10	4.0%
Tracheostenosis	1	0.4%
Supernumerary nipple	1	0.4%

4.2 Study of advanced age mothers

During the 3-year study period, 7799 births were recorded, and the total number of elderly pregnancies was 378 (4.8%); out of these, 374 were singleton and four were twin gestations.

The main characteristics of mothers in both groups are shown in Table 5. In the case group (older mothers), most of the mothers (43.3%) were 40 years old, and the oldest mother was 48 years old; the mean maternal age was 41.12±1.39 years, the median age was 41 years (interquartile range, IQR: 42-40=2). Among the elderly mothers, the rate of being married was 53.2%, but the number of mothers who had a life-partner was also high (37.2%). 11 mothers (2.9%) confessed to smoking during pregnancy, and 99.2% of them attended prenatal care regularly, but 3 mothers (0.8%) never attended; 318 mothers (85.0%) had a history of previous gestation(s).

In the control group (younger mothers), most of the mothers were 29 years old (32%); the mean maternal age was 27.51±1.33 years. The rate of women who were married or had a life partner was similar (54.8% vs. 40.7%). In this group, nine mothers smoked during pregnancy (2.4%), and every mother in this group attended prenatal care regularly, and 55.0% of them had previous gestation(s).

The rate of maternal complications during pregnancy is also presented in Table 5. The frequency of GDM and preeclampsia was significantly higher in the case (older) group than in the control group (16.8% vs. 6.9 % and 17.9% vs. 1.6%, respectively). The frequency of threatened preterm delivery (5.6 % vs 1.8%) and the use of IVF-ET (4.5% vs. 0.0%) were significantly higher in the case group.

Mean gestational age (38.22±2.30 vs. 38.85±1.49 weeks) was significantly lower in the case group, while the number of Caesarean sections (58.6% vs. 29.4%) was significantly higher in the case group.

Table 5 Characteristics of study participants

Parameters	**Women aged ≥40 years (n=374)**	**Women aged 25–29 years (n=378)**	**P-value**
Mothers			
Median maternal age in years (IQR)	41 (42-40=2)	28 (29-26=3)	<0.001[#]
Maternal age, years (mean±SD)	41.12±1.39	27.51±1.33	<0.001[#]
Marital status			0.021[##]
Single, n (%)	36 (9.6)	17 (4.5)	
Having a life partner, n (%)	139 (37.2)	154 (40.7)	
Married, n (%)	199 (53.2)	207 (54.8)	
Smoking during pregnancy, n (%)	11 (2.9)	9 (2.4)	0.633[##]
Attending prenatal care, n (%)	371 (99.2)	378 (100.0)	0.123[###]
IVF-ET, n (%)	17 (4.5)	0 (0.0)	<0.001[###]
Gestational diabetes mellitus, n (%)	63 (16.8)	26 (6.9)	<0.001[##]
Preeclampsia, n (%)	67 (17.9)	6 (1.6)	<0.001[##]
Threatened preterm delivery, n (%)	21 (5.6)	7 (1.8)	0.006[##]
Gestational age, weeks (mean±SD)	38.22±2.30	38.85±1.49	<0.001[#]
Caesarean section, n (%)	219 (58.6)	111 (29.4)	<0.001[##]
Newborns			
Sex			0.276[##]
Male, n (%)	185 (49.5)	202 (53.4)	
Female, n (%)	189 (50.5)	176 (46.6)	
Mean birth weight, g, (mean±SD)	3282.37±658.11	3347.89±504.41	0.414[#]
Mean birth length, cm, (mean±SD)	49,61±2.61	49.67±2.20	0.783[#]
Low birth weight, n (%)	37 (11.2)	18 (5.2)	0.004[##]
Fetal macrosomia, n (%)	43 (12.8)	31 (8.6)	0.076[##]
Preterm birth, n (%)	44 (11.8)	26 (6.9)	0.021[##]
Congenital malformation, n (%)	21 (5.6)	26 (6.9)	0.474[##]
Apgar score at 5 min <7, n (%)	4 (1.1)	0 (0.0)	0.060[###]
Umbilical cord blood pH <7.1, n (%)[&]	10 (2.8)	22 (5.9)	0.041[##]
Admission to neonatal intensive care unit, n (%)	35 (9.4)	19 (5.0)	0.021[##]

Note: The table shows the main characteristics of mothers in both age-groups.
IQR: interquartile range, SD: standard deviation, IVF-ET: in vitro fertilization-embryo transfer
[&]Measurement was not performed in all cases (18 and 6)
[#]Mann-Whitney U test, [##]Chi-squared test, [###]Fischer's Exact test

Data of perinatal outcome in the case and in the control groups are summarized in Table 5. The frequencies of preterm birth and LBW were significantly higher in the study group compared to the control group (11.8% vs. 6.9% and 11.2% vs. 5.2%, respectively). The rate of fetal macrosomia was higher in the case group (12.8% vs. 8.6%), although the difference was not significant. A significant difference was found, however, in the number of admissions to NICU (9.4% vs. 5.0%). The frequency of registered congenital malformations (mainly heart defects and urogenital defects) was similar (5.6% vs. 6.9%) in both groups. There was no significant difference in the Apgar score at 5-min <7 (1.1% vs 0.0%), whereas the frequency of low umbilical cord blood pH (<7.1) was significantly lower in the case group (2.8% vs. 5.9%).

The results of logistic regression analyses are presented in Table 6.

Age had a significant effect on various maternal outcomes. The odds of GDM (OR: 2.74; AOR: 2.81), preeclampsia (OR:13.53; AOR: 13.05), threatened preterm delivery (OR: 3.15; AOR: 3.62), and Caesarean section (OR: 3.40; AOR: 3.31) were significantly higher in older than younger mothers in unadjusted and adjusted models as well.

The odds of adverse neonatal outcomes, such as LBW (OR: 2.30; AOR: 2.56) and admission to NICU (OR: 1.95; AOR: 2.03), were significantly higher in older vs. younger mothers in both models. The odds of preterm birth (OR: 1.80; AOR: 1.67) and low level of umbilical cord blood pH (OR: 0.46, AOR: 0.70) were significant in the unadjusted models, but these relationships were no longer statistically significant after the adjustment for marital status, smoking status, primigravity, IVF-ET, and attendance of prenatal care. There was no significant effect of maternal age on the frequency of fetal macrosomia and congenital malformations.

Table 6 Adverse maternal and neonatal outcomes in older mothers vs younger mothers (logistic regression analyses)

Parameters	OR (95% CI)	P-value	AOR (95% CI)	P-value
Maternal outcomes				
Gestational diabetes mellitus	2.74 (1.69–4.44)	<0.001	2.81 (1.66–4.76)	<0.001
Preeclampsia	13.53 (5.79–31.62)	<0.001	13.05 (5.46–31.19)	<0.001
Threatened preterm delivery	3.15 (1.32–7.51)	0.009	3.62 (1.44–9.10)	0.006
Neonatal outcomes				
Low birth weight	2.30 (1.28–4.13)	0.005	2.56 (1.34–4.91)	0.005
Fetal macrosomia	1.55 (0.95–2.53)	0.077	1.54 (0.92–2.60)	0.103
Preterm birth	1.80 (1.09–3.00)	0.023	1.67 (0.95–2.92)	0.072
Congenital malformation	0.81 (0.44–1.46)	0.475	0.73 (0.39–1.39)	0.342
Umbilical cord blood pH <7.1	0.46 (0.21–0.99)	0.046	0.70 (0.31–1.58)	0.388
Admission to neonatal intensive care unit	1.95 (1.09–3.48)	0.023	2.03 (1.06–3.86)	0.032

Note: Logistic regression analyses were used to assess the contribution of maternal age (older vs. younger age-group) to various maternal and neonatal outcomes. Adjustment was performed for marital status, smoking status, primigravity, IVF-ET, attendance of prenatal care.
OR: odds ratio, CI: confidence interval, AOR: adjusted odds ratio

4.3 Study of sex chromosome trisomy

During the study period (18 years) 31,287 birth and 14,990 terminations were registered at Department of Obstetrics and Gynecology, University of Szeged. Out of these 12 cases (0.026%) were diagnosed with sex chromosome trisomy prenatally. No new case was identificated during the 3–5-day long observation after birth. 481 terminations (3.2%) were performed according to medical indication, out of these 140 cases (0.9%) were numerical chromosome abnormality (Table 7). Out of these 140 cases six were trisomies of sex chromosome (three Klinefelter syndrome and three triple X syndrome). There were other six prenatally diagnosed cases, which resulted in delivery according to mothers's choice. Out of the six newborns two have Klinefelter syndrome, two have Jacob syndrome and two have triple X syndrome. In the in utero diagnosed cases mosaic cell line was not detected

by FISH (fluorescence in situ hybridization) (Department of Medical Genetics, University of Szeged).

Table 7 Terminations because of numerical chromosome abnormality (n=140)

Disease	Number of cases
Klinefelter syndrome	3
Triple X syndrome	3
Down syndrome	91
Edwards syndrome	22
Patau syndrome	5
Triploidy	4
Turner syndrome	8
Other autosomal trisomy	4

Cases of terminations because of fetal aneuploidy (n=140): trisomies of sex chromosome in six cases (4,3%), autosomal trisomies in 122 cases (87,1%)

The average age of the 12 pregnant women was 38.7 years, the youngest was 35 years old, the oldest was 47 years old. The indication of fetal karyotyping was maternal age in all (12) prenatally diagnosed cases, and also increased fetal nuchal translucency thickness were observed in two cases as well.

The average age of the six pregnant women deciding for delivery was 36.3 years. Fetal karyotyping was performed during amniocentesis in all six cases, the mean gestational age was 17.5 weeks at the time of procedure. The number of previous pregnancies was 1.2, the number of previous deliveries was 0.8. All of the six pregnancies resulted in delivery between 37th and 41st weeks of gestation (mean gestational age: 37.8 weeks). The mean birth weight of newborns was 3015.7 g, the mean Apgar score at 5 minutes was 8.3.

The average age of the six women who chose termination was 41.3 years. Fetal karyotyping was performed during amniocentesis (three cases, mean gestational age: 18.3 weeks) and chorionvillus sampling (three cases, mean gestational age: 13.6 weeks). The mean gestational age was 20.3 weeks at the date of termination. In one case there was a major congenital malformation (cystic adenomatoid malformation) described by pathological examination (and it was identified by prenatal ultrasound examination, too). The number of previous pregnancies was 3.5, the number of previous deliveries was 2.7.

Increased fetal nuchal translucency thickness was observed in two cases (1-1 case in both group). Both cases were similar to each other: the fetal nuchal translucency thickness was 4.1 mm and Triple X syndrome was diagnosed. The pathological examination did not describe any kind of malformation which could have been identified by ultrasound examination during pregnancy (except cystic adenomatoid malformation mentioned before). Other screening methods like extended ultrasound diagnostics, maternal serum markers and free fetal deoxyribonucleic acid (DNA) based tests (noninvasive prenatal tests, NIPT) were not forgone by these affected pregnant women.

4.4 Study of lifestyle factors

Table 8 shows the basic demographic characteristics of women. The frequency of the different components of lifestyle is shown by Table 9. Most of the mothers had daily fruit (1178, 78.5%) and vegetable (955, 63.8%) consumption, but they eat fish less frequently than once per week (905, 60.8%). Majority of mothers eat sweets regularly (1205, 80.3%). Each lifestyle field had given points (see Table 9). Assessing the points of dietary habits 602 (41.3%) of included women had healthy diet, 134 (9.0%) were physically active and attended special pregnancy exercise classes, 1279 (84.4%) did not drink alcohol and 1447 (93.5%) were not smoking during present pregnancy.

Table 8 Demographic characteristics of pregnant women (N=1548)

Characteristics	**n**	**%**
Age group (years)		
–24	147	9.5
25–34	949	61.3
35–	452	29.2
Partnership status		
Single	147	10.3
In partneship	1286	89.7

Table 9 Lifestyle characteristics of pregnant women and given points of each field (N=1548)

Characteristics	**n**	**%**	**Given points**
Vegetable consumption			
Daily	955	63.8	2
Weekly	472	31.5	1
Less frequently	71	4.7	0
Fruit consumption			
Daily	1178	78.5	2
Weekly	293	19.5	1
Less frequently	29	1.9	0
Fish consumption			
Weekly	584	39.2	1
Less frequently	905	60.8	0
Fast foods			
Monthly or never	1270	84.8	1
More frequently	228	15.2	0
Salty snacks			
Monthly or never	1067	71.7	2
Weekly	360	24.2	1
Daily	61	4.1	0
Sweets			
Monthly or never	296	19.7	2
Weekly	815	54.3	1
Daily	390	26.0	0
Soft drinks			
Monthly or never	993	66.7	2
Weekly	387	26.0	1
Daily	109	7.3	0
Physical activity			
Yes	755	50.5	1
No	741	49.5	0
Pregnancy exercise			
Yes	174	11.4	1
No	1349	88.6	0
Smoking during pregnancy			
No	1447	93.5	3
Yes	101	6.5	0
Alcohol consumption during pregnancy			
No	1279	84.4	3
Yes	236	15.6	0

The associations between the different components of healthy lifestyle and maternal age and patnership status are shown in Table 10.

Healthy diet was more prevalent among older women (35 or older). Regular physical activity was more frequent among 25- and 34-year-old mothers. Smoking during pregnancy was significantly associated with younger maternal age. No alcohol consumption during pregnancy was significantly higher among younger mothers. Marital status can affect a pregnant woman's lifestyle. Healthy diet and non-smoking behavior were significantly associated with living in partnership.

Table 10 Association between the separate field of health behaviour and demographic characteristics (Chi-square test)

Characteristics	**Healthy diet (N=602)**		**Regular physical activity (N=134)**		**Nonsmoking (N=1447)**		**No alcohol consumption (N=1279)**	
	n (%)	**p**	**n (%)**	**p**	**n (%)**	**p**	**n (%)**	**p**
Age group (years)		<0.001		0.001		<0.001		0.006
–24	27 (20.6)		2 (1.4)		121 (82.3)		132 (93.6)	
25–34	364 (40.6)		99 (10.9)		893 (94.1)		775 (83.2)	
35–	211 (49.0)		33 (7.7)		433 (95.8)		372 (84.2)	
Partnership status		0.013		0.067		<0.001		0.414
Single	47 (31.8)		8 (5.1)		137 (82.5)		142 (86.6)	
In partnership	555 (42.4)		126 (9.5)		1309 (94.9)		1135 (84.1)	

5. Discussion

The aim of this thesis was to characterize the association between mother's age and adverse maternal, perinatal and neonatal outcomes. To solve this aim we analyzed the relationship between teenage pregnancy and adverse perinatal outcome (congenital malformations), advanced maternal age and various adverse maternal and neonatal outcomes, and the association between demographic factors and lifestyle factors in pregnant women. Additionally, we investigated the cases with in-utero-diagnosed trisomies of sex chromosome.

Our results showed that younger maternal age was significantly associated with lower mean birth weight, higher risk of congenital malformations and increased admission rate to NICU. Older maternal age was significantly associated with maternal complications, higher frequency of using IVF-ET, higher rate of Caesarean-section, prematurity, increased admission rate to NICU, and lower mean gestational age. We expected significantly higher rate of congenital malformations in the case group of older mothers, but our results showed that advanced maternal age was not associated with higher rate of birth defects.

The frequency of prenatal recognition of sex chromosome trisomies lags behind autosomal trisomies. The causes are the following: low sensitivity of the screening methods used in the investigated period and the various clinical appearance of sex chromosome trisomies. The decision concerning the fate of the pregnancy is a much more difficult challenge for parents in case of sex chromosome trisomy than in case of autosomal trisomy. The parents can only make their decision based on extensive information given by a multidisciplinary team (consisting of a clinical genetician, obstetrician, pediatrician, endocrinologist, and professionals of developing treatments).

