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Pregnancy, Childbirth and Puerperium Health Problems in Women Over 35 Years of Age

Problemy zdrowotne u kobiet po 35 roku życia w ciąży, podczas porodu oraz wczesnego połogu

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Abstract: *Background:* Due to the choice of postponing motherhood, the average age of women giving birth in Poland has moved into older age groups. This study was conducted to assess pregnancy complications and birth outcomes in women of advanced maternal age (AMA, over 35 years of age) compared with women aged 35 years. *Material and Methods:* Data on births was obtained from two third-degree hospitals in Warsaw, Poland for the years 2017 – 2019. Maternal and perinatal outcomes for women of advanced maternal age (n = 3,766) were analyzed using Chi-square tests and the ANOVA Kruskal-Wallis test. Comparisons between the following age groups of women were conducted: age 35 (control group), 36 – 39, 40 – 44 and over 45 years of age. Results of the analysis are presented with unadjusted odds ratios, 95 percent confidence intervals and p-values. *Results:* The incidence of pregnancy-induced hypertension (PIH) was found to increase with age in the 36 – 39 (OR 1.76, CI 1.09 – 2.87), 40 – 44 (OR 2.72, CI 1.56 – 4.73) and in the over 45 (OR 6.34, CI 2.04 – 19.69) age groups. The risk of gestational diabetes was seen to increase in women aged 40 – 44 (OR 1.49, CI 1.13 – 1.97) and increases almost three times in women over the age of 45 (OR 2.88, CI 1.41 – 5.87). The frequency of births by Cesarean section was observed to increase by one quarter in the 36 – 39 age group (OR 1.26, CI 1.07 – 1.48), by half in the 40 – 44 age group (OR 1.5, CI 1.28 – 1.96) and almost three times in women over 45 (OR 2.88, CI 1.41 – 5.87). There was no statistical significance for the incidence of preterm delivery, induction of labor and postpartum anemia or the health status of newborns in the studied age groups. *Conclusions:* Maternal age of over 35 years old is an independent risk factor for higher rates of pregnancy and perinatal complications in the Polish population.
Keywords: advanced maternal age, pregnancy, childbirth

Abstrakt: *Wprowadzenie:* Ze względu odraczanie macierzyństwa, średni wiek kobiet rodzących w Polsce przesuwa się na starsze roczniki. Celem pracy było porównanie powikłań w ciąży i podczas porodu u kobiet w wieku 35 lat i powyżej 35 roku życia (AMA).

Materiał i metody: Retrospektywne badanie zostało przeprowadzone w 2 szpitalach trzeciego stopnia referencyjności w Warszawie w okresie od 1.02.2017 do 31.01.2019. dane dotyczące kobiet po 35 roku życia (n = 3 766) przeanalizowano za pomocą testu Chi-kwadrat oraz testu ANOVA Kruskala-Wallisa. Porównano następujące grupy wiekowe kobiet: 35 lat (grupa kontrolna), 36-39 lat, 40-44 lata i powyżej 45 lat. Wyniki analizy przedstawiono za pomocą nieskorygowanych ilorazów szans, 95-procentowych przedziałów ufności i wartości p.
Wyniki: Stwierdzono wzrost częstości występowania nadciśnienia indukowanego ciążą (PIH) wraz z wiekiem w grupach wiekowych 36 - 39 (OR 1,76, CI 1,09 - 2,87), 40 - 44 (OR 2,72, CI 1,56 - 4,73) oraz w grupie wiekowej powyżej 45 lat (OR 6,34, CI 2,04 - 19,69). Ryzyko wystąpienia cukrzycy ciążowej wzrasta o połowę u matek w wieku 40 - 44 lat (OR 1,49, CI 1,13 - 1,97) oraz prawie trzykrotnie w grupie matek powyżej 45 roku życia (OR 2,88, CI 1,41 - 5,87). Częstość porodów drogą cięcia cesarskiego wzrasta o jedną czwartą w grupie wiekowej 36 - 39 lat (OR 1,26, CI 1,07 - 1,48), o połowę w grupie wiekowej 40 - 44 lat (OR 1,5, CI 1,28 - 1,96) i prawie trzykrotnie u kobiet powyżej 45 roku życia (OR 2,88, CI 1,41 - 5,87). Nie stwierdzono istotnego statystycznie wpływu na częstość występowania porodu przedwczesnego, indukcji porodu i niedokrwistości poporodowej oraz na stan zdrowia noworodków w badanych grupach wiekowych.
Wnioski: Wiek matki powyżej 35 roku życia jest niezależnym czynnikiem ryzyka wyższych wskaźników powikłań ciążowych i okołoporodowych w populacji polskiej.
Słowa kluczowe: zaawansowany wiek matki, ciąża, poród

