Archives of Gynecology and Obstetrics (2019) 300:1591–1600
https://doi.org/10.1007/s00404-019-05361-z

The impact of neuropsychiatric disease on fetal growth: a case–control study

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Received: 13 June 2019 / Accepted: 25 October 2019 / Published online: 6 November 2019

Abstract

Purpose To determine the impact of depression, epilepsy and drug abuse during pregnancy on delivery and fetal outcome. Due to the worldwide increasing prevalence of neurological and psychiatric diseases and drug abuse, the number of affected pregnant women is increasing.

Methods A large-scale retrospective case–control analysis of pregnancies affected by depression, epilepsy or drug abuse with and without medication was conducted in two German perinatal centres between 2013 and 2017. The case group consisted of 706 pregnant women who had a diagnosis of depression, epilepsy or drug abuse vs. 12,574 pregnant women without neuropsychiatric diagnosis (control group). The analysis included the rate of intrauterine growth restriction, birth weight and length, neonatal head circumference.

Results Significant differences in the subgroups were found in the parameters intrauterine growth restriction, birth weight, length and head circumference. Women with epilepsy were affected less often than women with depression and substance abuse. Major differences were found in the group of women with substance abuse. Negative associations were found within the non-pharmacologically managed disease group itself compared to women exposed to medication.

Conclusion The present results demonstrated a negative association between maternal neurological or psychiatric disease and pregnancy outcome in the examined parameters. However, the non-pharmacologically treated maternal disease was identified as a risk factor itself.

Keywords Germany · Case–control study · Neuropsychiatric disease · Pregnancy outcome · Perinatal outcome · Birth parameters

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Introduction

The prevalence of neurological and psychiatric disease in the general population increases constantly. A longitudinal study from China showed that the prevalence of major depression, alcohol abuse and alcohol dependence as well as the suicide incidents increased significantly over the study period of 3 decades [1]. Yin et al. detected a lifetime prevalence of 23.6% for mental disorders. Especially mood disorders, anxiety disorders and substance abuse had the highest prevalence within the cohort [2].

As a result, the number of women in reproductive age affected by neurological or psychiatric disease increases constantly. Different studies from North America and Australia identified that up to 24.5% of the children are born to mothers with a mental health disorder such as depression [3, 4]. The prevalence of depression in third trimester pregnancies is up to 73.5% in Brazil [5].

Studies about substance abuse and drug consumption showed that 50% of women in reproductive age consume alcohol regularly, 20% consume tobacco products and 13% indicated the use of other drugs [6]. The prevalence of opioid abuse within pregnant women increased by 127% during the years 1998 and 2011 up to 0.39% in the USA [7]. The prevalence of neurological diseases like epilepsy is relevant as well when looking at the prevalence in pregnant women. Preliminary investigations showed that in the USA 5–7 per 1000 deliveries happened to woman affected by epilepsy which results in a frequency of 0.5–0.7% [8]. Data from central Germany, evaluated from our working group combined the different neuropsychiatric diseases and identified the prevalence for depression in pregnant women with 3.5%, for women with substance abuse with 0.7% and for epilepsy with 0.8% [9].

This leads to an increasing relevance for perinatal medicine and obstetrics. Maternal disease on medication as well as the untreated one implicate risk factors for maternal and fetal outcomes as studies have shown [10]. While a disease-specific medication and substance abuse increase the risk for small for gestational age (SGA), caesarean section, congenital malformations and intrauterine growth retardation (IUGR) [7, 11, 12] the increasing number of pharmaceuticals and their prescriptions in pregnancy increase the need for expert advice [13, 14]. Also the non-pharmacologically treated maternal neuro psychiatric disease is a risk factor for SGA, IUGR and prematurity as study results have shown [15–19].

It is known that parameters describing the neonatal growth like head circumference and gestational age are predictors for the newborn's welfare and their future development [20, 21].

Due to the worldwide increasing trend, we undertook the present study in central Germany to determine the impact of depression, epilepsy and drug abuse during pregnancy on fetal growth.

The second aim of the study was to assess the rate of pregnancies exposed to neuropsychiatric diseases with pharmacological or non-pharmacological treatment. In our study the different diagnoses have been validated and classified unlike published register studies.