From the point of the lifestyle of the mothers during pregnancy, our results showed significant association between maternal age and health behaviour. With the exception of alcohol consumption older mothers showed healthier lifestyle (healthy diet, regular physical activity, non-smoking).

5.1 Study of teenage mothers

Over the last decades, remarkable changes have been noticed in family life and in sexual activity before marriage. Sexual provocation has increased through the media and contraceptives are easierly available than before. All these factors have led to the earlier sexual activity and the increased number of teenage pregnancies throughout the world [20].

In the study of Orvos et al. in 1999 [7], most of the teenage mothers were single and almost one fifth of these mothers have never attended prenatal care (data were collected immediately after the political structure change of Hungary). In our study, changes have been noticed in the proportion of single mothers and of those who had a partner in life. Having a husband or a partner during pregnancy could mean appreciable support to the mother, and it can explain the high rate of attending prenatal care.

Several previous studies have already shown association between teenage pregnancy and adverse perinatal outcome. Mahavarkar et al. [8], Loto et al. [10], Gilbert et al. [12], Serunjogi et al. [26] described LBW among the babies of teenagers, but we found difference only in the mean birth weight, which was lower in teenage mother than in the control. It is in contrasts with the findings of Dewan et al. [93], who found no significant differences between the mean birth weight and the proportion of LBW babies between adolescens and adults. Our results could not prove higher rate of IUGR like Amini [13] and Fraser [14] or prematurity like Todhunter [27], Exarchos [28] and Akseer [29]. The study of Sandal et al. demonstrated that the rate of NICU admission was higher in teenage mothers [23], our observations confirmed their statement. We have found significant risk of congenital malformations in teenage group, similarly to Eckmann-Sholz [19], Csermely [20] and Reefhuis et al. [21].

Csermely et al. [20] examined the risk of congenital anomalies in young pregnant women in Hungary: according to their results, a higher risk of gastroschisis, congenital hearts defects, particularly left-sided obstructive defects, undescended testis and clubfoot was found in the youngest age group (19 years or less). Hollier et al. reported also a high risk of gastroschisis and polydactyly [89]. In the study of Serunjogi [26] offsprings of teenage mothers had an increased risk of major external birth defects, specifically gastroschisis.

In the study of Eckmann-Scholz gastroschisis and fetal heart defects were the most frequent malformations [19]. Chen et al. found no increased risk for circulatory/respiratory or urogenital anomalies, but reported higher risk for congenital anomalies in central nervous, gastrointestinal and musculoskeletal systems [22]. Our study agrees with Hollier (polydactyly), Csermely (undescended testis), and Chen (musculoskeletal defects), but in our study gastroschisis was noticed only in one case.

During the analysis of maternal complications, GDM was significantly lower among teenage mothers. The prevalence of GDM has been increasing with maternal age [90], thus, our results were not unexpected. Preeclampsia is more specific in younger age and in

nulliparous women, our findings are similar: preeclampsia was more common in teenage mothers, than in the control, but there was no significant difference.

To identify the causes of congenital anomalies, prematurity, LBW, and other adverse perinatal outcomes is a really complex task. Lam suggests that young mothers who smoke cigarettes or marijuana or are malnourished have a high risk of having an infant with gastroschisis [91]. Reefhuis claims that lifestyle factors – inadequate prenatal care, smoking, drinking alcohol, taking drugs and malnutrition (lack of using folic acid and multivitamins) – seem to be the most likely explanation for the increased risk of congenital abnormalities [21]. In Hungary, Paulik et al. had similar results: the regular use of folic acid was important to prevent neural tube defects [92]. Smoking is a well-known risk factor of low birth weight and prematurity, Dewan reported that the mean birth weight of babies of smoking mothers was significantly lower than for non-smoking mothers and the risk of LBW was significantly increased in teenage mothers who smoked [93]. Gortzak-Uzan confirmed that nutritional status, insufficient folate intake, lack of prenatal care are risk factors in teenage pregnancies [9].

5.2 Study of advanced maternal age

Older gravida is usually described as a pregnant woman over the age of 35 years, but recent studies has regarded the age of 40 years to be the age threshold. It is due to the fact that in many high-income countries the maternal age at childbirth has increased [45]. Considering this tendency, which is also present in Hungary, we analysed the data of mothers aged 40 years or over.

In our study, most of the mothers in both groups were married or had a life partner and attended prenatal care regularly. Only some of them smoked during pregnancy.

Several previous studies have found an association between advanced maternal age and adverse perinatal outcome. Several authors (Favilli et al. [36]; Karabulut et al. [37]; Kenny et al. [45], Glick et al. [53], Elci et al. [54]) have described a higher rate of prematurity in older mothers, and our findings correlate with their statement. Favilli et al. [36] have also reported higher rate of Caesarean-section among mothers over 40 years. Our results highlighted the same tendency similarly to the studies of Chan and Lao [38], Marozio et al. [39] and Claramonte Nieto et al. [44]. Nonetheless, we did not find higher rate of macrosomia like Schimmel et al. [41] and AlJahdali et al. [56].

Likewise, several studies (Zapata-Masias et al. [40]; Koshida et al. [47]; Laopaiboon et al. [50]; Akin et al. [51]) and our observations also demonstrated that the rate of NICU admission was higher in older mothers.

Our data showed significant difference in the use of IVF-ET. In the case group, the rate of IVF-ET was significantly higher than in the control group. According to Chan et al. [38] older pregnant women have often been nulliparous previously, and they have delayed pregnancy by choice. A significant proportion of these women needed assisted reproductive technology to have their own babies. Salem Yaniv et al. [34] and Materna-Kiryluk et al. [49] have revealed that the frequency of congenital malformations is significantly higher in advanced age, but our research did not have the same results.

Our observations are in contrast with the findings of Celik et al. [59] and Alshami et al. [60] who have reported no significant difference between advanced maternal age and adverse perinatal outcome.

During the analysis of maternal complications, GDM was found to be significantly higher among older mothers. The prevalence of GDM increases with maternal age, and our results were in line with this finding. It might be explained by the impairment of carbohydrate metabolism in older age [39]. There was also a significant difference in preeclampsia and threatened preterm delivery. Marozio et al. [39] suggest that age-related dysfunction of the vascular endothelium can cause preeclampsia in older age.

According to the literature there are some controversies from the point of adverse perinatal outcomes: increased risk of malformations has been found in case of younger and older mothers. In our study of teenage mothers, we analysed the frequency of congenital defects among teenage mothers, and we found significantly higher rate of malformations among adolescens than in the control group. In the present study we supposed that the risk of malformations will be higher in older mothers, too, but the results showed different situation: the incidence of foetal malformations was similar in the case group and in the control group. The risk of chromosomal aberrations is increasing with age, but our study found only one case (one newborn with Down's syndrome) in the older group. Probably the high rate of prenatal care attendance resulted in the low number of malformations. Owing to adequate prenatal care and the availability of cytogenetic and molecular genetic methods, in most cases, severe malformations could be diagnosed intrauterinely. In that case, the mother can choose whether to deliver the foetus with the diagnosed malformation or terminate the pregnancy (the Hungarian law accepts the termination in case of a severe, life-threatening malformation).

5.3 Study of sex chromosome trisomy

In Hungary the diagnostic methods of trisomies of sex chromosome are prenatal cytogenetic methods (amniocentesis, chorionvillus sampling, analysis of fetal blood, similar to autosomal trisomies) in most of the cases. These invasive methods are recommended only in high-risk pregnancies. Detection of high-risk pregnancies are based on ultrasound examination during first and second trimester. According to the professional policy of Ministry of Human Capacities about Prenatal screening and diagnostics of Down syndrome all pregnant women aged 37 or above must be refered to genetic consultation because maternal age is one of the determining factors of genetical aberrations [94]. At the same time maternal age is not a risk factor for sex chromosome aberrations. In our study the mean age of the 12 affected pregnant women was increased (38.7 years) with regard to the fact that the indication of the cytogenetic analysis was older maternal age (37 years and above). In case of trisomies of sex chromosome sensitivity of NIPT does not achieve the same level as in case of autosomal trisomies and is not supported by social insurance.

Several studies confirmed the importance of prenatal diagnostics of sex chromosome trisomes. Informing the parents correctly and properly (in collaboration with other professions) about the circumstances and potential outcomes is essential to decide responsibly. Early recognition of trisomies of sex chromosome are important to increase intervention for emerging developmental problems and apply hormonal substitution if it's necessary, potentially improving their quality of life [64,67].

In our study out of 31,287 deliveries and 14,990 terminations there were 12 prenatally diagnosed cases: five Klinefelter, five triple X and two Jacob syndromes. No mosaicism was identified. The indication of fetal karyotyping was maternal age in all (12) prenatally diagnosed cases, and also increased fetal nuchal translucency thickness was observed in two cases as well. The most common reason of fetal karyotyping in prenatally diagnosed cases is maternal age also in the international literature [63].

In our study there were 12 prenatally identified cases, out of these 6 was led to termination. One of the international studies claims that the rate of termination is 36% in the in utero diagnosed cases [61]. The six pregnant women deciding on termination were older and had more previous pregnancies than the 6 women deciding on delivery. The potential cause is that the mother doesn't want to give birth to a baby with disease if she has healthy child(ren). A french study found the same statement: women who gave birth before chose termination more often than women with no child [65]. In 2011 in the

EUROCAT (European Surveillance of Congenital Anomalies) study 41% of pregnant women younger than 35 years and only 33% of women older than 35 years asked for termination in prenatally diagnosed cases.[61]

In our study the mean gestational week of identification of chromosome aberrations was 19.5 weeks. In EUROCAT study the mean gestational week was 16 weeks, the earliest case was in Denmark (11 weeks), the latest case was in Poland (21 weeks) [61].

The detection rate of sex chromosome trisomies was significantly higher in countries where the prenatal detection rate of Down syndrome was also high. Moreover both group showed significant correlation in rate of in utero identification. It means that high detection rate of in utero diagnosed Down syndrome went hand in hand with high detection rate of in utero diagnosed sex chromosome trisomies [61].

No specific ultrasound marker exists for sex chromosome aberrations. None of the universal markers using for routine screening has notable predictive value in cases of sex chromosome trisomies because discrepancies of nuchal thickness, nasal bone, ductus venosus or tricuspidal flow are not tipical of these trisomies. In addition, serious fetal disorders observable by ultrasound examination are not characteristic too. Older maternal age does not count for screening of sex chromosome trisomies because the incidence of these diseases doesn't increase with maternal age unlike Down syndrome [68]. Some studies observed contrary [61,65]. The risk of sex chromosome trisomy does not increase with gestational age and the rate of spontaneous abortion is not higher compared to healthy pregnancies. It makes difficulties to screen for these trisomies [68,94]. For instance, the relative frequency of Edwards syndrome is 90% smaller nearby term than in first trimester because of spontaneous abortions, but in case of sex chromosome trisomy the rate of spontaneous abortions corresponds with the rate of spontaneous abortions in healthy pregnancies [68]. The phenotypical aberrations of sex chromosome trisomies are not so serious just like Edwards or Patau or Turner syndrome, even so patients can have symptoms and they want solutions for their problems from doctors.

Viuff et al. [64] examined the prenatal detection rate of Down syndrome and aneuploidies of sex chromosome in a screening programme in Denmark. In this study 275,037 case were analysed and they found that 85% of Down syndrome was detected, the detection rate of Klinefelter syndrome was 13%, of Triple X syndrome was 16% and of Jacob syndrome was only 5%. The screening programme used combined test based on fetal nuchal thickness, maternal serum β-HCG (beta-human choriogonadotropin) and PAPP-A (pregnancy-associated plasma protein-A). The reached 85% detection rate of Down

syndrome is high, but the extremely low detection rate of sex chromosome trisomies is thought-provoking. Fetal nuchal thickness was significantly higher, serum level of PAPP-A was significantly lower in group of sex chromosome trisomy compared to healthy control group. Furthermore, in Klinefelter syndrome serum level of β-HCG was lower. Statistical significancy does not mean automatically that these markers can be used for screening (for example maternal serum alpha-fetoprotein and Down syndrome have mathematical connection and a lot of false legal conclusion based on this connection apropos of medical lawsuits). Viuff found higher rate of obstetric complication in case of sex chromosome trisomy like higher rate of prematurity in Triple X syndrome. In conclusion, they made clear that their prenatal screening programme functions in case of Down syndrome, but not in case of sex chromosome trisomies. Probably development of another algorithm based on nuchal thickness and serum markers is needed to create useful screening programme for sex chromosme trisomies [64].

Sebire et al. examined the efficiency of screening programme used to detect Down syndrome in first trimester in case of sex chromosome trisomy. Risk calculation was performed from nuchal thickness and maternal age. If calculated risk exceeded 1:300 they offered fetal karyotyping. The primary goal of karytyping was identifying Down syndrome. In this study out of 59,131 cases there were ten Klinefelter, five Jacob and five Triple X syndroma. MoM (multiple of the median) of nuchal thickness was 1.35 compared to healthy fetuses which was statistically significant. In 8 cases (40%, out of the 20 affected fetuses) the nuchal thickness was over 95 percentiles. In conclusion, if studies don't apply fetal karyotyping in every case, prevalence of sex chromosome trisomy will be underestimated and sensitivity of screening method for detecting it will be overestimated. The frequency of sex chromosome trisomies in first trimester and by birth and the 4% of spontaneous abortion showed that „screen positivity" of their method was only 9% reffering to sex chromosome trisomies [95].

Analysis of free fetal DNA sequences in maternal circulation is new and promising opportunity in modern prenatal genetics but this method is appropriate for screening Down syndrome in the first place. In a study sequential and DNA based screening were compared. In point of all aneupoidy the detection rate of sequential screening was 81.6% (with 4.5% false positivity) and the detection rate of DNA based method was 77.1% (with 3.7% false positivity). The two compared methods are effective mostly in screening for autosomal trisomies. In case of sex chromosome trisomy detection rate of sequential screening was

58.9% and of DNA based method was 93.7%. „Screen positivity" of DNA based method was 99.2% and of sequential screening was 92.9% [96].

In our study (with small case number) the rate of termination was 50% in prenatally diagnosed cases of sex chromosome trisomy. In a study with large case number this rate was only 24–48% (Klinefelter syndrome: 48%, Jacob syndrome: 29%, Triple X syndrome 24%) [64]. According to the results of EUROCAT study huge differences can be observed among europian countries in prenatal identification of sex chromsome trisomy and number of terminations [61].

The prenatal diagnosis of sex chromosome trisomies is not as efficient as of the autosomal trisomies.

At the beginning of the 1990s, when the nuchal thickness had been introduced as an ultrasound marker, prenatal genetics started on its journey by screening for Down syndrome. Whitout any doubt it is unquestionable that the problem caused by 21 trisomy is one of the greatest professional challenges in these days, but it has to be stated that prenatal genetics consists of more than screening for Down syndrome only.

The frequency of prenatal recognition of sex chromosome trisomies lags behind autosomal trisomies. The causes are the following: low sensitivity of the screening methods used in the investigated period and the various clinical appearance of sex chromosome trisomies. The real frequencies of diseases are underestimated by most of the studies because they are not paired with as serious clinical symptoms as autosomal trisomies. Much of them are not diagnosed immediately after birth, and some of the people suffering from Klinefelter syndrome do not get diagnosed even in their whole lifetime.