1. Introduction

The average age of women giving birth in Poland has increased into older age groups. The proportion of births requiring temporary feeding route (TFR) begins to increase in women between 30 and 34 years of age and systematically increases in women in the age group between 35 and 39 years of age (Waligórska, 2014). Women feel that they are better prepared emotionally and financially for motherhood after the age of 35, largely due to financial stability and personal independence (Aldrighi, Wall, Souza, Cancela, 2016).

Women are increasingly choosing to postpone motherhood, despite age being an important factor that impacts the ability to become naturally pregnant, with many believing in the possibilities of modern medicine to assist them with their pregnancies (Pedro, Brandão, Schmidt, Costa, Martins, 2018). Postponement may also be influenced by media messages that create images of women for whom it is never too late for motherhood (Mills, Lavender R, Lavender T, 2015; O'Brien, Wingfield, 2019). Ovarian reserves decrease beginning at age 30. Chronic diseases such as hypertension and diabetes, which appear with age, can also make pregnancy difficult. Moreover, women over 35 years of age are being increasingly treated for infertility, which is defined as the lack of pregnancy after one year of intercourse without any protection. Infertility treatment is a broad medical area that includes both assisted procreation procedures like in vitro fertilization (IVF), medical counselling, diagnosis of causes and pharmacological and surgical treatments with psychological support (Fuchs, Monet, Ducruet, Chaillet, Audibert, 2018; Shirasuna, Iwata, 2017; Ustawa z dnia 25 czerwca 2015 r. o leczeniu niepłodności).

The consequences of pregnancy in advanced maternal age (AMA) may include an increased risk of health problems caused by pregnancy such as cholestasis, hypertension and diabetes. Diseases occurring during pregnancy may also affect the incidence of premature birth and labor may more frequently end in Cesarean section (De Viti, Malvasi, Busardò, Beck, Zaami, Marinelli, 2019). The costs of complications of pregnancy and childbirth in AMA are not only financial expenses incurred due to longer hospitalization of the mother and child, but also social and family costs (Attali, Yogev 2021; Frey, Klebanoff, 2016).

In the present study, we compared health problems during pregnancy, childbirth and early purpureum in women 35 years of age, 36 – 39, 40 – 44 and over 45 years of age.

2. Materials and methods

This was a retrospective case control study involving women who gave birth after the age of 35 at two third-degree hospitals in Warsaw between February 1, 2017 and January 31, 2019. The study was based on data collected from electronic hospital databases and medical records.

We defined criteria for inclusion (n = 3,766) as age at birth ≥35 years, birth after the 22nd week of pregnancy, single pregnancy and head position. The exclusion criteria were: age <35 years, birth before 22 weeks of pregnancy, multiple pregnancy and pelvic or oblique position. We rejected 7 cases due to incomplete data.

Term birth was defined as delivery after the 37th week of pregnancy. Infertility treatment was defined as interventions in the diagnosis and restoration of fertility through conservative and surgical methods. Time of hospitalization was defined as the continuous number of days that a patient was hospitalized from the moment of admission to the hospital, to discharge after delivery. Pregnancy-induced hypertension (PIH) and gestational diabetes mellitus (GDM) were defined according to Polish guidelines and recommendations. Data on pre-pregnancy diabetes, placenta praevia and cholestasis were excluded due to insufficient numbers. Due to incomplete data on early puerperal complications, we decided to omit them from the analysis.