Materials and methods

In a retrospective cohort study, including data from two 'level 1' maternity departments (MD) in Saxony-Anhalt, Germany, women diagnosed with a neurological or psychiatric disease or illicit drug abuse were identified under all pregnant women delivered between 01.01.2013–31.03.2017. We manually and electronically evaluated routine clinical hospital data of pregnant women. The diagnosis was validated by neurological and psychiatric experts and in case of substance abuse based on the woman self-report and urine drug screening. Therefore, all pregnant women with a validated neuropsychatric disease were included and classified by ICD10 German Modification (GM) version 2017 [22]. For maternity department 1 (MD1) this resulted in a case number of 604 women defined as case group compared to a number of 7590 women without neuropsychiatric disease defined as control group. For maternity department 2 (MD2) we evaluated 178 women for the case group and 4984 women for the control group. Twin pregnancies were excluded from the study cohort.

Information on pregnancy, intrauterine growth retardation (IUGR) and the fetal growth was obtained from labor documentation program (Nexus, PDM, Version 6.3.3.1), and was provided in pseudonymous form for further processing in Microsoft Excel 2010.

After scanning the files and giving a characteristic ID number to the cases, the case group were classified in subcategories by the frequency of the three most assigned diagnoses (depression, substance abuse and epilepsy). Furthermore, a disease-specific medication in pregnancy was detected to differentiate whether the primary disease was treated pharmacologically or not. Cases with other neurological or psychiatric diseases were excluded from the case group as well as from the control group (MD1: $n=39$, MD2: $n=37$). This resulted in a final number of 565 women in the case group and 7590 women in the control group for MD1, and 141 women in the case group and 4984 women in the control group for MD2 (Fig. 1).

Statistical analysis was conducted using SPSS Version 24 (IBM SPSS Statistics). As a graphical check of the three endpoints body weight, body length, and head circumference

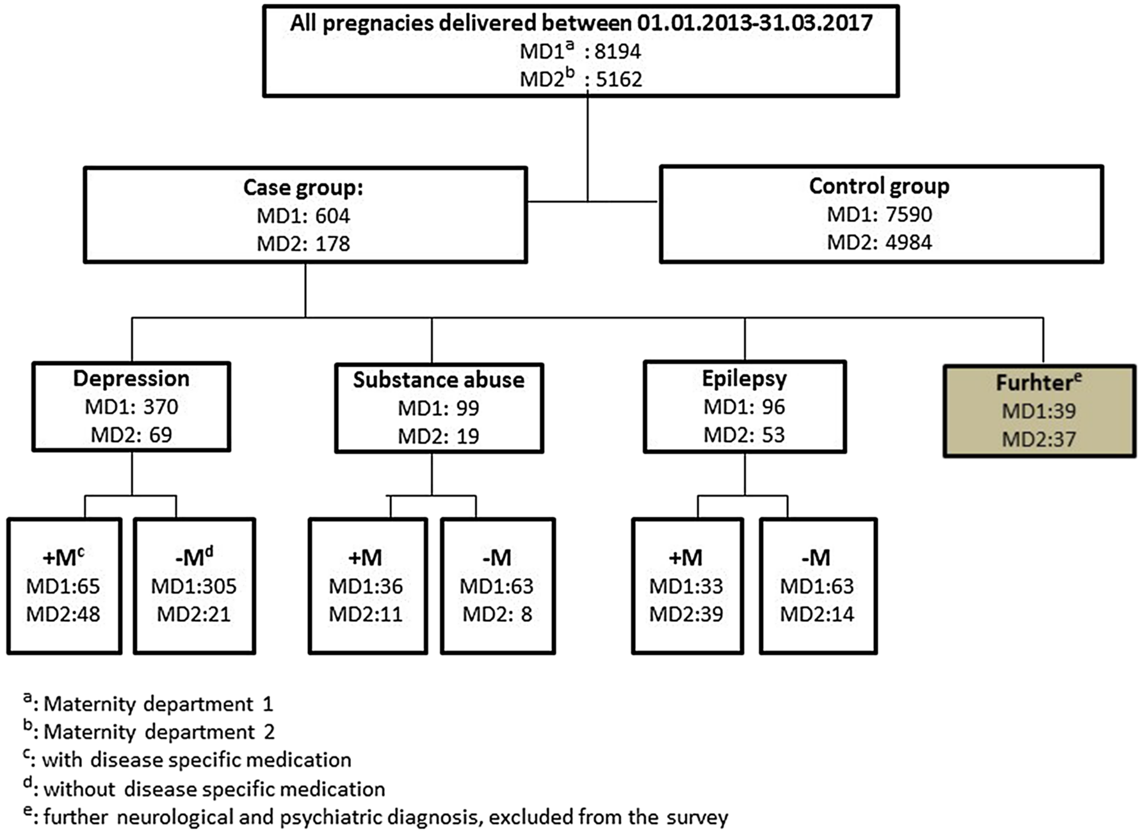

Fig. 1 Overview of the study cohort (all singletons born in the study period January 2013 to March 2017, case group and control group)