The decision concerning the fate of the pregnancy is a much more difficult challenge for parents in case of sex chromosome trisomy than in case of autosomal trisomy. The parents can only make their decision based on extensive information given by a multidisciplinary team (consisting of a clinical genetician, obstetrician, pediatrician, endocrinologist, and professionals of developing treatments).

5.4 Study of lifestyle factors

Our results showed that advanced maternal age was significantly associated with healthier lifestyle components. Our results are in line with previous studies which suggested that maternal dietary behaviour would be strongly connected with socioeconomic status including maternal age. Jardí et al. [97] investigated the adherence to Mediterranean diet

of pregnant women; while Wesolowska et al. [98] examined the correlation between educational, socioeconomic status of women and quality of diet during pregnancy. Their results were similar to ours, according to which a healthier diet was observed in case of advanced maternal age. However, advanced maternal age means a higher health risk, some investigations suggest that advanced age is associated with higher health literacy level, and more health-conscious lifestyle and behaviour. Advanced age women tend to consume less unhealthy snacks and drinks during pregnancy compared with the younger mothers [99]; nonetheless, compulsory genetical pregnancy screenings over 35 years can also lower the health risks [100]. Our results show that advanced maternal age is associated with the examined lifestyle fields, except alcohol consumption during pregnancy.

5.5 Limitations of studies

The findings of our studies have to be seen in light of some limitations. One important limitation of all studies is their retrospective nature. The generalizability of our results is influenced by the small sample size in case of studies of teenage and advanced age mothers. It is also notable, that all studies were delivered in a single institution, but this institute has a regional responsibility, what increases the generalizability of our results.

No data were available about level of education, income of the mothers, folate or vitamin intake, diet habits, if mothers smoked before pregnancy, and there was no detailed medical follow-up of the transferred neonates, because NICU is located in another department. The missing of these data limited the detailed characterization of the factors potentially associated with adverse maternal and neonatal outcomes.

The data on pregnancy related lifestyle characteristics of mothers came from self-reports that may influence the answers. It is also possible that some risk factors (e.g. smoking during pregnancy) were underreported because of social desirability.

6. Summary of findings

- Younger maternal age was significantly associated with lower mean birth weight, higher risk of congenital malformations and increased admission rate to NICU. Teenage mothers should be informed about the potential complications during an adequate prenatal care program and recommended to deliver in a regional centre to avoid adverse perinatal outcome.

- Our data suggest that older maternal age was significantly associated with maternal complications, higher frequency of using IVF-ET, higher rate of Caesarean section, prematurity and increased admission rate to NICU. We expected significantly higher rate of congenital malformations in the older mothers' group, but our results showed that advanced maternal age was not associated with higher rate of birth defects. It may prove that adequate prenatal care and modern genetic diagnostic methods are able to screen congenital anomalies, thereby much fewer neonates are born with severe congenital defects.
- Today, health care providers pay more attention to older mothers because of the risks of advanced age, but our results showed that the early detection of congenital malformations may be important in every age group, especially in the teenage mothers. It is important to inform women about the consequences of delayed childbearing. Older mothers may need more attention during an adequate prenatal care program provided by obstetricians, midwives, and health visitors, and they are recommended to deliver in a regional centre to decrease adverse perinatal outcomes.
- The indication of fetal karyotyping was advanced maternal age in all prenatally diagnosed cases; maternal age is an independent factor in case of sex chromosome trisomy. However, importance of early diagnosis followed by treatment should always be emphasised to reach a better quality of life.
- Sex chromosome trisomies are identified most commonly by amniocentesis performed in consequence of maternal age. It can be expected that the efficiency of prenatal recognition of sex chromosome trisomies will increase measurably in Hungary thanks to the spreading of free fetal DNA based tests (NIPT). This tendency increases the importancy of medical teams specialized in these trisomies.
- The lifestyle of the mothers during pregnancy can strongly determine their own and their infant's health. From the point of prevention, the fulfilment of the four health behaviour components – healthy diet and physical activity, avoidance of smoking and alcohol consumption – is the best solution. The differences between age groups may suggest further promotion and improvement of pregnancy planning and pregnancy care among younger women.

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APPENDICES

I.

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Adverse perinatal outcome in teenage pregnancies: an analysis of a 5-year period in Southeastern Hungary

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ORIGINAL ARTICLE

Adverse perinatal outcome in teenage pregnancies: an analysis of a 5-year period in Southeastern Hungary

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ABSTRACT

Objective: To determine the risks of adverse perinatal outcomes of teenage mothers.

Material and methods: A retrospective analysis was performed on teenage mothers (under 20 years of age) who delivered in the period of 2010–2014 at the Department of Obstetrics and Gynecology, University of Szeged (study group). All mothers who delivered in Hungary during the same period were studied as a control group. The following parameters were analyzed: demographic data of the mothers, maternal complications, perinatal outcome and congenital malformations of the newborns. The binominal test, Student's *t*-test and Poisson's regression were applied using STATA 9.0 (StataCorp, College Station, TX, USA) statistical software ($p < .05$ was considered to be statistically significant).

Results: During this 5-year period, 12,845 births were recorded at the Department, of these 274 (2.1%) were teenage pregnancies with 275 newborns. The offsprings of teenage mothers had significantly lower mean birth weight (3110.2 ± 564.03 g versus 3247 g), higher rate of congenital malformations (8.0 versus 5.0%) and higher admission to neonatal intensive care unit (12.4 versus 8.0%) than the infants in the control group.

Conclusions: Younger maternal age was significantly associated with lower mean birth weight, higher risk of congenital malformations, and increased admission rate to neonatal intensive care unit.

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KEYWORDS
Teenage pregnancy; congenital malformation; prenatal care

Introduction

The population including the total number of deliveries has been decreased in the last decades in Hungary. Despite of this tendency, the incidence of adolescent pregnancies has increased [1].

Teenage pregnancy and its effect on perinatal outcome has been brought into focus by a lot of studies. Many of them reported higher rate of low birth weight [2–10], prematurity [2–8,10–12], intrauterine growth retardation (IUGR) [1,7,8], congenital malformations [3,13–16], neonatal intensive care admission [4,17] and perinatal mortality [4,6,7] among teenage pregnancies. Marital status, low educational level, poverty, and lack of prenatal care are also risk factors of poor perinatal outcome among these young mothers [3,18,19]. On the other hand, there are some studies in the literature, which assert the contrary that young maternal age does not mean higher risks of adverse perinatal outcome [20].

The aim of this study was to determine if teenage pregnancy is associated with adverse perinatal outcome with particular regard to congenital malformations.

Materials and methods

A retrospective analysis was done on teenage mothers (under 20 years of age) with more than 24 complete weeks of gestation, who delivered between 1 January 2010 and 31 December 2014 at the Department of Obstetrics and Gynecology, University of Szeged (study group). The following parameters were analyzed: demographic data of the mothers, maternal complications, neonatal data including congenital malformations. Gestational age was established by the last menstrual period, first-trimester ultrasonography or the examination of newborn. Preterm delivery was considered before 37 complete gestational weeks, intrauterine growth retardation (IUGR) means birth weight below the 10th percentile for gestational age according to sex. Prenatal care was adequate when the first visit was registered below 16 weeks of gestation or at least four check-ups were done

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during pregnancy. We compared the data of teenage mothers with the data of all mothers who delivered in Hungary (Hungarian Central Statistical Office) during the study period (control group). Our department is a regional healthcare center, which means that high-risk pregnancies are transferred from the Southeastern part of Hungary to here.

The binomial test was applied to compare proportions of the anomalies observed in Szeged to the Hungarian rates. Furthermore, Student's *t*-test was applied to compare the average birth weight between the two groups. The trends in incidence of adolescent deliveries were investigated using Poisson's regression.

All statistical analyses were carried out using STATA (StataCorp, College Station, TX, USA) 9.0 statistical software, $p < .05$ was considered to be statistically significant.

Results

During the 5-year study period, 12,845 births were recorded at the Department. The total number of teenage pregnancies was 274 (2.1%). Out of these, 273 were singleton gestations and one was twin pregnancy. In Hungary, the total number of births was 448,852, out of these 27,777 (6.18%) were teenage pregnancies.

Table 1 shows the main characteristics of the teenage mothers. Most of them (41.0%) were 19 years old and only one was under 14 years. Among adolescents the rate of marriage is 11.7%, but the number of single mothers and number of mothers who had a partner in life was nearly the same. A total of 66 mothers (24.0%) reported smoking during pregnancy, 94.5% of them attended prenatal care regularly, but seven mothers (2.5%) never attended. 90 mothers (32.8%) had history of previous gestation(s) and 14.2% of the mothers had at least one previous delivery.

The rate of maternal complications during pregnancy is demonstrated in Table 2. Gestational diabetes was significantly lower among adolescent mothers than in the control group. Preeclampsia was common in teenagers, but there was no significant difference.

Table 2 also summarizes the data of the perinatal outcome in the control and in the study group. The rate of premature deliveries was worse in the study group (10.2%) than the national rate (8.9%), but it was not significant. Frequency of spontaneous vaginal delivery and caesarean section were similar in the two groups (66.5 versus 65.2 and 33.5 versus 34.8%). IUGR occurred a little bit more often in the teenage group. Significant difference was found in mean birth weight, in rate of congenital malformation, and in admission to Neonatal Intensive Care Unit (NICU).

Table 1. Characteristics of teenage mothers (274 mothers).

	n	%
Maternal age		
<14 years	1	0.4
14 years	6	2.4
15 years	6	2.4
16 years	28	11.0
17 years	47	16.9
18 years	72	25.9
19 years	114	41.0
Marital status		
Single	119	43.4
Partner in life	123	44.9
Married	32	11.7
Smoking during pregnancy		
Yes	66	24.0
No	208	76.0
Attending prenatal care		
Regularly	259	94.5
Irregularly	8	3.0
Never	7	2.5
Number of previous gestations		
0	184	67.2
1	65	23.7
2 or more	25	9.1
Number of previous deliveries		
0	235	85.8
1	32	11.7
2 or more	7	2.5

Table 2. Maternal complications during pregnancy (274 mothers) and perinatal outcome of newborns (2010–2014, 275 newborns).

	Teenagers		Control[b]	*p*
Maternal complications				
Gestational diabetes	5	1.8%	6.3%	<.001*
Preeclampsia	21	7.6%	6.0%	.250
Threatened preterm delivery	22	8.0%	8.0%	1.000
Perinatal outcome of newborns				
Premature	28	10.2%	8.86%	.450
Mode of delivery				
Vaginal delivery	183	66.5%	65.2%	
Caesarean section	92	33.5%	34.8%	.660
Mean birth weight (g)	3110.2 ± 564.03		3247	<.001*
IUGR	26	9.4%	8.0%	.370
Congenital malformation	22	8.0%	5.0%	.036*
Apgar score at 5 min <7	4	1.5%	data not available	
Umbilical cord blood pH <7.2[a]	51	18.5%	data not available	
Newborn transferred to NICU	34	12.4%	8.0%	.014*

[a]Measurement was not performed in all cases (14).
[b]National data.
*Significance at $p < .05$.

Table 3 shows the types of congenital malformations registered in the study group. 22 babies from the 275 newborns of adolescent mothers had congenital malformations (8.0%), three of them had multiple malformations.

Discussion

Over the last decades, remarkable changes have been noticed in family life and in sexual activity before marriage. Sexual provocation has increased through the media and contraceptives are easier available

Table 3. The incidence of various fetal malformations.

Defects	Incidence	
Neural tube defects/hydrocephalus	2	0.8%
Heart defects	2	0.8%
Single umbilical artery	1	0.4%
Abdominal wall defect (gastroschisis)	1	0.4%
Urogenital defects	7	2.8%
Musculoskeletal defects	10	4.0%
Tracheostenosis	1	0.4%
Supernumerary nipple	1	0.4%

than before. All these factors have led to the increased number of adolescent pregnancies throughout the world [21].

In the study by Orvos et al. in 1999 [1], most of the teenage mothers were single and almost one fifth of adolescent mothers have never attended prenatal care (data were collected immediately after the political structure change). In our study, changes have been noticed in the proportion of single mothers and of those who had a partner in life. Having a husband or a partner during pregnancy could mean appreciable support to the mother, and it can explain the high rate of attending prenatal care.

Several previous studies have already shown association between teenage pregnancy and adverse perinatal outcome. Mahavarkar et al. [2], Loto et al. [4], Gilbert et al. [6] described low birth weight among the babies of teenagers, but we found difference only in the mean birth weight, which was lower than in control. It contrasts with the findings of Dewan et al., who found no significant differences between the mean birth weight and the proportion of low birth weight babies between teenagers and adults [22]. We could not prove higher rate of prematurity and IUGR like Amini [7] and Fraser [8]. The study of Sandal et al. demonstrated that the rate of NICU admission was higher in adolescent mothers [17], our observations confirmed their statement. We have noticed significant risk of congenital malformations similarly to Eckmann-Sholz [13], Csermely [14], and Reefhuis [15] et al.

Csermely et al. examined the risk of congenital anomalies in young pregnant women in Hungary: according to their results, a higher risk of gastroschisis, congenital heart defects, particularly left-sided obstructive defects, undescended testis and clubfoot was found in the youngest age group (19 years or less) [14]. Hollier et al. reported also a high risk of gastroschisis and polydactyly [23]. In the study by Eckmann-Scholz gastroschisis and fetal heart defects were the most frequent malformations [13]. Chen et al. found no increased risk for circulatory/respiratory or urogenital anomalies, but reported higher risk for congenital anomalies in central nervous, gastrointestinal and musculoskeletal systems [16]. Our study agrees with Hollier (polydactyly), Csermely (undescended testis) and Chen (musculoskeletal defects), but gastroschisis was noticed only in one case.

During the analysis of maternal complications, gestational diabetes was significantly lower among adolescent mothers. The prevalence of gestational diabetes has been increasing with maternal age [24], thus, our results were not unexpected. Preeclampsia is more specific in younger age and in nulliparous women, our findings are similar: preeclampsia was common in teenagers, but there was no significant difference.

To identify the causes of congenital anomalies, prematurity, low birth weight and other adverse perinatal outcome is a really complex task. Lam suggests that young mothers who smoke cigarettes or marijuana or are malnourished have a high risk of having an infant with gastroschisis [25]. Reefhuis claims that lifestyle factors seem to be the most likely explanation for the increased risk of congenital abnormalities: inadequate prenatal care, smoking, drinking alcohol, taking drugs, and malnutrition (lack of using folic acid and multivitamins) [15]. In Hungary, Paulik et al. had similar results: the regular use of folic acid was important to prevent neural tube defects [26]. Smoking is a well-known risk factor of low birth weight and prematurity, Dewan reported that the mean birth weight of babies of smoking mothers was significantly lower than for non-smoking mothers and risk of low birth weight was significantly increased in teenagers who smoked [22]. Gortzak-Uzan confirmed that nutritional status, insufficient folate intake, lack of prenatal care are risk factors in teenage pregnancies [3].

The limitations of our study are its retrospective nature and the small sample size in the examined groups despite of being a regional center. No data were available about level of education, income of the mothers, folate or vitamin intake, diet habits, if mothers smoked before pregnancy, and there was no detailed medical follow-up of the transferred neonates, because NICU is located in another department.

In conclusion, we can summarize that in our study group younger maternal age was significantly associated with lower mean birth weight, higher risk of congenital malformations and increased admission rate to neonatal intensive care unit. The possible causes need further investigation, but our findings confirm the relevancy of screening congenital malformations in younger mothers and the necessity of NICU. Teenage mothers should be informed about the potential complications during an adequate prenatal care program

and recommended to deliver in a regional center to avoid adverse perinatal outcome.

