

Research Article

Cannabis Use in Pregnancy and Risk for Placental Abruption

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OPEN ACCESS**Abstract**

Study design: Retrospectives study including 167 women, who used cannabis during the pregnancy or before and were admitted to the Family Clinic in Region Zealand and delivered singletons in the period from July 2012 to June 2016.

We divided the pregnant in 3 groups depending on cannabis use in pregnancy: previous cannabis users, users who stopped at the beginning of pregnancy and users who continued smoking cannabis late in pregnancy. We compared the groups and compared the number of placenta abruption with data from The Medical Birth Register.

Results: The pregnant women were younger, shorter educated, smoked more cigarettes and were more unemployment than other pregnant. However, there are no differences between the three groups on many basic parameters.

We found significantly greater risk of placental abruption in the group of pregnant women who used cannabis later in pregnancy, OR 21.3. This risk was not found in the other groups.

Conclusions: Cannabis use in pregnancy may increase the risk of placental abruption, which is a rare and serious obstetric complication with far-reaching consequences for the children.

Keywords

- Placental abruption
- Cannabis use
- Pregnancy
- Risk factor

INTRODUCTION

Cannabis is widely used throughout the world, and is used by women of childbearing age. With the legalization, one can fear that more pregnant women will use cannabis. Cannabis during pregnancy might increase adverse outcomes for mothers and their neonates [1]. The correlation between cannabis and adverse obstetric outcomes is still unresolved and more research is needed to further assess this relationship [1-3].

Within the last 8 years, Denmark has increased the focus on pregnant drug users and their children and the antenatal care for pregnant drug users has been centralized. It allows for better detection of the risks drug causes.

Placental abruption is rare, but a very serious obstetric complication that can have far-reaching consequences for the children. Therefore, there is a great interest in identifying risk factors so that increases can be made with the aim of reducing the number of adverse obstetric complications

Considering the lack of firm knowledge on the associations between cannabis use in pregnancy and severe obstetrical outcomes, we decided to assess the association among cannabis users in the Family Clinic in Region Zealand. Cannabis consumption is often seen with other factors that can affect

adverse obstetric outcomes eg cigarette smoking, drug use and short school education.

In an effort to take into account these factors, we have chosen to compare adversity outcomes among a group of active cannabis users with a group of pregnant women who have previously used cannabis as they often have the same socio-social risk factors.

MATERIAL AND METHODS

In Denmark, all pregnant women who have used drugs during the pregnancy or two years prior are admitted to antenatal care by a special unit, the Family Clinic, which is an outpatient clinic. Denmark is divided into five administrative regions and each region has a Family Clinic. The staff in the Family Clinic performs the antenatal care and follows the women throughout their pregnancy. Every pregnant is connected to a midwife, a doctor and a social worker in the Family Clinic.

When a woman realizes that she is pregnant, she goes to her general practitioner. He or she will fill in a pregnancy medical file and sends it to the hospital. Among other questions the woman will be asked, if she has taken drugs and if so what types. If the pregnant woman admits any drug use, or if such use is suspected, the pregnant woman will be referred to the Family Clinic. All midwives ask the pregnant women about their lifestyle and drug

use, and refers them to the Family Clinic have they used drugs during pregnancy or two years prior. The participants of the present study thus constitute a cohort of pregnant cannabis users living in Region Zealand, Denmark.

This is a historical cohort study and all information was found in the patients' medical reports.

All women, who used cannabis during the pregnancy or in the last two years before pregnancy, and who were admitted to the Family Clinic in Region Zealand and delivered singletons in the period from July 2012 to June 2016, were included in the study. Exclusion criteria were twin deliveries (N=3) and loss to follow-up due to immigration to another country during the pregnancy (N=3).

In order to determine cannabis consumption, we examined the urine for THC. At the first visit in the Family Clinic every pregnant had a urine test. During pregnancy, we asked the pregnant woman about her cannabis consumption and tested her to get an overview of her consumption. At the beginning of the study period, we sent all urine sampling to the laboratory, later we used Nanosticka® from Ferle and only sent urine to the laboratory was the Nanosticka® positive. The laboratory used LC-MS [MS] analyses.

Medical history was taken from all women primary by one doctor [VV]. Gestational age was determined by ultrasound in all cases.