showed approximate normal distributions, mean and standard deviation were used for descriptive statistics. Originally, it was planned to analyse both maternal departments in a common ANCOVA model with department as one of the factors. Preliminary analyses showed, however, significant differences between the control groups of both departments with respect to important characteristics of mothers (e.g., age, body length and BMI before pregnancy, smoking), to parameters in relation to delivery (e.g., mode of delivery, length of stay in department, gestational age), and fetal outcome (e.g., APGAR 1, APGAR 5, body weight and head circumference) in respective Chi-squared tests and Mann–Whitney *U* tests. Therefore, we decided to analyse both departments separately, thus also giving hints to the variability between departments.

We did not perform a formal sample size calculation in this retrospective trial. Instead, we intended a complete inclusion of all births in the two departments over the study period (which was chosen because of a constant mode of coding over this time). Though department 2 with the smaller sample sizes (particular in the case groups) has lower power in the statistical tests, one can at least check for similar trends in the outcome. Given the observed rates and standard deviations in the control group, the given sample sizes allow to detect differences between the control group and the case group (as a whole) with a power of 80% in respective two-sided tests at an error level of 5% if the rate of intrauterine growth retardation differs by more than about 2% in MD 1 (and about 4% in MD 2) and the three metrical outcome variables differ by more than 55 g body weight, 0.28 cm body length, and 0.17 cm head circumference in MD 1 (100 g, 0.51 cm, and 0.30 cm in MD 2).

For the main analyses, we excluded multiple birth cases (because of risk for adverse pregnancy outcome in general). Furthermore, only births were included in the analyses for the metrical outcome variables if actual date of birth was less than 30 days before and less than 10 days after the planned date of birth.

The effect of the diseases and their specific medication on the three continuous was tested in a general linear model (ANCOVA) with the respective outcome as dependent variable, disease group, smoking habits of mother (yes/no) and fetal gender as categorical factors and gestational age as covariable. The disease groups were considered in three hierarchical levels: (1) case vs. control (2) depression, substance abuse and epilepsy vs. control group, and (3) the latter case groups further subdivided by special medication (yes/no). As test decisions we used the pairwise comparisons of the respective disease groups vs. the control group. Here we reported the unadjusted p values (test version LSD) together with marks for unadjusted significance (*) or for Bonferroni-corrected significance (**) at the error level of 5% (Bonferroni-factor 3 for the main disease groups and 6 for the combination with medication). The rate of intrauterine growth retardation was compared in a similar fashion in a generalized linear model for binary outcome (corresponding to logistic regression) with the same specification of disease groups and corresponding pairwise comparisons. Here, only smoking of mothers (yes/no) was included as additional factor. Ethical approval was obtained from the institutional Ethics Committee of the Medical Faculty of the Otto-von-Guericke University Magdeburg, Germany.

Results

565 pregnant women, excluding those with twin pregnancies, with a neuropsychiatric disease were identified as case group (6.9%) in MD1. The three most frequently assigned diagnoses were depression ($n=370$, 65.5%), drug abuse ($n=99$, 17.5%) and epilepsy ($n=96$, 17.0%) (Fig. 1).

65 women in the depression group were treated with antidepressants (17.6%), while 305 did not get any antidepressant medication during pregnancy (82.4%). 36 women in the drug abuse group were part of a substitution program (36.4%), while 63 women who were not part of a program declared the use of illegal substances and were tested positive by urine screening (63.6%). In the group of women affected by epilepsy, 33 had an anticonvulsive medication (34.4%), while 63 did not get anticonvulsants (65.6%). These pregnancies were compared to 7590 women without a neuropsychiatric disease referred as the control group (92.6%).

The analysis of data from MD2 resulted in a case number of 141 women with neuropsychiatric disease (2.7%) (Fig. 1). Depression ($n=69$, 48.9% not all results did show statistical significance), drug abuse ($n=19$, 13.5%) and epilepsy ($n=53$, 37.6%) were the three most assigned diagnoses. In the depression group 48 had an antidepressant medication (69.6%) while 21 did not take antidepressants during pregnancy (30.4%). From 19 drug abusing women of the case group 11 were part of a substitution program (57.9%). Eight pregnant women who were not part of a program declared the use of illegal substances and were tested positive by urine screening (42.1%). In the epilepsy group 39 pregnant women had an anticonvulsive medication (73.6%) and 14 did not take antiepileptic medication during pregnancy (26.4%).