The study was approved by the Bioethics Committee of Warsaw Medical University: AKBE/214/2017.

The analyses were performed in Statistica 13.1 (StatSoft Poland). Statistical significance levels of 0.05 and test power of 80% were set. Nominal variables were compared using the Chi-square test and ordinal variables, after checking the normality of distribution, using the Shapiro-Wilk test, were compared with the ANOVA Kruskal-Wallis test and presented as medians and their minimum and maximum values. Odds Ratio (OR) was calculated taking into account 95% confidence intervals.

3. Results

During the study period, both hospitals had a total of 17,145 deliveries that took place, where women over 35 years of age accounted for 23.7% of the group (N = 4,071). The oldest primipara was 49 years old (it was her third pregnancy) and the oldest multipara was 56 years old (6 pregnancies and 4 births). The characteristics of the group are presented in Table 1.

Table 1a. Characteristics of the Group

	Maternal age				
	35 (n=953)	36 – 39 (n=2192)	40 – 44 (n=589)	≥45 (n=32)	p value
Pregnancy					
1	242 (25%)	429 (20%)	105 (18%)	8 (25%)	p<0.0013* χ^2 =103.60
2	390 (41%)	779 (36%)	138 (23%)	5 (16%)	
3 or more	321 (34%)	984 (44%)	246 (59%)	19 (59%)	
Birth					
1	316 (33%)	563 (26%)	154 (26%)	11 (34%)	p<0.0014* χ^2 =85.73
2	443 (46%)	976 (45%)	196 (33%)	9 (28%)	
3 or more	194 (21%)	651 (29%)	239 (41%)	12 (38%)	
Previous Cesarean	191 (20%)	559 (24%)	141 (24%)	6 (19%)	p=0.0098* χ^2 =11.37
Miscarriages					
0	708 (75%)	1,521(69%)	334 (57%)	17 (53%)	p<0.0012* χ^2 =80.41
1	193 (20%)	460 (21%)	157 (27%)	7 (22%)	
2	40 (4%)	151 (7%)	60 (10%)	5 (16%)	
3 or more	12 (1%)	60 (3%)	38 (6%)	3 (9%)	
IVF pregnancy	46 (4%)	101 (5%)	41 (7%)	9 (28%)	p<0.0013* χ^2 =39.42
Health status before pregnancy					
Hypertension	10 (1%)	32 (1%)	13 (2%)	4 (12%)	p<0.0013* χ^2 =28.18
Infertility treatment	8 (1%)	27 (1%)	22 (4%)	6 (19%)	p<0.0014* χ^2 =97.39
Pregnancy-related problems					
Pregnancy-induced hypertension (PIH)	21 (2%)	84 (4%)	34 (6%)	4 (12%)	p=0.0002* χ^2 =19.55
Gestational diabetes	126 (13%)	402 (13%)	109 (19%)	9 (28%)	p=0.0023* χ^2 =17.07
Delivery					

Table 1b. Characteristics of the Group

	Maternal age				
	35 (n=953)	36 – 39 (n=2192)	40 – 44 (n=589)	≥45 (n=32)	p value
In term	915 (96%)	2068 (94%)	553 (94%)	30 (94%)	p=0.2028 $\chi2$ =4.64
Cesarean section	294 (31%)	789 (36%)	244 (41%)	18 (56%)	p<0.0010* $\chi2$ =24.14
Induction	177 (19%)	566 (18%)	117(20%)	4 (12%)	p=0.3948 $\chi2$ =1.87
Stillbirth	2 (0.2%)	2 (0.2%)	5 (0.8%)	0	p=0.1893 $\chi2$ =4.81
Secondary anemia	38 (4%)	105 (5%)	25 (4%)	2 (6%)	p=0.7243 $\chi2$ =1.32
Hospitalization time >7 days	157 (16%)	438 (20%)	121 (21%)	7 (22%)	p=0.0987 $\chi2$ =6.26

* p<0.05

The estimation of the odds ratio for variables that had significant differences between groups is presented in Table 2.