Disclosure statement

The authors report no conflicts of interest.

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II.

MAGYAR NŐORVOSOK LAPJA • 2020; 83: 90–94.

A nemi kromoszómákat érintő triszómiák in utero felismerésének gyakorisága

A Szegedi Tudományegyetem Szülészeti és Nőgyógyászati Klinika beteganyagában 2003–2015. között

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Célkitűzés: Magzati korban felismert nemi kromoszóma-triszómiák típusának és a várandósság kimenetelének elemzése.
Anyag és módszer: 2003–2015 között a Szegedi Tudományegyetem (SZTE) Szülészeti és Nőgyógyászati Klinikáján szülések és terhességmegszakítások kerültek elemzésre az alábbi szempontokat vizsgálva: milyen arányban történt terhességmegszakítás magzati citogenetikai vizsgálattal igazolt számbeli kromoszóma-rendellenesség miatt, ezen belül az esetek hány százalékában volt a nemi kromoszómák triszómiája a megszakítás oka. Egyidejűleg elemeztük 2003–2015 között az SZTE Orvosi Genetikai Intézetben prenatális citogenetikai vizsgálattal azonosított összes nemi kromoszóma-triszómiát, valamint a várandósság kimenetelét.
Eredmények: Tizenkét nemi kromoszóma-triszómia került in utero diagnosztizálásra ebben a periódusban. A vizsgált intervallumban (13 év) 31 287 szülés és 14 990 terhességmegszakítás történt az SZTE Szülészeti és Nőgyógyászati Klinikáján. A terhességmegszakítások közül 481 eset (3,2%) történt orvosi javallat alapján, ebből 140 esetben (0,9%) magzati számbeli kromoszóma-rendellenesség miatt. A 140 esetből hat volt nemi kromoszómát érintő triszómia (három *Klinefelter-szindróma,* három tripla X-szindróma). Hat olyan prenatálisan felismert eset volt, amelyeknél a várandós a terhesség kiviselése mellett döntött. Mind a hat újszülöttnél postnatalis kromoszómavizsgálat igazolta a nemi kromoszóma-triszómiát (két *Klinefelter-szindróma,* két *Jacob-szindróma,* két tripla X-szindróma). A terhesség kihordása mellett döntő hat várandós átlagos életkora 36,3 év, a hat terhességmegszakítást választó átlagos életkora 41,3 év volt. A tizenkét in utero diagnosztizált nemi kromoszóma-triszómia esetében a magzati kromoszómameghatározás javallatának oka minden esetben az anyai életkor volt, két esetben megvastagodott tarkóredő is társult hozzá.
Következtetések: A nemi kromoszóma triszómiáinak prenatális felismerése jóval elmarad az autoszomális triszómiák felismerési gyakoriságától, ami várhatóan jelentős mértékben növekedni fog hazánkban is az egyre inkább elterjedő nem invazív, szabad magzati DNS (dezoxiribonukleinsav) kimutatásán alapuló tesztek révén. Ezen esetek ellátása multidiszciplináris együttműködést igényel.

Kulcsszavak: nemi kromoszóma-triszómia, prenatális felismerés

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In utero-diagnosed trisomies of sex chromosome: an analysis of frequency at the Deparment of Obstetrics and Gynecology, University of Szeged between 2003 and 2015

Aim: Our purpose was to determine the type of trisomies of sex chromosome by prenatal identification and outcome of these pregnancies.

Materials and methods: We analyzed the data of deliveries and abortions at the Department of Obstetrics and Gynecology, University of Szeged between 2003 and 2015. The following parameters were examined: frequency of pregnancy termination, medical indications of termination (the rate of numerical chromosome abnormalities based on fetal karyotyping and out of these the rate of sex chromosomal trisomies). Simultaneously all of the sex chromosome trisomies diagnosed by prenatal cytogenetic methods and the outcome of these pregnancies were investigated at the Department of Medical Genetics, University of Szeged between 2003 and 2015.

Results: During the study period 12 sex chromosome trisomies were diagnosed in utero. Between 2003 and 2015 (13 years) 31287 deliveries and 14990 terminations were performed at the Department of Obstetrics and Gynecology, University of Szeged. Out of these terminations, 481 (3.2%) were based on medical indication including fetal numerical chromosomal aberration in 140 (0.9%) cases. Out of these 140 cases six were trisomies of sex chromosome (three Klinefelter syndrome three triple X syndrome). There were other six prenatally diagnosed cases, which resulted in delivery according to mothers' choice. Out of the six newborns 2 have Klinefelter syndrome, 2 have Jacob syndrome, and 2 have triple X syndrome. All of the sex chromosome trisomies were verified by postnatal analysis of the chromosomes. The average age of the six pregnant women deciding for delivery was 36.3 years, the average age of the six women who choose termination was 41.3 years. The indication of fetal karyotyping was maternal age in all (12) prenatal diagnosed cases, and also increased fetal nuchal translucency thickness were observed in two cases as well.

Conclusions: The frequency of prenatal diagnosis of sex chromosome trisomies is not as high as of the autosomal trisomies. The number of successfully diagnosed sex chromosome trisomies will probably increase in Hungary, due to the spread of non-invasive, free fetal DNA (deoxyribonucleic acid) detecting methods. The adequate care of these cases requires multidisciplinary effort.

Keywords: trisomy of sex chromosome, prenatal diagnosis

Bevezetés

A nemi kromoszómát érintő triszómiák gyakoriságukhoz képest viszonylag kevésbé reprezentáltak a szakirodalomban [1]. A nemi kromoszómák triszómiája meiotikus non-disjunctio következtében jön létre [1, 2, 3]. Az extra X-kromoszóma nőkben tripla X-szindrómát, férfiakban *Klinefelter-szindrómát* eredményez, míg az extra Y-kromoszóma jelenlétét férfiakban *Jacob-szindrómának* (dupla Y-szindrómának) nevezik.

A tripla X-szindrómában érintett nők kariotípusa 47,XXX. A nemi kromoszóma-triszómiái közül ez kerül legritkábban méhen belül felismerésre. A szindróma ritkán okoz súlyos fenotípusos elváltozásokat, és jellegüket tekintve azok is igen széles határok között változhatnak [3]. A betegek magasak, fertilitásuk megtartott, jellemző lehet a microcephalia, az epicanthus és a görbe ötödik ujj, ritkán tanulási problémák, izomhipotónia és veseérintettség előfordul. Az élveszületésekre vonatkoztatott gyakorisága 1:1000 (1:900–1200) [1, 4, 5, 6].

A *Klinefelter-szindróma* kariotípusa 47,XXY, élveszületésekre vonatkoztatott gyakorisága 1:500–600 [6]. Jellemző tünetek a sterilitás, a gynecomastia, a pubertás zavara. Általában magasak, hosszú karokkal és lábakkal, nőies testalkattal. A gyér szőrzet és a hypogonadismus az alacsony tesztoszteronszint következményei. Az intelligenciájuk átlagos, de enyhe mentális retardáció, viselkedési zavar is előfordulhat [2].

A *Jacob-szindróma* (dupla Y-szindróma) kariotípusa 47,XYY, a férfiak magasak, acnés bőrrel, átlagos vagy átlag alatti intelligenciával. Tanulási és magatartási problémák jelentkezhetnek. Gyakorisága az élveszületett fiúgyermekekre vonatkoztatva 1:1000 [5, 6]. Az összes esetnek mindössze 15%-át sikerül diagnosztizálni, azokat is átlagosan 17 évesen [4, 7].

A nemi kromoszómák számának növekedésével súlyosbodnak a klinikai tünetek, a mozaikossággal pedig csökkennek.

A fentebb említett triszómiák közül egyik sem jár olyan súlyos fenotípusos elváltozásokkal, mint a 21-es, a 13-as, illetve a 18-as kromoszóma triszómiája [1]. Míg a *Patau-* és az *Edwards-szindróma* prenatális felismerési rátája eléri a 90%-ot, a *Down-szindrómáé* is 75% feletti, addig a nemi kromoszómák triszómiái esetében ez az arány mindössze 20% körül mozog az irodalom szerint [8]. A nemi kromoszómák fent ismertetett számbeli eltéréseinek a prenatális előrejelzésére a szűrőmódszerek közül sem az ultrahangdiagnosztika, sem az anyai szérummarkerek [4, 8], de még a szabad magzati DNS kimutatásán alapuló (noninvazív prenatális) tesztek sem érik el az autoszomális triszómiák kiszűrésére vonatkozó megbízhatóságát [9].

A nemi kromoszóma triszómiája – számbeli kromoszóma-rendellenesség révén – jogilag ugyanazon megítélés alá esik Magyarországon, mint az autoszomális triszómiáké, azaz a 24. terhességi hét előtt kiszűrt esetekben a várandós dönthet terhességének megszakítása vagy kiviselése között [10]. Ebben a kérdésben a szülők alapvetően az orvostól vár-

nak információt a megállapított kromoszómaeltérés talaján várhatóan kialakuló klinikai rendellenességekről. A szülők pontos, körültekintő és alapos tájékoztatása elengedhetetlen ahhoz, hogy felelősséggel tudjanak dönteni a magzat sorsáról. A korai felismerés további előnye, hogy a megszületett gyermeknél az időben elkezdett fejlesztés és az esetlegesen szükséges hormonális szubsztitúció sokat javíthat az egyén állapotán, életminőségén [3, 6].

Anyag és módszer

A Szegedi Tudományegyetem Szülészeti és Nőgyógyászati Klinikáján 2003 és 2015 közötti szülések és terhességmegszakítások kerültek elemzésre az alábbi szempontokat vizsgálva: milyen arányban történt terhességmegszakítás magzati citogenetikai vizsgálattal igazolt számbeli kromoszóma-rendellenesség miatt, ezen belül az esetek hány százalékában volt a nemi kromoszómák fent leírt számbeli eltérése a megszakítás oka. Egyidejűleg elemeztük 2003–2015 között az SZTE Orvosi Genetikai Intézetben prenatális citogenetikai vizsgálattal azonosított összes nemi kromoszóma triszómiáját, valamint a várandósság kimenetelét.

A magzati kariotípus-meghatározás G-sáv-technikával (SZTE Orvosi Genetikai Intézet) történt invazív mintavétellel (amniocentesis, chorionboholy-biopszia, SZTE Szülészeti és Nőgyógyászati Klinika) nyert magzati mintából. Az adatok a klinika írásos és elektronikus adatbázisából kerültek kigyűjtésre és elemzésre.

Eredmények

A vizsgált 13 év alatt 31 287 szülés és 14 990 terhességmegszakítás történt a klinikán. 481 esetben (3,2%) került sor orvosi javallat alapján terhességmegszakításra, ebből 140 esetben (0,9%) magzati számbeli kromoszóma-rendellenesség *(1. táblázat)*, ezen belül 6 esetben (0,026%) a nemi kromoszómák triszómiái miatt.

1. táblázat: Magzati számbeli kromoszóma-rendellenesség miatt terminált esetek (n=140)

Kórkép	Esetszám
Klinefelter-szindróma	3
Tripla X-szindróma	3
Down-szindróma	91
Edwards-szindróma	22
Patau-szindróma	5
Triploidia	4
Turner-szindróma	8
Egyéb autoszomális triszómia	4

Magzati számbeli kromoszóma-rendellenesség miatt 140 esetben történt terhességterminálás, közülük 122 (87,1%) esetben autoszomális triszómia, 6 (4,3%) esetben nemi kromoszóma-triszómia miatt.

Az SZTE Orvosi Genetikai Intézetben a vizsgálati időszakban tizenkét magzatnál prenatálisan diagnosztizáltak nemi kromoszómát érintő triszómiát, a szülők hat esetben a terhesség terminálása, hat esetben a terhesség kiviselése mellett döntöttek. Két *Klinefelter-szindrómás,* két *Jacob-szindrómás,* két tripla X-szindrómás újszülött született.

A 12 várandós átlagos anyai életkora 38,7 év, a legfiatalabb 35, a legidősebb pedig 47 éves volt.

A terhesség kihordása mellett döntő hat várandós átlagos életkora 36,3 év volt. Mind a hat esetben magzatvízből történt a magzati kariotípus meghatározása, az amniocentesis időpontjában az átlag terhességi kor 17,5 hét volt. A megelőző terhességek száma átlagosan 1,2, a szülések átlagos száma pedig 0,8 volt. Mind a hat terhesség szüléssel ért véget a 37. és a 41. terhességi hét között, átlagosan a 37,8 héten. Az újszülöttek átlagos születési súlya 3015,7 g, az 5 perces Apgar-értékek átlaga 8,3 volt.

A terhességmegszakítást választó hat várandós átlagos életkora 41,3 év volt. Három esetben amniocentesis, három esetben chorionboholy-mintavétel útján történt a magzati kromoszóma meghatározása. A beavatkozások időpontja amniocentesis esetén átlagosan a 18,3, chorionboholy-biopsziánál átlagosan a 13,6 terhességi hét volt. A terhesség befejezése átlagosan 20,3 hetesen történt. A kórbonctani vizsgálat egy esetben írt le major fejlődési rendellenességet: a tüdő cisztikus adenomatoid malformációját, ami prenatálisan már ultrahangvizsgálattal felismerésre került. (Ennél az esetnél az anyai életkor miatt történt magzati citogenetikai vizsgálat 47,XXY kariotípust igazolt.) A megelőző terhességek száma átlagosan 3,5, a megelőző szülések átlagos száma pedig 2,7 volt.

Kóros tartományba eső tarkóredő-vastagságot egy-egy esetben mértek a terhesség megszakítása, illetve a kiviselése mellett döntő várandósok között. Mindkét esetben 4,1 mm volt a mért tarkóredő-vastagság, és mindkét esetben tripla X-szindróma került diagnosztizálásra. A kórbonctani vizsgálat a már említett tüdő cisztikus adenomatoid malformációján kívül egyéb, ultrahangvizsgálattal felismerhető kóros eltérést nem írt le. Más prenatális szűrőmódszert a várandósok (pl. kiterjesztett ultrahangvizsgálat, noninvazív prenatális teszt, szérummarker-meghatározás) nem vettek igénybe.

Megbeszélés

A vizsgálati időszakban prenatálisan 12 nemi kromoszóma-triszómia került felismerésre: öt *Klinefelter-,* öt tripla X- és két *Jacob-szindróma.* A prenatálisan felismert esetek felében történt terhességmegszakítás.

Számos tanulmány bizonyítja, hogy a magzati számbeli kromoszóma-rendellenességek, köztük a nemi kromoszóma triszómiáinak diagnosztikája fontos. A várandós törvény adta joga, hogy tisztában legyen magzatának kromoszóma-rendellenességével, ennek a magzatra és újszülöttre való hatásával. A fenti célt szolgálja a várandósok szűrési- és diagnosztikai vizsgálati rendszere, ezekre vonatkozó legfontosabb útmutató az Emberi Erőforrások Minisztériuma

szakmai irányelve a *Down-kor* prenatális szűréséről és diagnosztikájáról [11]. Az irányelvben szereplő, anyai szérumból végezhető magzati szabad DNS-alapú, noninvazív szűrőtesztek (NIPT), mint másodlagos szűrések, államilag nem támogatottak. Azokban az országokban, ahol a *Down-szindróma* prenatális felismerése magas, ott a nemi kromoszómák triszómiáinak detekciós rátája is szignifikánsan jobb volt [1].