Intrauterine growth retardation

The prevalence of IUGR in the case group was 4.3% in MD1 and 2.7% in MD2 (Table 1). While the control group MD1 with a rate of 2.6% had lower rate of IUGR than the control group, the control group MD2 with a rate of 2.8% had a similarly high rate of IUGR than the case group. After adjustment for maternal nicotine consumption the differences between case and control group were not statistically significant for both maternity departments (MD1: $p=0.071$, MD2: 0.832).

Table 1 Intrauterine growth retardation (IUGR) classified by control group, case group and subgroups, according to pharmacological treatment

	Maternity department 1		Maternity department 2	
	Study cohort (n)/ proportion (%)	p value[c]	Study cohort (n)/ proportion (%)	p value
Control group	194/2.6		137/2.8	
Case group	24/4.4	0.071	5/2.7	0.832
Depression	11/3.0	0.871	0/0	< 0.001**
Depression + M[a]	0/0	< 0.001**	0/0	< 0.001**
Depression − M[b]	11/3.6	0.497	0/0	< 0.001**
Substance abuse	10/10.1	0.043*	3/15.8	0.189
Substance abuse + M	0/0	< 0.001**	1/9.1	0.546
Substance abuse −M	10/15.9	0.011*	2/25	0.227
Epilepsy	3/3.1	0.666	2/3.8	0.737
Epilepsy + M	0/0	< 0.001**	2/5.1	0.549
Epilepsy −M	3/4.8	0.362	0/0	< 0.001**

*Significant without Bonferroni correction

**Significant with Bonferroni correction

[a]With disease-specific medication (+ M)

[b]Without disease-specific medication (− M)

[c]Compared to the control group, $p < 0.05$ was considered significant

[d]Test adjusted for smoking

In both maternity departments the highest rate for IUGR was within the group of drug abuse (MD1: 10.1%, $p=0.043$, MD2: 15.8, $p=0.189$). Especially those without substitution treatment were affected (MD1: 15.9%, $p=0.011$, MD2: 25%, $p=0.227$). The data showed significant difference for the case group of MD1. Women from MD1 being part of a substitution program had lower rate of IUGR than the control group (0%, $p= <0.001$). Substituted women from MD2 had lower rate of IUGR than the non-substituted ones but higher rates than the control group (9.1%, $p=0.546$).

Within the group of women affected by depression the rates of IUGR were the lowest (MD1: 3.0%, $p=0.871$, MD2: 0%, $p<0.001$). Only women from MD1 without antidepressant medication showed cases of IUGR but not statistically significant compared to the control group (3.6%, $p=0.497$). None of the women who took antidepressants from MD1 (0%, $p<0.001$) and none of the depression group from MD2 had verified cases of IUGR (0%, $p<0.001$).

Women in the epilepsy group (MD1 + MD2) showed a less frequent rate of IUGR than the ones with substance abuse but higher rates than depression group (MD1: 3.1%, $p=0.666$, MD2: 3.8%, $p=0.737$). While in MD1 the without specific medication had higher rates of IUGR (4.8%, $p=0.362$), epilepsy group in MD2 those with antiepileptic medication had higher rates (5.1%, $p=0.549$).

Birth weight

The newborns in MD1 had an average birth weight of 3265.6 g, while the newborns of the control group weighed 3383.2 g (Table 2, Fig. 2). After adjusting these parameters for gestational age, maternal nicotine consumption and gender of the babies the statistical analysis revealed a significant difference between cases and controls ($p=0.002$). The data from MD2 showed that the infants of the case group (3304.9 g) weighed less than the control group (3399.7 g) but not statistically significant ($p=0.460$). Infants MD2 weighed more compared to infants MD1 (Table 2). More detailed analysis showed that in both departments (MD1 + MD2) neonates from the drug abuse group were the ones with the lowest birth weight (MD1: 3046.6, $p<0.001$, MD2: 3036.4, $p=0.027$). In MD1 depression group, without disease-specific medication (-M) the neonates were the ones with the highest birth weight (3336.5 g, $p=0.306$). In MD2 epilepsy group, with disease-specific medication the neonates were the ones with the highest birth weight (3472.9 g, $p=0.089$).