We divided cannabis users into two groups: those who stopped cannabis consumption early (negative screen test before GA 16, named group B), and those who continued (positive screen test after GA 16, named group A). Some did not meet one of two criteria, for example, if they came to the first consultation after GA 16 weeks, and the screen test was negative. The decision about which group the pregnant belonged was in each case based on the medical history and magnitude of the creatinine-cannabis ratio.

167 pregnant women were included. 102 had taken cannabis during the pregnancy, 62 in group A and 40 in group B. 65 pregnant where previous users (group C).

We have provided data for the background population for comparison. The frequencies are calculated on data originating from The Medical Birth Register (National Board of Health) [4], and relates to the period 2013-2016.

Statistics: Differences across groups were evaluated using Fischer's exact test for count variables and Van der Warden's test for continuous variables. The binomial distribution was applied in calculation of odds ratios, OR, in comparisons of our findings with regional and national Danish incidence rates. Such an OR is equivalent to the calculation of indirect standardized morbidity ratios but more straightforward to interpret in this context. To illustrate the GA for the three groups a scatter box-plot was made. Test probabilities below 0.05 were considered significant.

We have permission from the Patient Security Agency to read the medical reports and permission from Region Zealand's local part of the Danish Data Protection Agency to store data in a database in order to analyze it.

RESULTS AND DISCUSSION

Results

Basic information about the groups is shown in Table (1). It is seen that the 3 groups were comparable.

The participants in the three groups were younger than pregnant women in general in Denmark. The median age at birth was 23 years in group A while 30 years in Denmark. In the three groups (A+B+C) at least 50% of the women were under 25 years, compared to less than 13% in the general population. In Denmark, little more than half the women are multiparous, in the study there were far fewer. In our study ¾ of the women smoked when they came to the first visit in the Family Clinic, on a national level, 10.8 % of pregnant women smoke in the beginning of the pregnancy and 7.4 % at the delivery.

Two thirds of our patients had a psychiatric diagnosis. The most frequent was depression, followed by emotionally unstable personality disorder, often borderline and attention deficit hyperactivity disorder (ADHD). 11% of the pregnant women from all three groups took psychopharmacological medicine including antidepressant drugs.

In addition to psychopharmacological medicine, the most frequent use of medication during pregnancy was asthma medicine, painkillers and antiepileptic drugs, drug for metabolism, insulin and blood thinning medication. Two pregnant women were treated with blood thinning medicine (Tinzapin) due to blood-clotting disorders.

About half of the women had previously consumed other illegal drugs or overused alcohol. During pregnancy, 10% had taken other drugs, most of them alcohol or amphetamines, but all stopped at the acknowledgement of the pregnancy. None of the women who delivered very prematurely or had placental abruption had taken other drugs during pregnancy.

More than half of the women in this study had used cannabis before they were 15 years old. The youngest were 11 years old, when they smoked cannabis for the first time.

28.4% had not taken the primary school exam. Only 32% were employed or under training/education and the rest had some form of unemployment benefit. There was no significant difference between the 3 groups.

Information about the delivery is seen in Table (2). Figure (1) shows GA in the 3 groups.

Totally seven women had placental abruption. Six women from group A had placental abruption. In group C one woman got a little rip-off in week 28, but continued the pregnancy until the delivery in week 39. The seven women gave birth at GA 25, 26, 32, 33, 33, 39 and 40 weeks, respectively.

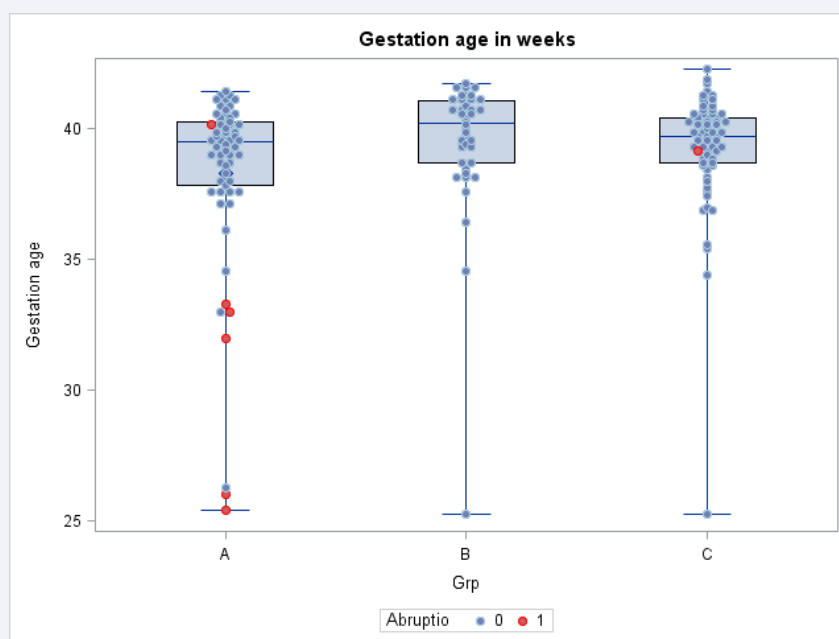
Two of the women were in treatment with Tinzaparin. One woman received high dose Tinzaparin (14,000ie) due to previous thrombosis x 3. She had an abruption in week 32 and had a cesarean section. The other woman (group C) was in prophylactic treatment with 4,500ie Tinzaparin.