Anyagunkban a 12 kiszűrt várandós átlagéletkora emelkedett – 38,7 év – volt, tekintettel arra, hogy 2003–2015 között a nemi kromoszóma-triszómiák felismerése magzati citogenetikai vizsgálattal történt, amelynek a vezető javallata az idősebb anyai életkor volt. Az általunk felismert eseteknél az invazív mintavétellel nyert chorionboholy- és magzatvízsejteket klasszikus G-sáv-technikával vizsgáltuk. Kromoszómaspecifikus FISH (fluorescence in situ hybridization) vizsgálatokat az esetleges mozaik sejtvonal felismerésére kiegészítő vizsgálatként alkalmaztunk. A nemi kromoszóma-triszómiák gyors diagnosztikájára alkalmas kvantitatív fluoreszcens polimeráz láncreakció (QF-PCR) módszer [12] az SZTE Orvosi Genetikai Intézetben nem volt elérhető. A nemzetközi irodalomban fellelhető tanulmányok szerint is a prenatálisan felismert esetekben a magzati kromoszómameghatározás leggyakoribb oka az anyai életkor [3]. Tekintettel arra, hogy az anyai életkor a nemi kromoszómák számbeli rendellenességeinek kockázatát nem növeli [8], feltételezhető, hogy az általunk megállapított 38,7 éves átlag anyai életkor nem tükrözi a nemi kromoszóma-triszómiás újszülöttek valós átlagos anyai életkorát. Az alkalmazott invazív diagnosztika a magzati fejlődési rendellenességre magas kockázatú várandósoknál történt meg.

A nemi kromoszómák eltéréseinek felismerésére specifikus ultrahangmarker ugyan nem ismert, mégis anyagunkban két esetben kóros tarkóredő-vastagság (4,1 mm) volt mérhető. A rutin szűrésben használt univerzális markerek közül egyik sem rendelkezik jelentős prediktív értékkel a nemi kromoszómák triszómiáira nézve, mivel a tarkóredő, az orrcsont, a ductus venosus vagy akár a tricuspidalis áramlás eltérései nem jellemzőek erre a betegségcsoportra. Ezenfelül a súlyos, ultrahangvizsgálat során észlelhető magzati szervi rendellenességek sem jellemzőek egyik vizsgált szindrómára sem.

Viuff és munkatársai Dániában a nemi kromoszóma aneuploidiák és a Down-szindróma prenatális detekciós rátáját vizsgálták a tarkóredő vastagságon és a szérummarkereken alapuló szűrőprogramban. Konklúzióként megállapították, hogy a prenatális szűrőprogramjuk jól működik Down-szindróma esetében, de a nemi kromoszóma triszómiáinak szűrésében nem. A probléma okát abban látták, hogy az utóbbiak szűrésénél valószínűleg a tarkóredővastagság és a szérummarkerek figyelembe vételéhez más algoritmus kidolgozása szükséges [4]. Sebire és munkatársai az I. trimeszterbeli Down-szűrőprogram hatékonyságát vizsgálták a nemi kromoszómák triszómiái esetében. Az általuk alkalmazott szűrőmódszernek a nemi kromoszóma triszómiáira vonatkoztatott „screen pozitivitása" mindössze 9% [13].

A saját kis esetszámú anyagunkban a prenatálisan felismert esetek felében (6/12) történt terhességmegszakítás. Egy nagy esetszámú tanulmányban a prenatálisan felismert nemi kromoszóma-triszómiákban a terhességek 24-48%-ában kérték a várandósok a terhesség megszakítását (Klinefelter-szindrómában 48%, Jacob-szindrómában 29%, tripla X-szindrómában 24%) [4]. Az EUROCAT (European Surveillance of Congenital Anomalies) vizsgálat szerint az európai országok között nagy eltérések tapasztalhatóak a nemi kromoszóma triszómiáinak prenatális felismerésében, valamint a terhességmegszakítások arányában is [1]. A vizsgálati anyagunkban a terminálás mellett döntő hat várandós idősebb volt és a paritások száma is magasabb volt a terhesség kiviselését választó várandósokhoz képest. Ennek oka az lehet, hogy az anya nem szeretne „beteg" gyermeket szülni egészséges testvér vagy testvérek mellé. Hasonló megállapításra jutott egy francia tanulmány is, ahol a már szült nők gyakrabban döntöttek a terhesség terminálása mellett a még gyermektelenekhez képest [5]. A 2011-es EUROCAT-vizsgálatban a 35 évnél fiatalabb nők 41%-a, míg a 35 évnél idősebbeknek csak a 33%-a kérte a terhesség megszakítását a méhen belül felismert esetekben [1].

A prenatálisan kiszűrt esetekben fontos a megfelelő felvilágosítás genetikai tanácsadás keretében. Szükséges megteremteni a várandós és családja számára több szakma képviselőivel (klinikai genetikus, szülész-nőgyógyász szakorvos, neonatológus, endokrinológus, gyermekneurológus, pszichiáter, gyermeksebész, szívsebész és fejlesztő terapeuták) történő kommunikáció lehetőségét, mivel csak így tudnak felelősségteljes döntést hozni a magzat sorsáról. A korai, pontos diagnózis teszi lehetővé az időben megkezdett fejlesztést, illetve hormonális szubsztitúciós terápia sokat javíthat a betegek életminőségén [6].

Következtetés

Az autoszomális és a nemi kromoszóma számbeli rendellenességek aránya közel azonos. A nemi kromoszóma triszómiáinak prenatális felismerési gyakorisága azonban elmarad az autoszomális triszómiákétól. Ennek oka a vizsgált időszakban használt szűrőmódszerek alacsony szenzitivitásából és a nemi kromoszómát érintő triszómiák klinikai megjelenéséből adódik. A kórképek valódi gyakoriságát a legtöbb tanulmány alábecsüli, mivel nem járnak olyan súlyos klinikai tünetekkel, mint az autoszomális triszómiák, nagy részük még születés után, sőt a Klinefelter-szindrómások egy része egész életükben sem kerülnek diagnosztizálásra. A terhesség sorsával kapcsolatos döntés meghozatala sokkal nagyobb kihívás a szülők számára, mint magzati korban felismert autoszomális triszómia esetén. A szülők csak multidiszciplináris team által adott, széles körű tájékoztatás alapján tudják meghozni a döntésüket. Leggyakrabban az anyai életkor miatt végzett magzati citogenetikai vizsgálat kapcsán, véletlenül kerülnek felismerésre. Várhatóan jelentős mértékben növekedni fog hazánkban is a nemi kromoszóma-triszómiák prenatális felismerésének a hatásfoka az egyre inkább elterjedő nem invazív, szabad magzati DNS kimutatásán alapuló

tesztek révén, ami ezen esetek ellátásához szükséges orvosi teamek jelentőségét növeli.

Érdekeltség, támogatás

A közleményben szereplő tudományos eredmények az „Intelligens élettudományi technológiák, módszertanok, alkalmazások fejlesztése és innovatív folyamatok, szolgáltatások kialakítása a szegedi tudásbázisra építve" című EFOP-3.6.1-16-2016- diszciplináris egészségügyi, egészségnevelési és egészségfejlesztési összefogás az egészséges gyermekvállalásért és az egészséges gyermekek megszületéséért a Dél-Alföldi régióban" alprojekt támogatásával jöttek létre.

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III.

Adverse Maternal and Perinatal Outcome of Women Aged 40 Years or Over: A Retrospective Study

Adrienn Karai, Zita Gyurkovits, Gábor Németh, Hajnalka Orvos, and Edit Paulik

BACKGROUND: Advanced maternal age is traditionally described to be 35 years of age or over. In recent years, new trends have suggested that it may be 40 years of age or over; this occurs in Hungary.

AIM: The aim of this study was to determine the association between advanced maternal age and various adverse maternal and neonatal outcomes.

METHODS: A retrospective analysis was performed among women who delivered between 2015 and 2017. All women aged 40 years or over (cases) were involved into the analysis (n = 374). The controls (n = 378) were randomly selected from women aged 25 to 29 years who delivered during the same period considering the number of previous gestations and previous deliveries. The data collected from the medical records comprised the mothers' demographic and obstetric characteristics and neonatal data. To assess the contribution of maternal age to various maternal and neonatal outcomes, multiple logistic regression analyses were used.

RESULTS: The logistic regression analyses showed higher odds of gestational diabetes (AOR, adjusted odds ratio: 2.81), preeclampsia (AOR: 13.05), threatened preterm delivery (AOR: 3.62), and cesarean section (AOR: 3.31) in mothers of higher age. The odds of low birth weight (AOR: 2.56) and intensive care (AOR: 2.03) were significantly higher in older vs. younger mothers, while no significant associations were between maternal age and fetal macrosomia and congenital malformations.

CONCLUSIONS: Considering our results, it is important to educate women about the consequences of delayed childbearing and the need of continuous observation within prenatal care.

KEYWORDS: antepartum management; maternal complications; neonatal care; regression analysis

INTRODUCTION

Advanced maternal age is traditionally described to be 35 years of age or over (Carolan et al., 2011), whereas in recent years, new trends have suggested that it may be 40 years of age or over. The number of women who delay the first pregnancy or planning of another pregnancy is increasing in many countries. The reasons could be various, such as longer time spent in education or career plans first (Berkowitz et al., 1990). These women give birth to their first child in their 30s or 40s (Huang et al., 2008).

In Hungary, the total number of deliveries has decreased in the past decades (148,673 live births in 1980; 125,679 in 1990; 97,047 in 2001; 90,335 in 2010; 91,577 in 2017; and 89,807 in 2018) (Hungarian Central Statistical Office, 2020). Although there is a decrease in the number of live births, the proportion of mothers

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over 40 years has increased, especially in the past 10 years (2.6% [2,354] in 2010 vs. 5.2% [4,802] in 2017) (Hungarian Central Statistical Office, 2020) similarly to the tendency in other developed countries. Due to the demographic changes, the Hungarian population can be described as an ageing society; thus, childbearing is a key-question, and the new tendencies (delaying childbirth or having a baby over 40 years of age) do not point towards the growth of the population. Childbearing would be preferable in mid-twenties to early thirties, every social and health care programme must prompt this age limit. Giving birth at a later age has more risks; therefore, it is highly important to support mothers over 40 during their pregnancy to deliver healthy babies.

Pregnancy at an advanced age and its effect on the perinatal outcome have been investigated by several studies. Many of them have reported that maternal complications, such as gestational diabetes mellitus and preeclampsia are frequent in older mothers (Chan & Lao, 2008; Claramonte Nieto et al., 2019; Favilli et al., 2012; Kahveci et al., 2018; Karabulut et al., 2013; Kenny et al., 2013; Klemetti et al., 2016; Marozio et al., 2017; Salem Yaniv et al., 2011; Schimmel et al., 2014; Simenc et al., 2018; Zapata-Masias et al., 2016). The frequency of Cesarean section is also higher among them (Chan & Lao, 2008; Claramonte Nieto et al., 2019; Favilli et al., 2012; Kahveci et al., 2018; Kanmaz et al., 2019; Karabulut et al., 2013; Kenny et al., 2013; Marozio et al., 2017; Simenc et al., 2018; Zapata-Masias et al., 2016). On the one hand, studies have found a higher rate of low birth weight, macrosomia, prematurity intrauterine growth retardation (IUGR), congenital malformations, neonatal intensive care admission and perinatal mortality in advanced age mothers and their babies (Akin et al., 2010; Chan & Lao, 2008; Favilli et al., 2012; Fuchs et al., 2018; Kahveci et al., 2018; Karabulut et al., 2013; Kenny et al., 2013; Klemetti et al., 2016; Koshida et al., 2019; Laopaiboon et al., 2014; Marozio et al., 2017; Materna-Kiryluk et al., 2011; Salem Yaniv et al., 2011; Schimmel et al., 2014; Zapata-Masias et al., 2016). On the other hand, some studies have asserted the contrary, that is, advanced maternal age is not associated with higher risks of adverse perinatal outcome (Celik et al., 2017; Alshami et al., 2011).

The aim of this study was to determine the association between advanced maternal age and various adverse maternal and neonatal outcomes.

MATERIALS AND METHODS

A retrospective case-control study was performed among women who delivered between January 1, 2015, and December 31, 2017, at the Department of Obstetrics and Gynaecology, University of Szeged, Hungary. Our department is a regional healthcare centre, high-risk pregnancies are transferred here from the south eastern part of Hungary (it means three counties out of 19, around 1,250,000 people out of nearly 10 million). The data collection was based on the hospital documentation of women and neonates. All data were registered anonymously. The study protocol was approved by the Regional and Institutional Human Medical Biological Research Ethics Committee of the University of Szeged, Hungary (No: 4046).

During the 3-year study period, 7,799 births were recorded at the Department of Obstetrics and Gynaecology. All women aged 40 years or over (4.8% of total births) were involved into the analysis as cases (n = 378); out of these, 374 were singleton gestations (four twin gestations were excluded from the analysis). The controls (n = 378) were selected from women aged 25 to 29 years (14.8% of total births) who delivered during the same period, the controls were matched according to the number of previous gestations and previous deliveries, in case of more than one option a random selection was applied. Twin gestations were excluded.

The data collected from the medical records comprised mothers' age, marital status (two subgroups were formed: single and married; the latter included common-law relationships as well), smoking habits, and the following obstetrical data: number of previous pregnancies (primigravida vs. multigravida), in vitro fertilization-embryo transfer (IVF-ET), attending prenatal care (it was considered adequate when at least four check-ups were attended during pregnancy), registered maternal complications (gestational diabetes mellitus or preeclampsia during actual pregnancy), threatened preterm delivery, weeks of gestation, and the mode of delivery. Neonatal data included birth weight and length, congenital malformations, Apgar score at 5-minute, umbilical cord blood pH, and admission to neonatal intensive care unit (NICU).

The variables of maternal outcome for statistical analysis were diagnosis of gestational diabetes mellitus, diagnosis of preeclampsia, threatened preterm

delivery, and mode of delivery (cesarean section vs. vaginal delivery). The variables of neonatal outcome for statistical analysis were preterm birth (birth before 37 completed gestational weeks), low birth weight (below 2,500 grams), macrosomia (birth weight of 4,000 grams and more), congenital malformations (detected by prenatal genetic sampling or during routine screening: ultrasound examinations during pregnancy or physical examination of the newborn), umbilical cord blood pH <7.1, and admission to NICU.

Simple descriptive statistics were used to describe the overall characteristics of the sample. The Chi-squared test, Mann–Whitney *U* test, and Fischer's Exact test were used to examine the differences between the case group and the control group. Simple and multiple logistic regression analyses were used to assess the contribution of maternal age (older vs. younger age-group) to various maternal and neonatal outcomes. Adjustment was performed for marital status, smoking status, primigravity, IVF-ET, and attendance to prenatal care. The determinations of the logistic regression models were based on the Hosmer–Lemeshow goodness of fit tests for each dependent variable (Hosmer & Lemeshow, 1989). Statistical significance was defined at $p < .05$. Odds ratios (ORs) and 95% confidence intervals (CIs) were calculated for each variable. All statistical analyses were performed with the IBM SPSS version 24.