Birth length

In addition, the analysis showed that in both clinics the newborn's length was lower in the case group (MD1: 50.6 cm, MD2: 50.8 cm) than in the control group (MD1: 51.3 cm, MD2: 51.2 cm) (Table 2, Fig. 3). The difference was significant for MD1 ($p<0.001$) but not for MD2 ($p=0.253$). Analogous to the birth weight, neonates born by women with substance abuse were the smallest (MD1: 49.3 cm, $p<0.001$, MD2: 49.5 cm, $p=0.018$), followed by MD1 newborns of the depressed with antidepressant medication group (49.5 cm, $p=0.028$). In MD1 infants born by women with depression and no antidepressant use were the tallest (51.1 cm, $p=0.452$), also in MD2 the infants born by women with epilepsy and anticonvulsive medication were the ones with the highest birth length (51.4 cm, $p=0.328$).

Neonatal head circumference

Infants of the case group had smaller neonatal head circumferences (mean MD1: 34.8 cm, Mean MD2: 34.3 cm) than infants of the control group (mean MD1: 35.0 cm, $p=0.011$, mean MD2: 34.6 cm, $p=0.390$) (Table 2, Fig. 4). While in MD1 neonates from the drug abuse group had the smallest head circumference (mean 34.5 cm, $p=0.096$), neonates from drug abuse group MD2 had the highest head circumference (mean 34.8 cm, $p=0.241$). Especially those from the subgroup without substitution program had higher head circumferences than infants from the control group (mean 37.2 cm, $p<0.001$). In MD1 newborns of women with epilepsy and anticonvulsive medication were the ones with the highest head circumference (35.0 cm, $p=0.693$).

Discussion

For subgroup MD1 and MD2 the most frequent disease was maternal depression with a proportion of 4.5% (MD1) and 1.3% (MD2). Study results from Sweden detected a prevalence of similar magnitude, the prevalence for major depression was 3.3% and 6.9% for minor depression [23]. The rate of depressive symptoms is often higher. Lee et al. calculated a prevalence of 37.1% for depressive symptoms in Chinese pregnant women, pregnant women in Nicaragua had depressive symptoms up to 57% [24, 25]. The relative frequency of antidepressant use was 17.6% in the depression group and 0.8% in the entire group for MD 1 and 69.6% in the depression group and 0.9% in the entire group for MD 2. Other studies detected a prevalence of antidepressant use in 2–9.6% among pregnant women [26–28]. The relatively low prevalence of depression and the relatively high use of antidepressants in cases from MD 2 indicating a selection bias for the depression group.

With a prevalence of 1.2% and 0.4% the proportion of pregnant women affected by epilepsy is detected as similar as study results from USA which calculated an epilepsy prevalence of 0.5–0.7% [8, 29]. The proportion of women on pharmacological treatment was lower in women of

Table 2 Overview of neonatal somatometric variables classified by control group, case group and subgroups, according to pharmacological treatment

	Maternity department 1		Maternity department 2	
	Mean ± SD[j]	Significance p[c]	Mean ± SD	Significance p
Weight (g)[f,g,h,i]				
Control group	3383,2 ± 470.2		3399,7 ± 484.3	
Case group	3265.6 ± 498.2	0.002*	3304.9 ± 453.6	0.460
Depression	3312.1 ± 477.3	0.153	3303.3 ± 405.6	0.496
Depression + M[a]	3193.3 ± 439.7	0.219	3293,0 ± 398.5	0.400
Depression −M[b]	3336.5 ± 481.7	0.306	3329.1 ± 434.8	0.956
Substance abuse	3046.6 ± 507.4	< 0.001**	3036.4 ± 667.3	0.027*
Substance abuse + M	3030.0 ± 499.0	0.008**	3004.4 ± 588.6	0.039*
Substance abuse −M	3055.6 ± 516.3	< 0.001**	3094.0 ± 864.8	0.337
Epilepsy	3236.9 ± 485.2	0.113	3407.9 ± 419.8	0.379
Epilepsy + M	3280.5 ± 486.3	0.855	3472.9 ± 436.2	0.089
Epilepsy −M	3213.2 ± 487.3	0.062	3237.7 ± 330.3	0.293
Length (cm)[f,g,h,i]				
Control group	51.3 ± 2.4		51.3 ± 2.4	
Case group	50.6 ± 2.6	< 0.001*	50.8 ± 2.2	0.253
Depression	50.9 ± 2.5	0.028**	50.8 ± 2.0	0.677
Depression + M	49.5 ± 2.1	< 0.001**	50.8 ± 2.1	0.617
Depression −M	51.1 ± 2.5	0.452	50.9 ± 2.0	0.992
Substance abuse	49.3 ± 2.6	< 0.001**	49.5 ± 2.8	0.018*
Substance abuse + M	49.1 ± 2.5	< 0.001**	49.3 ± 2.8	0.368
Substance abuse −M	49.5 ± 2.7	< 0.001**	49.8 ± 3.3	0.368
Epilepsy	50.8 ± 2.5	0.808	51.2 ± 2.3	0.567
Epilepsy + M	51.0 ± 2.5	0.749	51.4 ± 2.4	0.328
Epilepsy −M	50.7 ± 2.5	0.571	50.8 ± 2.2	0.638
Head circumference (cm)[f,g,h,i]				
Control group	35.0 ± 1.4		34.6 ± 1.5	
Case group	34.8 ± 1.4	0.011*	34.3 ± 1.8	0.390
Depression	34.8 ± 1.4	0.018*	34.3 ± 1.8	0.035*
Depression + M	34.2 ± 1.4	0.003**	34.0 ± 1.2	0.012*
Depression −M	34.9 ± 1.4	0.206	34.4 ± 0.9	0.966
Substance abuse	34.5 ± 1.5	0.096	34.8 ± 3.7	0.241
Substance abuse + M	34.3 ± 1.4	0.102*	33.4 ± 1.1	0.025*
Substance abuse −M	34.6 ± 1.5	0.392	37.2 ± 5.6	< 0.001*
Epilepsy	34.8 ± 1.5	0.434	34.5 ± 1.7	0.885
Epilepsy + M	35.0 ± 1.4	0.693	34.7 ± 1.6	0.457
Epilepsy −M	34.7 ± 1.6	0.191	33.9 ± 1.8	0.156