Table 2. Neonatal condition

	Maternal age				
	35 (n=953)	36 – 39 (n=2192)	40 – 44 (n=589)	≥44 (n=32)	p value
Weight (grams)	3.430 (600 – 5,130)	3.450 (430 – 6,330)	3.420 (420 – 4,900)	3.385 (450 – 4,730)	0.1573
Length (cm)	55 (26 – 64)	55 (23 – 64)	54 (28 – 63)	54 (31-62)	0.3705
Apgar score after 1 min	10 (0 – 10)	10 (0 – 10)	10 (0 – 10)	10 (1 – 10)	0.3291
Apgar score after 5 min	10 (0 – 10)	10 (0 – 10)	10 (0 – 10)	10 (0 – 10)	0.6564

Age 35 was used as a reference control group.

Table 3a. Odds ratio (reference group – age 35)

	Maternal age					
	36 – 39		40 – 44		≥45	
	p	OR (95% CI))	p	OR (95% CI))	p	OR (95% CI)
Pregnancy						
1	0.0003*	0.71 (0.60 – 0.86)	0.0006*	0.64 (0.49 – 0.82)	0.8875	0.98 (0.43 – 2.21)
2	0.0046*	0.78 (0.68 – 0.93)	<0.0001*	0.44 (0.35 – 0.56)	0.0071*	0.27 (0.10 – 0.70)
3 or more	<0.0001*	0.64 (0.52 – 0.77)	<0.0001*	2.58 (2.06 – 2.24)	<0.0001*	5.27 (2.56 – 10.84)

Table 3b. Odds ratio (reference group – age 35)

	Maternal age					
	36 – 39		40 – 44		≥45	
	p	OR (95% CI))	p	OR (95% CI))	p	OR (95% CI)
Delivery						
1	<0.0001*	0.70 (0.59 – 0.82)	0.0043*	0.71 (0.57 – 0.90)	0.8875	1.06 (0.50 – 2.22)
2	0.0009*	0.76 (0.66 – 0.90)	<0.0001*	0.57 (0.46 – 0.71)	0.0613	0.45 (0.21 – 0.98)
3 or more	<0.0001*	2.51 (2.06 – 3.06)	<0.0001*	3.68 (2.90 – 4.68)	0.0023*	3.24 (1.55 – 6.76)
Previous Cesarean	0.0011*	1.37 (1.13 – 1.64)	0.0807	1.26 (0.98 – 1.61)	0.8624	0.92 (0.37 – 2.27)
Miscarriages						
0	0.006*	0.78 (0.66 – 0.93)	<0.0001*	0.46 (0.37-0.58)	0.0135*	0.39 (0.19 – 0.80)
1	0.6801	1.05 (0.86 – 1.26)	0.0043*	1.43 (1.12 – 1.82)	0.0004*	6.39 (2.61 – 15.66)
2	0.0047*	1.68 (1.18 – 2.41)	<0.0001*	2.59 (1.71 – 3.92)	0.0212*	3.65 (1.34-9.92)
3 and more	0.1068	1.76 (0.93 – 3.32)	<0.0001*	5.41 (2.80 – 0.44)	0.0108*	8.11 (2.17 – 3.31)
IVF	0.8624	0.95 (0.67 – 1.36)	0.0984	1.48 (0.96 – 2.28)	<0.0001*	7.72 (3.38 – 45.58)
Health condition before pregnancy						
Hypertension	0.4502	1.40 (0.68 – 2.85)	0.1082	2.13 (0.93 – 4.89)	<0.0001*	13.47 (3.98 – 45.58)
Infertility treatment	0.8875	1.03 (0.45 – 2.37)	0.0001*	4.58 (2.03 – 10.36)	<0.0001*	27.26 (8.82 – 84.21)
Pregnancy-related problems						
Pregnancy-induced hypertension (PIH)	0.0257*	1.76 (1.09 – 2.87)	0.0004*	2.72 (1.56 – 4.73)	0.0071*	6.34 (2.04 – 19.69)
Gestational diabetes	0.6713	0.94 (0.75 – 1.19)	0.0062*	1.49 (1.13 – 1.97)	0.0225*	2.57 (1.16 – 5.68)
Delivery						
Cesarean section	0.0059*	1.26 (1.07 – 1.48)	<0.0001*	1.5 (1.28 – 1.96)	0.0044*	2.88 (1.41 – 5.87)
Hospitalization time >7 days	0.0239*	1.27 (1.04 – 1.55)	0.0509	1.31 (1.01 – 1.71)	0.5716	1.42 (0.60 – 3.34)