RESULTS

The main characteristics of mothers in both groups are shown in Table 1. In the case group, most of the mothers (43.3%) were 40 years old, and the oldest mother was 48 years old; the median age was 41 years (interquartile range, IQR: 2). Among the older mothers, the rate of

TABLE 1. Characteristics of Study Participants

PARAMETERS	WOMEN AGED ≥40 YEARS (*n* = 374)	WOMEN AGED 25–29 YEARS (*n* = 378)	*P*-VALUE
Mothers			
Median maternal age in years (IQR)	41 (2)	28 (3)	<.001[b]
Marital status			.021[c]
Single, *n* (%)	36 (9.6)	17 (4.5)	
Having a life partner, *n* (%)	139 (37.2)	154 (40.7)	
Married, *n* (%)	199 (53.2)	207 (54.8)	
Smoking during pregnancy, *n* (%)	11 (2.9)	9 (2.4)	.633[c]
Attending prenatal care, *n* (%)	371 (99.2)	378 (100.0)	.123[d]
Primigravity, *n* (%)	56 (15.0)	170 (45.0)	<.001[c]
IVF-ET, *n* (%)	17 (4.5)	0 (0.0)	<.001[d]
Gestational diabetes mellitus, *n* (%)	63 (16.8)	26 (6.9)	<0.001[c]
Preeclampsia, *n* (%)	67 (17.9)	6 (1.6)	<.001[c]
Threatened preterm delivery, *n* (%)	21 (5.6)	7 (1.8)	.006[c]
Gestational age, weeks (mean ± *SD*)	38.22 ± 2.30	38.85 ± 1.49	<.001[b]
Cesarean section, *n* (%)	219 (58.6)	111 (29.4)	<.001[c]
Newborns			
Sex			.276[c]
Male, *n* (%)	185 (49.5)	202 (53.4)	
Female, *n* (%)	189 (50.5)	176 (46.6)	
Mean birth weight, g, (mean ± *SD*)	3282.37 ± 658.11	3347.89 ± 504.41	.414[b]
Mean birth length, cm, (mean ± *SD*)	49,61 ± 2.61	49.67 ± 2.20	.783[b]
Low birth weight, *n* (%)	37 (11.2)	18 (5.2)	.004[c]
Fetal macrosomia, *n* (%)	43 (12.8)	31 (8.6)	.076[c]
Preterm birth, *n* (%)	44 (11.8)	26 (6.9)	.021[c]
Congenital malformation, *n* (%)	21 (5.6)	26 (6.9)	.474[c]
Apgar score at 5 min <7, *n* (%)	4 (1.1)	0 (0.0)	.060[d]
Umbilical cord blood pH <7.1, *n* (%)[a]	10 (2.8)	22 (5.9)	.041[c]
Admission to neonatal intensive care unit, *n* (%)	35 (9.4)	19 (5.0)	.021[c]

Note. The table shows the main characteristics of mothers in both age-groups.

IQR = Interquartile range, SD = Standard deviation, IVF-ET = In vitro fertilization-embryo transfer.

[a]Measurement was not performed in all cases (18 and 6).

[b]Mann–Whitney U test, [c]Chi-squared test, [d]Fischer's Exact test.

being married was 53.2%, but the number of mothers who had a life-partner was also high (37.2%). 11 mothers (2.9%) confessed to smoking during pregnancy, and 99.2% of them attended prenatal care regularly, but 3 mothers (0.8%) never attended, and 318 mothers (85.0%) had a history of previous gestation(s).

In the control group, most of the mothers were 29 years old (32%); the mean maternal age was 27.51 ± 1.33 years. The rate of women who were married or had a life partner was similar (54.8% vs. 40.7%). In this group, nine mothers smoked during pregnancy (2.4%), and every mother in this group attended prenatal care regularly, and 55.0% of them had previous gestation(s). There was a significant difference between the study and the control groups in the rate of mothers who never had a gestation before (15% vs. 45%, respectively).

The rate of maternal complications during pregnancy is also presented in Table 1. The frequency of gestational diabetes mellitus and preeclampsia was significantly higher in the case group than in the control group (16.8% vs. 6.9 % and 17.9% vs. 1.6%, respectively). The frequency of threatened preterm delivery (5.6 % vs. 1.8%) and the use of IVF-ET (4.5% vs. 0.0%) were significantly higher in the case group.

Mean gestational age (38.22 ± 2.30 vs. 38.85 ± 1.49 weeks) was significantly lower in the case group, while the number of cesarean sections (58.6% vs. 29.4%) was significantly higher in the case group.

Data of perinatal outcome in the case group and in the control group are summarized in Table 1. The frequencies of preterm birth and low birth weight were significantly higher in the case group compared to the control group (11.8% vs. 6.9% and 11.2% vs. 5.2%, respectively). The rate of fetal macrosomia was higher in the case group (12.8% vs. 8.6%), although the difference was not significant. A significant difference was found, however, in the number of admissions to NICU (9.4% vs. 5.0%). The frequency of registered congenital malformations (mainly heart defects and urogenital defects) was similar (5.6% vs. 6.9%) in both groups. There was no significant difference in the Apgar score at 5-min <7 (1.1% vs. 0.0%), whereas the frequency of low umbilical cord blood pH (<7.1) was significantly lower in the case group (2.8% vs. 5.9%).

The results of logistic regression analyses are presented in Table 2. Age had a significant effect on various maternal outcomes. The odds of gestational diabetes (OR: 2.74; AOR: 2.81), preeclampsia (OR: 13.53; AOR: 13.05), threatened preterm delivery (OR: 3.15; AOR: 3.62), and cesarean section (OR: 3.40; AOR: 3.31) were significantly higher in older than younger mothers in unadjusted and adjusted models as well. The odds of adverse neonatal outcomes, such as low birth weight (OR: 2.30; AOR: 2.56) and admission to NICU (OR: 1.95; AOR: 2.03), were significantly higher in older vs. younger mothers in both models. The odds of preterm birth (OR: 1.80; AOR: 1.67) and low level of umbilical cord blood pH (OR: 0.46, AOR: 0.70) were significant in the unadjusted models, but these relationships were no longer statistically significant after the adjustment for marital status, smoking status, primigravity, IVF-ET, and attendance of prenatal care. There was no significant effect of maternal age on the frequency of fetal macrosomia and congenital malformations.

TABLE 2. Adverse Maternal and Neonatal Outcomes in Older Mothers vs. Younger Mothers—Logistic Regression Analyses

PARAMETERS	OR (95% CI)	*P*-VALUE	AOR (95% CI)	*P*-VALUE
Maternal outcomes				
Gestational diabetes mellitus	2.74 (1.69–4.44)	<.001	2.81 (1.66–4.76)	<.001
Preeclampsia	13.53 (5.79–31.62)	<.001	13.05 (5.46–31.19)	<.001
Threatened preterm delivery	3.15 (1.32–7.51)	.009	3.62 (1.44–9.10)	.006
Neonatal outcomes				
Low birth weight	2.30 (1.28–4.13)	.005	2.56 (1.34–4.91)	.005
Fetal macrosomia	1.55 (0.95–2.53)	.077	1.54 (0.92–2.60)	.103
Preterm birth	1.80 (1.09–3.00)	.023	1.67 (0.95–2.92)	.072
Congenital malformation	0.81 (0.44–1.46)	.475	0.73 (0.39–1.39)	.342
Umbilical cord blood pH <7.1	0.46 (0.21–0.99)	.046	0.70 (0.31–1.58)	.388
Admission to neonatal intensive care unit	1.95 (1.09–3.48)	.023	2.03 (1.06–3.86)	.032

Note. Logistic regression analyses were used to assess the contribution of maternal age (older vs. younger age-group) to various maternal and neonatal outcomes. Adjustment was performed for marital status, smoking status, primigravity, IVF-ET, attendance of prenatal care.

OR = Odds ratio, CI = Confidence interval, AOR = Adjusted odds ratio.

DISCUSSION

Older gravida is usually described as a pregnant woman over the age of 35 years, but recent studies has regarded the age of 40 years to be the age threshold. It is due to the fact that in many high-income countries the maternal age at childbirth has increased (Kenny et al., 2013). Considering this tendency, which is also present in Hungary, we analysed the data of mothers aged 40 years or over (case group).

In our study, most of the mothers in both groups were married or had a life partner and attended prenatal care regularly. Only some of them smoked during pregnancy.

In the control group, the proportion of mothers who had never been pregnant before or never had a delivery before was significantly higher. The mothers in this group were between ages 25 and 29 years. Women in this age may get married and start a family, accordingly, it was their first pregnancy. In the case group, women were aged 40 years or over and had a longer history of previous pregnancies and deliveries, but there were mothers also who had their first pregnancy or delivery.

Several previous studies have found an association between advanced maternal age and adverse perinatal outcome. Several authors (Karabulut et al., 2013; Kenny et al., 2013; Favilli et al., 2012) have described a higher rate of prematurity in older mothers, and our findings correlate with their statement. Favilli et al. (2012) have also reported higher rate of cesarean section among mothers over 40 years. Our results highlighted the same tendency similarly to the studies of Chan and Lao (2008), Marozio et al. (2017) and Claramonte Nieto et al. (2019). Nonetheless, we did not find higher rate of macrosomia like Schimmel et al. (2014).

Likewise, several studies (Akin et al., 2010; Koshida et al., 2019; Laopaiboon et al., 2014; Zapata-Masias et al., 2016) and our observations also demonstrated that the rate of NICU admission was higher in older mothers.

Our data showed significant difference in the use of IVF-ET. In the case group, the rate of IVF-ET was significantly higher than in the control group. According to Chan et al. [10] older pregnant women have often been nulliparous previously, and they have delayed pregnancy by choice. A significant proportion of these women needed assisted reproductive technology to have their own babies. Salem Yaniv et al. (2011) and Materna-Kiryluk et al. (2011) have revealed that the frequency of congenital malformations is significantly higher in advanced age, but our research did not have the same results.

Our observations are in contrast with the findings of Celik et al. (2017) and Alshami et al. (2011) who have reported no significant difference between advanced maternal age and adverse perinatal outcome.

During the analysis of maternal complications, gestational diabetes was found to be significantly higher among older mothers. The prevalence of gestational diabetes increases with maternal age, and our results were in line with this finding. It might be explained by the impairment of carbohydrate metabolism in older age (Marozio et al., 2017). There was also a significant difference in preeclampsia and threatened preterm delivery. Marozio et al. (2017) suggest that age-related dysfunction of the vascular endothelium can cause preeclampsia in older age.

According to the literature there are some controversies from the point of adverse perinatal outcomes: Increased risk of malformations has been found in case of younger and older mothers. In our previous study (Karai et al., 2019), we analysed the frequency of congenital defects among teenage mothers, and we found significantly higher rate of malformations among teenagers than in the control group. In the present study we supposed that the risk of malformations will be higher in older mothers, too, but the results showed different situation: the incidence of fetal malformations was similar in the case group and in the control group. The risk of chromosomal aberrations is increasing with age, but our study found only one case (one newborn with Down's syndrome) in the older group. Probably the high rate of prenatal care attendance resulted in the low number of malformations. Owing to adequate prenatal care and the availability of cytogenetic and molecular genetic methods, in most cases, severe fetal malformations could be diagnosed. In that case, the mother can choose whether to deliver the fetus with the diagnosed malformation or terminate the pregnancy (the Hungarian law accepts the termination in case of a severe, life-threatening malformation).

The limitations of our study were its retrospective nature and the small sample size both in the case group and the control group. No data were available about the mother's level of education, income, drug intake (folic acid, vitamins, or any other medication), and dietary habits. Smoking status was based on self-assessment. There was no detailed medical follow-up of the neonates transferred to NICU as NICU is located in another department.

CONCLUSION

Our data suggest that older maternal age was significantly associated with maternal complications, higher frequency of using in vitro fertilization-embryo transfer, higher rate of cesarean section, prematurity, increased admission rate to NICU, and lower mean gestational age. We expected significantly higher rate of congenital malformations in the case group, but our results showed that advanced maternal age was not associated with higher rate of birth defects. It may prove that adequate prenatal care and modern genetic diagnostic methods are able to screen congenital anomalies, thereby much fewer neonates are born with severe congenital defects.

In Hungary, infant mortality has decreased in recent years, but among the causes of infant deaths, the rate of congenital malformations is the same (25%). It is a notable number, which should not be ignored. Today, health care providers pay more attention to older mothers because of the risks of advanced age, but our results showed that the early detection of congenital malformations may be important in every age group.

Considering our results, it should be important to inform women about the consequences of delayed childbearing. Older mothers may need more attention during an adequate prenatal care program provided by obstetricians, midwives, and health visitors, and they are recommended to deliver in a regional centre to prevent adverse perinatal outcomes.

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IV.

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Association between sociodemographic, obstetric, and lifestyle factors among Hungarian pregnant women—A cross-sectional study

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Abstract

Aim: To learn the association between sociodemographic and obstetric factors and lifestyle characteristics of pregnant women, and to identify factors that can influence pregnant women's health consciousness.

Methods: A cross-sectional, questionnaire-based study was performed among women who gave birth in Szeged in 2014–2015. Data collection was based on a self-administered questionnaire and health documentations. Overall maternal health promoting behavior (MHPB) index was defined by summarizing the scores obtained from diet, physical activity, smoking status, and alcohol consumption.

Results: The final analysis included 1548 mothers; 41.3% ($n = 602$) of the sample had healthy diet, 9.0% ($n = 134$) were physically active and attended special pregnancy exercise classes, 84.4% ($n = 1279$) did not drink alcohol, and 93.5% ($n = 1447$) were nonsmokers. Regarding the MHPB index, 0.8% ($n = 11$) of the women reached the maximum score (20), while the average was 14.8 (SD = 2.58). Advanced maternal age ($p < 0.001$), having a spouse or partner ($p < 0.001$), higher educational level ($p < 0.001$), planned pregnancy ($p < 0.001$), and early visit at pregnancy care ($p = 0.046$) were significantly associated with higher MHPB index.

Conclusion: The lifestyle of pregnant women can have a great impact on the developing fetus, either in a positive or negative way. In order to evaluate maternal lifestyle, overall health behavior should be considered. Lifestyle of the included women was not satisfactory, an improvement in health consciousness is needed at every social level; however, the differences between the various social classes may suggest the importance of further promotion and improvement of pregnancy planning and pregnancy care among younger and lower educated women.

Key words: health behavior, health literacy, healthy lifestyle, maternal behavior, pregnancy.

Introduction

Promotion of healthy life start is one of the priorities of the World Health Organization's (WHO) Health 2020 policy, and it plays an important role in other WHO programs (e.g., Life Course Approach to Health) as well. They emphasize that promotion of health should start before conception, as maternal lifestyle before and during pregnancy is as important as sociodemographic factors and previous health status

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of the mother. Moreover, there is a strong suggestion that healthy lifestyle and social status of the mother cannot be strictly separated,[1,2] and other factors such as involvement of family members play an important role as well.[3]

Demography is globally changing, and it affects many of the nonmodifiable factors of pregnancy outcome. Maternal age is relevant because besides the fact that the birth rates are globally decreasing, the average maternal age at first child's birth is increasing; actually, in developed countries it is over 30 years of age, and it is gradually growing. In case of age-specific fertility rates, a shift can also be observed: while among the 15–19 and 20–24 age groups, it drops; in groups over 30, it shows an increasing tendency.[4] In Hungary, the situation is the same: in 2018, the average maternal age at first child's birth was 28.8 years, and during the last decades, age-specific fertility rate of women under 30 dropped by 30%, whereas in women over 30, it tripled.[5] Advanced maternal age comes with higher health risks for the fetus and the pregnant woman as well. Lean et al.[6] have investigated the correlation between fetal adverse events and advanced maternal age. Maternal age was significantly associated with stillbirth, fetal growth restriction, infant death, and severe infant health conditions. Sheen et al.[7] have found that advanced maternal age is significantly correlated with more severe maternal complications during delivery. Moreover, maternal education level is also an important nonmodifiable sociodemographic determinant of pregnancy outcome. Lower education may be associated with poorer health literacy and health behavior, which can affect the lifestyle, and therefore the maternal and fetal/newborn health. However, there are studies which have described that more educated women reported inferior lifestyle status compared to women from the general population.[8]

Diet, physical activity, alcohol consumption, and smoking status are the four most important lifestyle factors, which can positively or negatively affect fetal health. The overall effect of maternal diet[9,10] and the effect of specific diets[11,12] during pregnancy have been widely investigated. Gestational diabetes mellitus, hypertension, depressive symptoms during pregnancy, preterm birth, small for gestational age show significant correlation with maternal diet during pregnancy.[9] Besides pregnancy outcomes and fetal health, maternal diet can also affect the child's later health; cognitive functions, development of allergic diseases, and diabetes mellitus can also be correlated with maternal eating patterns.[13,14] Dietary supplementation may be considered in order to achieve higher micronutrient intake levels during pregnancy. Daily folic acid is recommended to prevent neural tube defects.[15] Additionally, daily folic acid and iron supplementation is suggested to prevent low birth weight, maternal anemia, and iron deficiency,[16] and daily calcium intake to lower the risk of preeclampsia.[17] However, recommendations about physical activity during pregnancy are equivocal,[18] though physical activity can prevent excessive gestational weight gain, gestational diabetes mellitus, preeclampsia, and several adverse neonatal outcomes.[19] Smoking during pregnancy can seriously affect the development and future health of the child; it can be the causative agent of growth restriction and congenital disorders,[20] hyperactivity, cognitive dysfunctions,[21] and childhood obesity as well.[22] Alcohol consumption during pregnancy can affect fetal growth,[23] and it is associated with several socioeconomic factors, such as income and educational level; however, the evidence is not clearly stated.[24]

These lifestyle factors have been widely investigated in several studies separately; however, the overall lifestyle and health behavior are often more informative and should be considered together.