*Significant without Bonferroni correction

**Significant with Bonferroni correction

[a]With disease-specific medication (+ M)

[b]Without disease-specific medication (− M)

[c]Compared to the control group, $p < 0.05$ was considered significant

[f]Test adjusted for smoking

[g]Test adjusted for gestational age

[h]Test adjusted for gender

[i]Included only cases with actual date of birth between 30 days before and 10 days after calculated date of birth

[j]Standard deviation

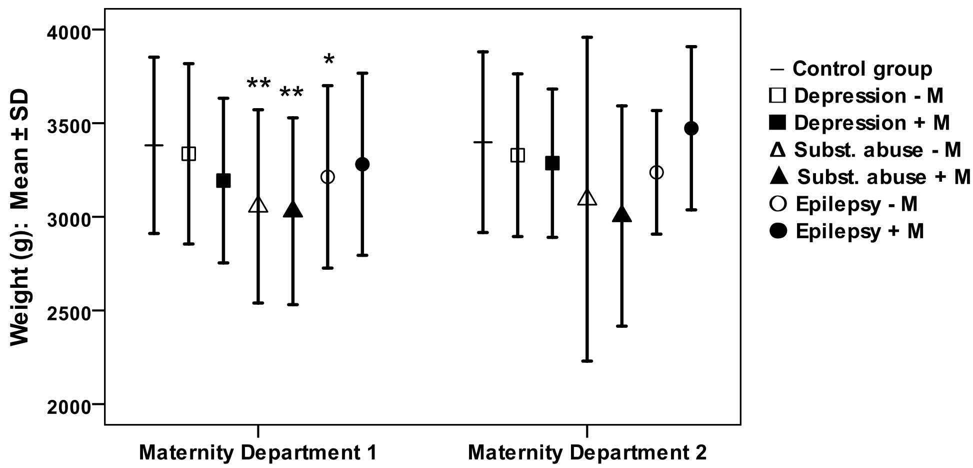

Fig. 2 Mean and standard deviation of birth weight in data MD1[a] and MD2[a]. ([a]Cases were included in the analysis when actual date of birth was less than 30 days before and not more than 10 days over the expected date of birth. *Significant without Bonferroni correction. **Significant with Bonferroni correction)