The five women who delivered before week 35 all had acute cesarean sections. Both women who gave birth at GA 39 and 40

Table 1: The table shows mainly percent, and in few lines median and range.

Group	A	B	C	Statistic A,B&C P
Number	62	40	65	
Age ¹	23 (17-39)	25 (16-37)	22 (17-41)	NS
Age < 25years	50.8	50.0	69.2	NS
Nulliparous	72.6	90.0	90.8	0.02
Cigarette smoking at 1. consultation	85.2	65.0	70.3	0.04
Daily cigarettes ¹	8 (0-23)	6 (0-20)	8 (0-20)	NS
Smoking ≥ 15 cigarettes	17.7	12.5	11.0	NS
Age at cannabis debut ^{1,2}	16 (11-30)	15 (12-30)	15 (11-29)	NS
Ever daily cannabis use	66.7	70.2	72.3	NS
Use of other drugs before pregnancy	50.0	56.4	46.0	NS
Use of other drugs in pregnancy	11.3	10.0	3.0	NS
Medicine in pregnancy	22.6	20.0	26.2	NS
Psychiatric diagnose	56.5	72.2	72.6	NS
Living with the farther	62.9	65.0	64.6	NS
Not taken the primary school exam ²	33.3	17.9	30.4	NS
Working or under training/education	32.3	32.5	41.6	NS

¹Median (range)
²Stated in about 70 % in all three groups

**Figure 1** GA in the 3 groups the cases with placental abruption is marked.

delivered vaginally.

Five out of the seven women who had placental abruption reported smoking more than 15 cigarettes daily before acknowledged pregnancy. One did not smoke. At the first consultation in the Family Clinic, two of the women reported that they had stopped smoking. The four others women who got placental abruption reported that they smoked cigarettes: one

woman smoked less than five cigarettes a day, two women smoke up to 10 cigarettes daily and one women smoke 15-20 cigarettes daily.

Compared to the known risk factors for placental abruption, very few were seen in our population. None of these seven women had taken other illegal drugs or alcohol during pregnancy. Except for the two pregnant women who used blood thinning medication,

there was only one woman who used medicine (antidepressant SSRI). Six women were nulliparous; one of the women had previously delivered once. None of the women was less than 20 years or more than 35 years old. None of the seven women had had a trauma, none had preterm rupture of the membrane and none had hypertension.

There were no perinatal deaths among the seven children.

The risk of placental abruption for pregnant who did not stop using cannabis when they become pregnant [group A] was significantly increased compared to normal Danish births, see Table (3). OR was 21.3 [7.5-49.4] for pregnant, who used cannabis late in the pregnancy. The cases with placental abruption are marked in Figure (1).

Discussion

Prevalence of placental abruption are roughly 0.5 % in Denmark [4,5]. We found a highly increased risk for placental abruption among pregnant cannabis users.

The women in our study [group A, B and C] were younger, shorter educated and smoked more cigarettes than average. Besides, there was an overrepresentation of women supported by unemployment benefit in all three groups compared to the background population in Denmark.

However, there are no differences in most of the basic

parameters between the three groups. We found a greater risk of placental abruption in the group of pregnant women who continued to smoke cannabis during pregnancy. This risk was not found among pregnant women who stopped early in pregnancy or who had stopped before getting pregnant.