The aim of this study was to determine the association between sociodemographic and obstetric factors, and lifestyle characteristics of pregnant women who delivered in Szeged, Hungary; moreover, to identify the factors that can influence pregnant women's health consciousness.

Methods

Study design and participants

A cross-sectional, questionnaire-based study was performed among women delivering at the Department of Obstetrics and Gynecology, University of Szeged in 2014–2015. Participation was offered to each adult (>18 years) woman who delivered her baby at the clinic during the study period. Altogether 1669 women were included into the study, who filled out the questionnaire 1 or 2 days after delivery. Multiple pregnancies were excluded from the present analysis. Finally, due to multiple pregnancies ($n = 49$) and missing data, 1548 mothers were involved into the final analysis.

Study variables

Data collection was based on a self-administered questionnaire and the health documentation of mothers and newborns. The self-administered questionnaire

contained general, sociodemographic, lifestyle, conception, and previous and current pregnancy-related questions. Health documentation comprised the mothers' health characteristics during pregnancy and right after delivery; data about delivery type and complications; and health characteristics of the newborn.

Maternal sociodemographic status included maternal age, education level (three categories: low [primary education or lower, vocational school], medium [secondary education], and high [university] level), type of residence and partnership status (single or in partnership). Additional questions were pregnancy planning, number of previous pregnancies, previous miscarriage, preterm delivery, and congenital disorder. The number of pregnancy week at first pregnancy care attendance was also asked, and three categories were formed: early visit (week 0–12), midterm visit (week 13–28) and late visit (week 29 or later). The self-reported use of folic acid, before and during pregnancy, was also measured.

Lifestyle-related questions included diet, physical activity, smoking, and alcohol consumption. The questionnaire and its evaluation protocol were formulated according national and international recommendations. Healthy diet was considered the most significant lifestyle factor because according to previous studies, it is the most important component of adherence to health.[25] Given that physical activity may be contradicted in case of endangered pregnancies it is weighing less. As smoking and alcohol consumption both have undoubtable consequences on maternal and fetal health, these factors were scored strictly with higher points. Dietary habits of mothers were measured by the frequency of vegetable, fruit, fish, fast food, salty snack, sweets, and soft drink consumption. Physical activity was evaluated by a question asking whether the mother was regularly physically active or not during the current pregnancy, without any specification of the exercise type. Smoking status was divided into two subgroups: smokers and nonsmokers (never smokers and ex-smokers). Alcohol consumption was divided into "no alcohol consumption" and "alcohol consumption during pregnancy" groups. First, maternal diet, physical activity, smoking, and alcohol consumption during pregnancy were expressed in diet, physical activity, alcohol consumption, and smoking scores. The dietary score included vegetable, fruit, fish, fast food, salty snack, sweets, and soft drink consumption. The physical activity score included physical activity during pregnancy and attendance at special pregnancy exercise classes. Smoking and alcohol consumption were categorized as "yes" or "no." The given points of each field and the particular scores could be seen in Table 1. The components of "healthy lifestyle" were defined according to the following: minimum 10 points in diet field were considered "healthy diet"; minimum 2 points in physical activity field, "regular physical activity"; and 3–3 points in smoking and alcohol consumption fields were considered as "non-smoking" and "no alcohol consumption."

In order to assess the overall adherence to healthy lifestyle of the included pregnant women, the maternal health promoting behavior (MHPB) index was formulated. The MHPB index was calculated by summarizing the scores obtained from diet, physical activity, smoking status, and alcohol consumption. The scale ranged between 0 to 20, where 0 means the poorest and 20 the highest level of health promoting behavior. Higher scores mean healthier lifestyle.

Birth weight was examined as fetal outcome in connection with the MHPB scores. Less than 2500 g was considered low birth weight (LBW); 2500–3999 g normal birth weight (NBW); and ≥4000 g high birth weight (HBW).

Statistical analysis

Characteristics of the study population were evaluated by descriptive statistics. The association between the separate components of healthy lifestyle (diet and physical activity) and sociodemographic characteristics and obstetric factors were analyzed with the chi-square test. The Kolmogorov–Smirnov test was used to test the normality of the MHPB score as a continuous variable. Because of non-normality, the association between the MHPB scores and sociodemographic and obstetric characteristics was analyzed by the non-parametric Kruskal–Wallis test. The level of statistical significance was set at $p < 0.05$.

Statistical analysis was performed by using IBM SPSS 26.0 program.

Ethics statement

The study protocol was approved by the Regional and Institutional Review Board of Human Investigation in the University of Szeged, Hungary (number: 3328). Participation was voluntary, and a written informed consent was obtained from each participant of the study.

Results

The sociodemographic and obstetric characteristics of the study population are shown in Table 2. The

TABLE 1 Given points of each lifestyle field of maternal health promoting behavior index

Lifestyle factor	Given points
Dietary habits	
Vegetable consumption	
Daily	2
Weekly	1
Less frequently	0
Fruit consumption	
Daily	2
Weekly	1
Less frequently	0
Fish consumption	
Weekly	1
Less frequently	0
Fast foods	
Monthly or never	1
More frequently	0
Salty snacks	
Monthly or never	2
Weekly	1
Daily	0
Sweets	
Monthly or never	2
Weekly	1
Daily	0
Soft drinks	
Monthly or never	2
Weekly	1
Daily	0
Maximum total diet score	12
Physical activity	
General physical activity	
Yes	1
No	0
Pregnancy exercise	
Yes	1
No	0
Maximum total physical activity score	2
Smoking during pregnancy	
No	3
Yes	0
Maximum total smoking score	3
Alcohol consumption during pregnancy	
No	3
Yes	0
Maximum total alcohol score	3
Maximum overall lifestyle score	20

frequency of the different components of lifestyle is presented in Table 3. Assessing the points of dietary habits, 602 (41.3%) of the included women followed a healthy diet, 134 (9.0%) were physically active and attended special pregnancy exercise classes, 1279 (84.4%) did not drink alcohol, and 1447 (93.5%) did not smoke during the present pregnancy.

The association between the different components of healthy lifestyle and the mothers' characteristics are shown in Table 4. Healthy diet was significantly associated with older age ($p < 0.001$), higher educational level (<0.001), nonsingle partnership status ($p = 0.013$), planned pregnancy ($p = 0.023$), diagnosis of gestational diabetes mellitus (<0.001), negative diagnosis of anemia ($p = 0.049$), and taking folic acid before and during pregnancy ($p = 0.021$ and $p < 0.001$, respectively). Regular physical activity was significantly associated with higher maternal age ($p = 0.001$), higher educational level (<0.001), living in county town (<0.001), planned pregnancy ($p = 0.009$), first pregnancy (<0.001), and folic acid before and during pregnancy ($p < 0.001$ and $p = 0.003$, respectively). Nonsmoking behavior was significantly associated with higher maternal age ($p < 0.001$), higher educational level ($p < 0.001$), nonsingle partnership status ($p < 0.001$), living in nonrural area ($p = 0.040$), planned pregnancy ($p < 0.001$), first pregnancy ($p < 0.001$), diagnosis of high blood pressure ($p = 0.027$), and folic acid intake before and during pregnancy ($p < 0.001$ and $p < 0.001$, respectively). No alcohol consumption was significantly associated with younger maternal age ($p = 0.006$), lower educational level ($p < 0.001$), living in a town or village ($p < 0.001$), earlier presentation at pregnancy care ($p = 0.021$), diagnosis of gestational diabetes mellitus ($p = 0.035$), and no folic-acid intake during pregnancy ($p = 0.020$). Our results show that planned pregnancy had a positive impact on all four investigated fields; however, early visit at pregnancy care had no effect on maternal health behavior. More conscious dietary habits were observed in case of gestational diabetes; however, those who had high blood pressure or anemia tended to follow a more unhealthy diet. Mothers who obtained a high dietary score were more likely to consume folic acid; moreover, pregnancy vitamin and folic acid consumption were associated with physical activity and nonsmoking behavior as well.

Figure 1 shows the distribution of overall MHPB index: 11 (0.8%) women reached the maximum score, while the average result was 14.8 (SD = 2.58), and the median was 15.00.[4–20] A threshold can be established at 15 points: at and above 15 points there is no need for intervention, the maintenance of good lifestyle habits should be strengthened; below 15 points the adherence to healthy lifestyle is poor, information and further education of the mother is needed. Additionally, 0 points in any lifestyle field (i.e., dietary habits, physical activity, smoking, alcohol consumption)

TABLE 2 Main characteristics of study population

Characteristics	*n*	%
Sociodemographic characteristics		
Age group (years)		
−24	147	9.5
25–34	949	61.3
35–	452	29.2
Educational level		
Low	273	17.7
Medium	506	32.8
High	763	49.5
Partnership status		
Single	147	10.3
In partnership	1286	89.7
Residence		
County town	920	60.0
Town	270	17.6
Village	343	22.4
Obstetric characteristics		
Planned pregnancy		
Yes	1306	84.6
No	237	15.4
First pregnancy		
Yes	751	48.7
No	791	51.3
Presence at pregnancy care		
Early (0–12)	1379	91.3
Midterm (13–28)	126	8.4
Late (29–)	5	0.3
Previous miscarriage		
Yes	278	18.1
No	1262	81.9
Previous preterm delivery		
Yes	62	8.1
No	708	91.9
Previous congenital disorder		
Yes	29	3.8
No	740	96.2
High blood pressure		
Yes	118	7.6
No	1430	92.4
Gestational diabetes mellitus		
Yes	156	10.1
No	1392	89.9
Anemia		
Yes	228	14.7
No	1320	85.3
Folic acid before pregnancy		
Yes	519	34.1
No	1004	65.9
Folic acid during pregnancy		
Yes	1047	70.4
No	440	29.6

should be considered as a critical situation, and smoking or alcohol consumption should not be ignored even if the overall score is above 15 points.

TABLE 3 Frequency of obtained lifestyle scores among study population

Lifestyle factor	*n*	%
Vegetable consumption		
Daily	955	63.8
Weekly	472	31.5
Less frequently	71	4.7
Fruit consumption		
Daily	1178	78.5
Weekly	293	19.5
Less frequently	29	1.9
Fish consumption		
Weekly	584	39.2
Less frequently	905	60.8
Fast foods		
Monthly or never	1270	84.8
More frequently	228	15.2
Salty snacks		
Monthly or never	1067	71.7
Weekly	360	24.2
Daily	61	4.1
Sweets		
Monthly or never	296	19.7
Weekly	815	54.3
Daily	390	26.0
Soft drinks		
Monthly or never	993	66.7
Weekly	387	26.0
Daily	109	7.3
Physical activity		
Yes	755	50.5
No	741	49.5
Pregnancy exercise		
Yes	174	11.4
No	1349	88.6
Smoking during pregnancy		
No	1447	93.5
Yes	101	6.5
Alcohol consumption during pregnancy		
No	1279	84.4
Yes	236	15.6

Table 5 presents the association between the overall MHPB scores and maternal characteristics. Advanced maternal age ($p < 0.001$), nonsingle partnership status ($p < 0.001$), higher educational level ($p < 0.001$), planned pregnancy ($p < 0.001$), and early visit at pregnancy care ($p = 0.046$) were significantly associated with higher MHPB index. Type of residence, first pregnancy, previous miscarriage, preterm delivery, or congenital diseases were not associated with the health promoting behavior of pregnant women.

Maternal high blood pressure during pregnancy was not associated with the overall lifestyle score; however, a strong correlation was found between

TABLE 4 Association between the separate field of health behavior and population characteristics (chi-square test)

Characteristics	Healthy diet		Regular physical activity		Nonsmoking		No alcohol consumption	
	n (%)	*p*	*n* (%)	*p*	*n* (%)	*p*	*n* (%)	*p*
Sociodemographic characteristics								
Age group		**<0.001**		**0.001**		**<0.001**		**0.006**
−24	27 (20.6)		2 (1.4)		121 (82.3)		132 (93.6)	
25–34	364 (40.6)		99 (10.9)		893 (94.1)		775 (83.2)	
35–	211 (49.0)		33 (7.7)		433 (95.8)		372 (84.2)	
Educational level		**<0.001**		**<0.001**		**<0.001**		**<0.001**
Low	50 (21.7)		3 (1.2)		209 (76.6)		239 (92.6)	
Medium	178 (37.2)		25 (5.2)		473 (93.5)		430 (86.7)	
High	374 (50.1)		106 (14.2)		759 (99.5)		605 (80.1)	
Partnership status		**0.013**		0.067		**<0.001**		0.414
Single	47 (31.8)		8 (5.1)		137 (82.5)		142 (86.6)	
In partnership	555 (42.4)		126 (9.5)		1309 (94.9)		1135 (84.1)	
Residence		0.125		**<0.001**		**0.040**		**<0.001**
County town	374 (42.7)		107 (12.0)		866 (94.1)		732 (81.3)	
Town	107 (41.8)		15 (5.8)		257 (95.2)		237 (89.1)	
Village	114 (36.2)		11 (3.5)		311 (90.7)		300 (89.6)	
Obstetric characteristics								
Planned pregnancy		**0.023**		**0.009**		**<0.001**		0.964
Yes	527 (42.5)		124 (9.9)		1245 (95.3)		1082 (84.5)	
No	74 (34.3)		10 (4.4)		197 (83.1)		194 (84.3)	
First pregnancy		0.297		**<0.001**		**0.034**		0.519
Yes	283 (39.9)		100 (13.8)		713 (94.9)		626 (85.1)	
No	317 (42.6)		34 (4.5)		730 (92.3)		649 (83.9)	
Presence at pregnancy care		0.230		0.644		0.163		**0.021**
Early (0–12)	544 (41.7)		120 (9.1)		1294 (93.8)		1133 (84.0)	
Midterm (13–28)	47 (40.2)		13 (10.7)		113 (89.7)		113 (91.9)	
Late (28–)	0 (0.0)		0 (0.0)		5 (100)		3 (60.0)	
Previous miscarriage		0.051		0.813		0.123		0.871
Yes	123 (46.6)		23 (8.6)		254 (91.4)		232 (84.7)	
No	476 (40.1)		110 (9.1)		1185 (93.9)		1040 (84.3)	
Previous preterm delivery		0.498		0.672		0.715		0.731
Yes	25 (47.2)		2 (3.4)		56 (90.3)		52 (85.2)	
No	284 (42.4)		31 (4.6)		649 (91.7)		579 (83.5)	
Previous congenital disorder		0.824		0.244		0.688		0.066
Yes	11 (40.7)		0 (0)		26 (89.7)		27 (96.4)	
No	299 (42.9)		34 (4.8)		679 (91.8)		605 (83.4)	
High blood pressure		0.107		0.334		**0.027**		0.060
Yes	37 (33.9)		7 (6.5)		116 (98.3)		105 (90.5)	
No	565 (41.9)		127 (9.2)		1331 (93.1)		1174 (83.9)	
Gestational diabetes mellitus		**<0.001**		0.898		0.687		**0.035**
Yes	100 (67.1)		14 (9.3)		147 (94.2)		139 (90.3)	
No	502 (38.3)		120 (9.0)		1300 (93.4)		1140 (83.8)	
Anemia		**0.049**		0.063		0.404		0.106
Yes	76 (35.2)		27 (12.4)		216 (94.7)		181 (80.8)	
No	526 (42.3)		107 (8.5)		1231 (93.3)		1098 (85.1)	
Folic acid before pregnancy		**0.021**		**<0.001**		**<0.001**		0.553
Yes	226 (45.5)		64 (12.9)		505 (97.3)		427 (83.9)	
No	370 (39.2)		67 (6.9)		919 (91.5)		836 (84.5)	
Folic acid during pregnancy		**<0.001**		**0.003**		**<0.001**		**0.020**
Yes	451 (44.5)		108 (10.7)		1005 (96.0)		854 (82.6)	
No	139 (34.4)		24 (5.6)		390 (88.6)		377 (87.5)	