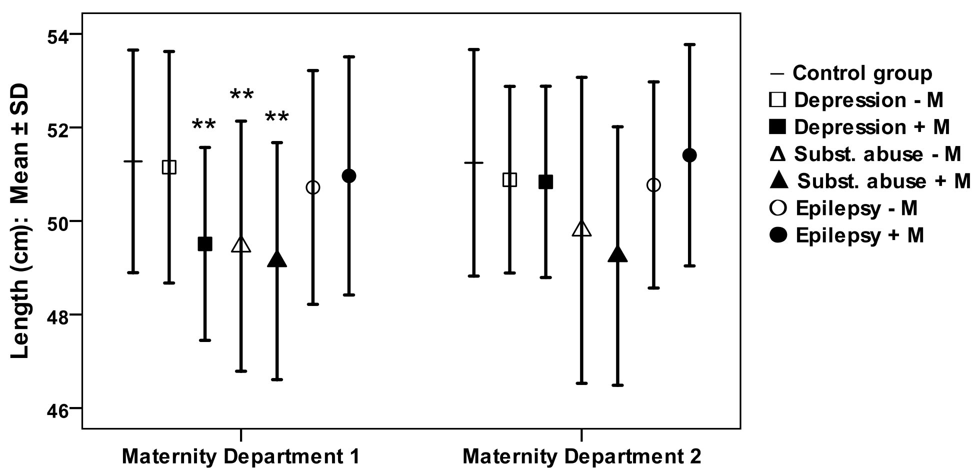

Fig. 3 Mean and standard deviation of birth length in data MD1 and MD2[a]. ([a]Cases were included in the analysis when actual date of birth was less than 30 days before and not more than 10 days over the expected date of birth. *Significant without Bonferroni correction. **Significant with Bonferroni correction)

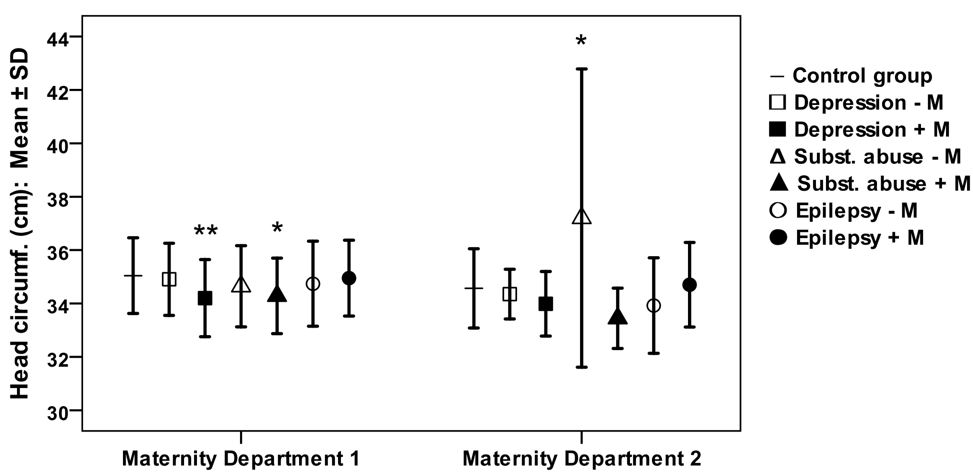

Fig. 4 Mean and standard deviation of head circumference in data MD1[a] and MD2[a]. ([a]Cases were included in the analysis when actual date of birth was less than 30 days before and not more than 10 days over the expected date of birth. *Significant without Bonferroni correction. **Significant with Bonferroni correction)

MD1 than in women of MD2 and compared with literature. While in the present study 34.4% (MD1) and 73.6% (MD2) were treated with anticonvulsants, Artama et al. detected a rate of 63% with antiepileptic medication [29].

The prevalence of drug abuse in pregnancy was 1.2% (MD1) and 1.0% (MD2). Compared to study results from McHugh et al. where the proportion in women of reproductive age was 13%, the subgroup in our study cohort is very low [6]. Although counselling on risks resulting from pregnancies exposed to illicit drug abuse is an essential part of the prenatal care this indicates that the proportion might be higher than the self-reported number.

Intrauterine growth restriction is one of the most predictive indicators and risk factors for fetal morbidity and mortality, irrespective of cause [30]. Starting with a high associated risk for SGA and prematurity, IUGR can lead to secondary diseases like necrotizing enterocolitis and retinopathy of the premature, as well as poorer neurodevelopmental and physical outcome. The lifetime risk for diabetes, immune dysfunction and neuropsychiatric diseases is increased [31–34].

In the present study, the rate of IUGR was only increased in the subgroup MD1 showed that especially women without disease-specific medication during pregnancy had higher rates of IUGR than the control group. In MD 2 especially neonates born by women with anticonvulsive medication and the drug abuse group showed higher rates of IUGR.

For maternal depression study results show that IUGR rate is higher compared to pregnancies not affected by depression [35–37]. Ciesielski et al. determined that the risk for IUGR does not depend on the pharmacological treatment. Compared to healthy controls, women with depression, regardless of treatment had higher IUGR rates [38].

A meta-analysis by Chen et al. from 2017 revealed that epilepsy is an important risk factor for IUGR and that antiepileptic medication does not decrease the rate of IUGR [39]. The present study showed that in subgroup MD 1 women without medication had a higher risk for IUGR. Indicating that the disease itself is the leading cause.