The only difference between the groups was fewer nulliparous and a little more who smoked cigarettes in group A. Although cigarettes are a known risk factor, this alone cannot explain the great difference in abruption.

Various factors can increase the risk of placental abruption, including previous placental abruption, high blood pressure, substance abuse (cigarette smoking or cocaine use during pregnancy), abdominal trauma, blood-clotting disorders, multiple pregnancy, premature rupture of the membranes and maternal age (older women, especially after age 40) [6]. Two of the pregnant women in the study were treated with blood thinning medicine due to blood-clotting disorders. Among the other five who had placental abruption, two did smoke cigarettes. No other known disposable factors were present in the seven women who had placental abruption.

In a newer systematic review and meta-analysis including 24 studies [1], it was concluded that use of cannabis during pregnancy might increase adverse outcomes for women and their neonates. There was found no association between exposure to cannabis in utero and placental abruption referring to one study

Table 2: Information about the delivery and the background population in Denmark 2013-2016.

	A	B	C	Denmark
Number	62	40	65	
GA	39+3 (25+3 - 41+3)	40+1 (25+2 - 41+5)	39+6 (25+2 - 42+2)	
BW	3060 g (730 -4130)	3280 g (875 - 5155)	3170 g (446-4570)	3440 g
Caesarian section	17 (27.4)	11 (27.5)	17 (26.2)	20.8
Preterm delivery GA <37	9 (14.3)	3 (7.5)	6 (9.2)	5.8
Very preterm delivery GA < 28	3 (4.8)	1 (2.5)	1 (1.5)	0.46
Placental abruption	6 (9.7)	0	1 (1.5)	0.47
Median and (range) or number and (%)				

[7]. This American study included records of 8,350 pregnant from the period 1983-85. They identified 417 pregnant who reported marijuana use but no other drugs. The incidence of abruption was non-significant between users and non-users.

One other study found that the occurrence of placental abruption increased with higher frequency of marijuana use [8]. Others studies did not find an increased risk for placental abruption [9,10]. It is remarkable that we found an OR at 21.3 when this difference has only been demonstrated in one other study. However, there is a difference in the way the drug users are identified and not all the studies distinguish between cannabis consumption in the second/third trimester or not.

In addition, contemporary marijuana products have higher

quantities of delta-9-tetrahydro-cannabinol (THC) than in the 1980s when some of the marijuana research was completed [3]. The effects on the pregnancy and fetus today may therefore be different than those previously seen.

To estimate OR we have compared to data from the Danish Medical Birth Registry. It may be problematic to merge data which have not been collected in the same way, but The Danish Medical Birth Registry collects reliable data, and all the 6 cases we found in group A resulted in action: one rupture of the membrane and 5 preterm acute cesarean sections.

We cannot expect to find all pregnant women using illegal drugs. Obviously, the result is confused if there are many pregnant women with substance abuse, which we do not find

Table 3: The frequency of placental abruption (%) and OR for group A compared to Denmark.

	A	B	C	2013-16. Region Zealand	2013-16. Denmark	OR for group A	Group A compared to DK
Placental abruption	9.7	0	1.5	0.49*	0.47*	21.3 (7.5-49.4)	p<0.0001

*from The Danish National Patient Registry
OR are calculated with 95 % upper and lower confidence limit

or if we cannot classify the pregnancy's consumption properly. In a Danish study, 608 pregnant women who came to early ultrasound (GA 12-14) were anonymously urine-tested. Three of the women (0.5%) were confirmed positive for cannabis [11]. In Region Zealand there are about 6,400 births a year. In our study we found 102 women, who used cannabis in the pregnancy, matching 0.4% of the pregnant in Region Zealand. This indicates that we have found the majority of pregnant cannabis users.

CONCLUSION

The pregnant women in our study (group A, B and C) used or had used cannabis. The pregnant women were younger, shorter educated, smoked more cigarettes and were more supported by unemployment benefit than other pregnant women. However, there are no differences between the 3 groups on most of the basic parameters.

We found greater risk of placental abruption in the group of pregnant women who used cannabis farther on in pregnancy, odds ratio 21.3 (7.5-49.4) compared to normal Danish births. This risk was not found among pregnant who had stopped using cannabis early in pregnancy or before they got pregnant.

Cannabis use in pregnancy may increase the risk of placental abruption, which is a rare and serious obstetric complication with far-reaching consequences for the children.

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