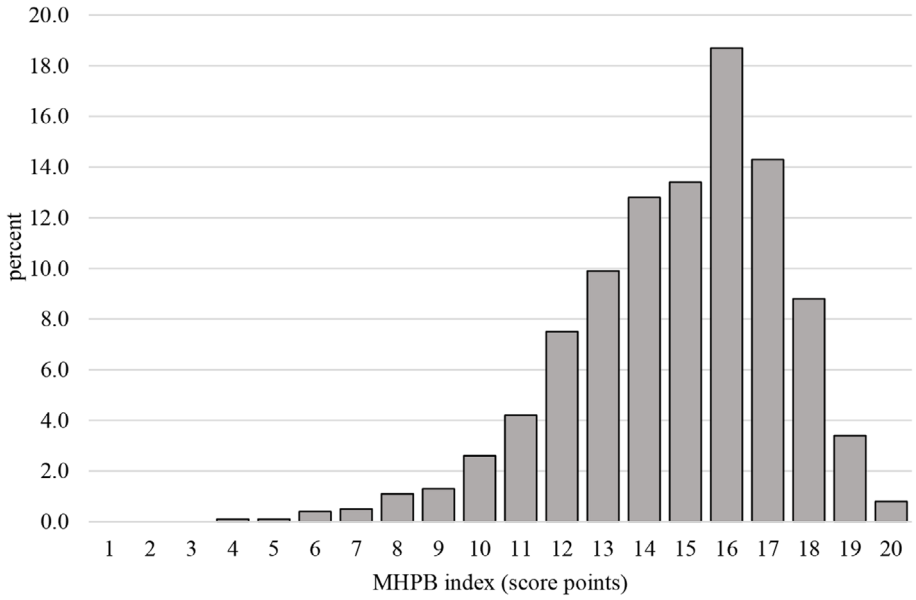

FIGURE 1 Maternal health promoting behavior (MHPB) index distribution ($N = 1391$). Obtained MHPB scores are shown on the horizontal axis, and the ratio (%) of pregnant women who obtained the certain scores are indicated on the vertical axis.

MHPB index and gestational diabetes mellitus ($p < 0.001$). Higher MHPB points were associated with gestational diabetes mellitus, which may be explained with the more conscious health behavior of diagnosed mothers. Anemia during pregnancy was also correlated with MHPB points: higher scores were associated with a negative diagnosis of anemia ($p = 0.036$); however, no other correlation was found between maternal disease burden and MHPB scores.

Folic acid intake before and during pregnancy was strongly correlated with the MHPB index: mothers who took some kind of folic acid before or during pregnancy reached significantly higher overall MHPB points ($p < 0.001$ and $p < 0.001$, respectively).

A significant correlation was found between birth weight of the newborn and the obtained maternal MHPB scores ($p = 0.003$). Significantly higher scores were obtained in women delivering a newborn with NBW compared to mothers who delivered LBW babies ($p = 0.006$). However, no significant correlation was found in case of HBW. The average MHPB score was 13.855 for LBW, 14.881 for NBW, and 14.580 for HBW.

Figure 2 demonstrates the associations among the investigated variables and MHPB index, implying that educational level and age group were proved to be the factors associated with the majority of the investigated variables considering sociodemographic characteristics. Furthermore, folic acid intake during pregnancy related to the group of obstetric characteristics.

Discussion

The aim of the study was to identify the socioeconomic and obstetric factors that can influence pregnant women's lifestyle (diet, physical activity, smoking, and alcohol consumption). Our results showed that maternal age, educational level, place of residence as sociodemographic factors, and planning of pregnancy and the use of folic acid as obstetric factors were significantly associated with healthier lifestyle components. Additionally, the answers were quantified by the MHPB index as the complex analysis of different lifestyle components. The overall MHPB index was strongly correlated with advanced maternal age, higher educational level, and planned pregnancy.

Our results are in line with previous studies that have suggested that maternal dietary behavior would be strongly connected with the socioeconomic status. Nonmodifiable factors not only directly, but also indirectly can affect maternal and fetal health via effects on maternal health consciousness and literacy. Jardí et al.[26] have investigated the adherence to Mediterranean diet of pregnant women, whereas Wesolowska et al.[27] have examined the correlation between educational and socioeconomic status of women, and quality of diet during pregnancy. Their results are similar to ours, according to which a healthier diet was observed in case of higher educational level, higher social status, and advanced maternal age. However,

TABLE 5 Overall MHPB scores and maternal characteristics (Kruskal–Wallis nonparametric test)

Characteristics	MHPB score			*p*-Value
	Mean (SD)	Minimum	Maximum	
Sociodemographic characteristics				
Age group (years)				**<0.001**
–24	13.38 (2.98)	5	20	
25–34	14.83 (2.57)	4	20	
35–	15.21 (2.31)	7	20	
Educational level				**<0.001**
Low	13.18 (3.13)	4	19	
Medium	14.58 (2.51)	6	20	
High	15.42 (2.20)	8	20	
Partnership status				**<0.001**
Single	13.86 (3.12)	5	20	
In partnership	14.91 (2.49)	4	20	
Residence				0.441
County town	14.87 (2.61)	5	20	
Town	14.78 (2.55)	4	20	
Village	14.66 (2.49)	7	20	
Obstetric characteristics				
Planned pregnancy				**<0.001**
Yes	14.96 (2.497)	4	20	
No	13.92 (2.90)	5	20	
First pregnancy				0.096
Yes	14.90 (2.65)	5	20	
No	14.71 (2.52)	4	20	
Presence at pregnancy care				**0.046**
Early (0–12)	14.84 (2.54)	4	20	
Midterm (13–28)	14.73 (2.96)	7	20	
Late (29–)	11.75 (1.50)	10	13	
Previous miscarriage				0.249
Yes	14.92 (2.64)	5	20	
No	14.77 (2.58)	4	20	
Previous preterm delivery				0.666
Yes	14.70 (2.56)	4	20	
No	14.596 (2.38)	8	19	
Previous congenital disorder				0.427
Yes	15.04 (2.68)	7	19	
No	14.70 (2.54)	4	20	
High blood pressure				0.877
Yes	14.94 (2.06)	10	19	
No	14.79 (2.62)	4	20	
Gestational diabetes mellitus				**<0.001**
Yes	16.13 (2.25)	6	20	
No	14.66 (2.58)	4	20	
Anemia				**0.036**
Yes	14.51 (2.64)	6	20	
No	14.86 (2.57)	4	20	
Folic acid before pregnancy				**<0.001**
Yes	15.23 (2.38)	7	20	
No	14.62 (2.63)	4	20	
Folic acid during pregnancy				**<0.001**
Yes	15.06 (2.45)	6	20	
No	14.24 (2.77)	4	20	

Abbreviation: MHPB, maternal health promoting behavior.

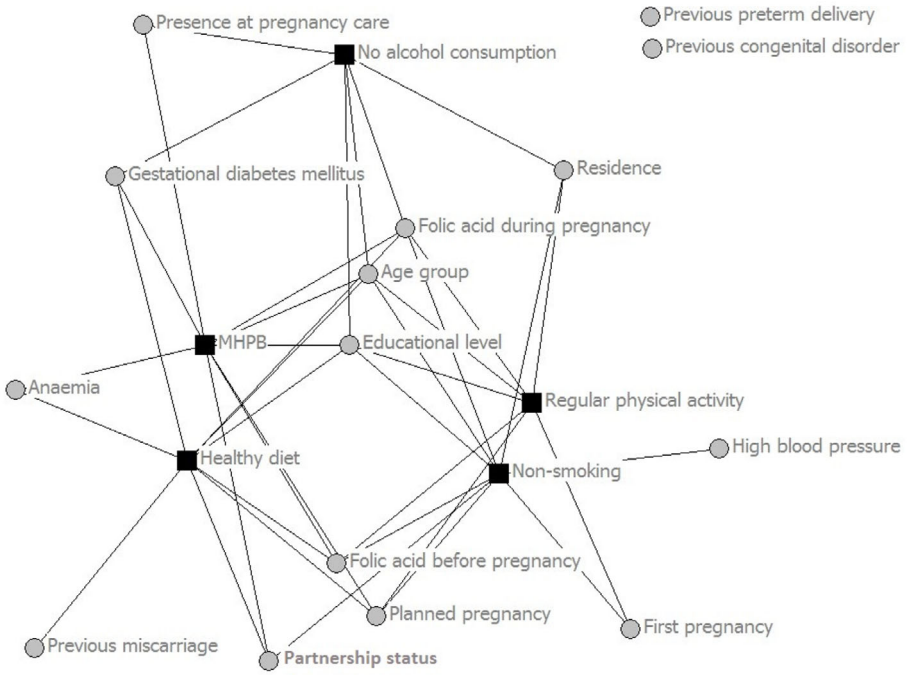

FIGURE 2 Associations among the investigated variables and maternal health promoting behavior (MHPB) index. The figure maps the pattern of relations among the variables investigated in the paper in order to offer a summarizing overview. Squares show the lifestyle factors used for forming the MHPB index, and circles show the analyzed characteristics. The position of the variables illustrates the number of connections: the elements displayed in the central part of the structure have more relations with other indices. Accordingly, it can be said in this sense, that some sociodemographic characteristics (education level, age-group) and folic acid during pregnancy prove to be variables correlated with multiple other indices. In contrast, the factors of previous preterm delivery and previous congenital disorder are not related to any of the indices.

maternal advanced age means a higher health risk; some investigations suggest that advanced age is associated with higher health literacy level, and more health-conscious lifestyle and behavior. Advanced age women tend to consume less unhealthy snacks and drinks during pregnancy compared with younger mothers.[28] Nonetheless, compulsory genetic pregnancy screenings over 35 years can also lower the health risks.[29] Our results show that advanced maternal age is associated with the examined lifestyle fields, except for alcohol consumption during pregnancy. Mothers 25–34 years of age with higher educational level, in nonsingle partnership, living in county towns showed more frequent physical activity. The overall lifestyle score was also in connection with advanced maternal age and higher educational level. According to Barrett and Wellings,[30] pregnancy planning plays a crucial role in the health behavior of the mother. The primary scope of the MHPB index was not to measure the risk, but the adherence to healthy lifestyle, which is well reflected in the index, as it shows the classical correlations with age, education and marital status. The index was formulated by considering the most important lifestyle factors during pregnancy. The questions were composed by professionals, using recent evidences of lifestyle medicine, therefore the face validity of MHPB index is suggested. Additionally, significant correlation was found assessing the connection between the separate lifestyle factors (i.e., healthy diet, physical activity, nonsmoking, no alcohol consumption) and the overall index. Considering obstetric factors, planned pregnancy may contribute to a more conscious lifestyle during the preconception and childbearing period, therefore improving maternal and fetal health status. Planned pregnancy was associated with healthy diet, regular physical activity, nonsmoking behavior, and higher MHPB overall scores.

The lifestyle of mothers during pregnancy can strongly determine both their health and their infant's

health. Not only healthy diet, but physical activity is also an important component of the definition of healthy lifestyle. However, during pregnancy, it should be considered with limitations because of the contradicting evidence, and considering pregnancy as a specific health condition. Besides healthy diet and physical activity, abstaining from smoking and alcohol consumption is also an important criterion of appropriate health behavior, not only for a pregnant woman. From the point of prevention, the fulfillment of the four health behavior components is the best solution.

This study had some limitations. The participation in the study was offered to all eligible women, but the final decision about the enrolment was given by the participants. The lifestyle characteristics during pregnancy were collected after the delivery. The retrospective and self-administered questionnaire-based form of the study could influence the answers; this bias can originate from the selective memory, or it is possible that respondents reported more positive behaviors during pregnancy because of social expectations/prejudice. Although the study was run in a single institution, this institute has a regional responsibility, which increases the generalizability of our results. Data were obtained in 2014 and 2015, therefore it would not completely represent the present situation; however, the examined variables were mostly variables, which does not show significant changes at population level over the course of few years. Additionally, there were no central or local healthy lifestyle promoting programs implemented for pregnant women, which could radically change the adherence to healthy lifestyle.

Despite these limitations, the study provides a complex analysis on the behavior of pregnant women in Hungary.

In conclusion, our study revealed that the lifestyle of the included women was not satisfactory, and an improvement in health consciousness is needed in every social level. Nonetheless, the differences between the various social classes may suggest the importance and further promotion and improvement of pregnancy planning and pregnancy care among younger and lower educated women. Dietary and physical activity recommendations should be improved in case of younger and lower educated mothers. Precise suggestions are needed for the quality, quantity, and frequency of recommended food, preferably considering the preferences of the mother. Exact suggestions are needed for physical activity as well, considering the capability and possible health consequences of the pregnant woman. Professional consulting regarding healthy lifestyle should be incorporated into the regular pregnancy care sessions by giving precise information about the recommended lifestyle changes. Locally organized pregnancy exercise classes, within the pregnancy care sessions, would help mothers prepare their body for childbirth. Listing the possible positive and negative effects of the lifestyle factors is also needed in order to improve adherence to healthy lifestyle.

The introduced MHPB index and the formulated short questionnaire could be used as a simple measuring tool to assess the overall adherence to healthy lifestyle of pregnant women, as it only needs to answer a few, lifestyle-based questions. However, further studies are needed in order to establish the everyday use of MHPB index.

Author contributions

Evelin Polanek: conceptualization, analysis and interpretation of data, writing original draft; Adrienn Karai: interpretation of data, writing original draft; Regina Molnár: conceptualization, methodology; Gábor Németh: supervision, writing review and editing; Hajnalka Orvos: conceptualization, investigation; Péter Balogh: statistical analysis; Edit Paulik: conceptualization, investigation, writing review and editing. All authors have read and agreed to the published version of the manuscript.

Conflict of interest

The authors have no conflict of interest to declare.

Data availability statement

The data that support the findings of this study are available from the corresponding author upon reasonable request.

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