The highest IUGR rate in our study cohort displayed the drug abuse group MD1 without substitution. Compared to the published data which measured a rate up to 34% for opioid and cocaine consumption, the rate of 10.1% (MD1) and 15.8% (MD2) in this study is lower, but still alarming [7, 40].

Nevertheless, the data were not significant and in some subgroups, there were no cases of IUGR at all. Although IUGR is a known risk factor, the prevalence in general population is relatively low (between 3–7%) [41]. Further studies with higher case numbers are needed.

Looking at weight and length of the newborns, the study in both subgroups (MD1, MD2) showed that infants from the drug abuse group were significantly lower, especially in substituted women. The literature shows that substitution enables better outcome for the fetus. Nevertheless, substitution itself is a risk factor for prematurity, low birthweight and SGA [42, 43]. However, our study is limited by a relatively low sample size in the not-substituted drug abuse group.

The neonatal head circumferences in infants born from the drug abuse group were significantly lower in MD1 compared to the control group. Bier et al. found a negative association between maternal methadone dose and neonatal head circumference, 2019 published data from Tennessee also showed smaller head circumferences within newborn exposed to chronic opioid abuse [44, 45]. Another study from 2011 showed that the neonatal head circumference is negatively associated with the methadone concentration in the placenta [46]. Inconclusive results shown in the subgroup drug abuse MD2 without maternal substitution infants presented a significantly higher neonatal head circumference. Again, a low sample size in this subgroup might be the reason for these findings.

Although some results were not statistically significant, in subgroups MD1 and MD2 infants born by women with depression had generally lower birth weight, birth length and neonatal head circumference than infants born from the control group. Results published from Iran in 2017 support these findings and displayed that depression itself has significant effects on the somatometric parameters of the newborns [47]. Compared to the unexposed pregnancies, those exposed to intrauterine antidepressant medication had lower growth outcomes as other study results have shown [48, 49].

The neonatal growth parameters in the infants from epilepsy group differ the least from data of the control group. Comparing the group with anticonvulsive medication with the non-pharmacological one, the group with disease-specific medication had a better outcome. In contrast, previous study results show that use of anticonvulsive medication is a risk factor for lower gestational age at birth, and SGA [15, 50, 51]. Liu et al. published data in 2009 that displayed poorer outcome for infants of epileptic women without antiepileptic treatment, analogous to the results of the present study [52]. Consequently, the isolated and untreated epilepsy might be a risk factor for poorer somatometric outcome but not as much as the other neuropsychiatric diseases have demonstrated.

Limitation

By including data from two different major maternity departments, a high validity within the data could be obtained. Nevertheless, some case numbers of subgroups were relatively small, statistical effects might have been lost in comparison to the high number of controls. Man-made mistakes in the data and incorrect information by the pregnant women self-report of drug abuse also cannot be fully excluded.

Conclusion

Although not all results show statistical significance, impact of maternal neuropsychiatric diseases can be demonstrated in neonatal growth. While the relevant literature often considers gynaecologic and paediatric parameters separately, this study does not consider maternal disease and its effect on the newborn's welfare isolated but analyses them in their wholeness. In conclusion, our data suggest both pharmacological and non-pharmacological-treated neuropsychiatric disease may have influence on fetal growth outcome. The proportion of affected pregnancies in our data clearly demonstrates the clinical relevance of the topic.

Author contributions GJ: critical revision of the article, final approval. SDC: critical revision of the article, final approval. SK: statistical support, critical revision of the article, final approval. SS: data collection, critical revision of the article, final approval. AR: data collection, critical revision of the article, final approval. AR: data collection, critical revision of the article, final approval. LZ: data collection, critical revision of the article, final approval. AR: project development, data collection, data analysis and interpretation, critical revision of the article, final approval. LS: project development, data collection, data analysis and interpretation, manuscript writing.

Funding This paper was Lara Südekum's doctoral thesis, and she obtained financial support from the Otto-von-Guericke-University Medical Faculty Magdeburg, Germany, as a doctoral scholarship.

Compliance with ethical standards

Conflict of interest The authors declare that they have no conflict of interest.

Ethical approval The institutional Ethics Committee of the Medical Faculty of the Otto-von-Guericke University Magdeburg (113/14), Germany approved the study. All procedures performed in this study were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki Declaration and its later amendments or comparable ethical standards.

Informed consent For this retrospective type of study formal consent was not required. Requirement for inform consent has been waived by the institutional Ethics Committee due to the retrospective nature of the study, and pseudonymization of data.

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