* p<0.05

The age 35-control group represented 25% (n = 242) of the entire study group. The chance of giving birth to the first child after 35 years of age was found to be similar in the 36 – 39 (OR 0.70, CI 0.59 – 0.82) and 40 – 44 (OR 0.71, CI 0.57 – 0.90) age groups. The number of women who did not have any miscarriages decreased with age, while miscarriages reached 60% in the over 45 age group (OR 0.39, CI 0.19 – 0.80). Moreover, the highest percentage of pregnancies conducted in vitro was observed in this age group, being seven times more frequent than in the 35 years of age control group (OR 7.72, CI 3.38 – 45.58). After age 40,

women were treated more often for infertility issues before pregnancy: more than four times in women 40 – 44 (OR 4.58, CI 2.03 – 10.36) and almost thirty times more in women over the age of 45 (OR 27.26, CI 8.82 – 84.21) compared to the control group.

The incidence of pregnancy-induced hypertension (PIH) increases with age. It was found to increase by more than half in the 36 – 39 age group (OR 1.76, CI 1.09 – 2.87), more than double in the 40 – 44 age group (OR 2.72, CI 1.56 – 4.73) and more than six times in the above 45 age group (OR 6.34, CI 2.04 – 19.69) compared to the control group. Similarly for gestational diabetes, where the chance of occurrence increased by more than half in women aged 40 – 44 (OR 1.49, CI 1.13 – 1.97), it was almost three times in women over 45 (OR 2.88, CI 1.41 – 5.87).

The frequency of births by cesarean section increased with age – increasing by one quarter in the 36 – 39 age group (OR 1.26, CI 1.07 – 1.48), by half in the 40 – 44 group (OR 1.5, CI 1.28 – 1.96) and by almost three times in women over 45 (OR 2.88, CI 1.41 – 5.87) compared to the control group.

Statistical significance was not demonstrated for the incidence of preterm delivery, induction of labor or postpartum anemia in the studied age groups. There are no statistical differences in the birth weight, length and health status of newborns in both groups.

Discussion

Most studies compare advanced age groups to younger women between the ages of 20 and 34. In the present study, women aged 35 years old were used as a reference group, representing 25% of the total number of respondents. Health status was evaluated in three groups of pregnancies: 36 – 39 years of age, 40 – 44 years of age and above 45 years of age.

Women over 35 years of age are more likely to undergo infertility treatment, which may also result in a higher incidence of miscarriages than younger women. In a study by Casteleiro et al., a smaller percentage of women in this age group were treated for infertility, which may be due to differing definitions of infertility treatment that may only include assisted reproductive technologies (Casteleiro, Paz-Zulueta, Parás-Bravo, Ruiz-Azcona, Santibañez, 2019). There is also a trend that the older the mother, the more miscarriages she is likely to have had. In a Norwegian study, the risk of miscarriage increased rapidly after age 30, reaching 53% in women aged 45 and over (Magnus, Wilcox, Morken, Weinberg, Håberg, 2019). The present study shows that multiple miscarriages occur approximately five times more often in mothers between the ages of 36 and 39, and about eight times more often over the age of 45. This is not only due to biological factors, but also because older women having a longer maternal history than younger women.

The rising trend of increased cesarean sections among women of advanced maternal age has been observed worldwide (Casteleiro et al.,2019; Radoń-Pokracka, Adrianowicz,

Płonka, Danił, Nowak, Huras, 2019; Rydahl, Declercq, Juhl, Maimburg, 2019). Among similar age groups compared in a study by Claramonte et al. in Spain, the frequency of cesarean sections increased by one third in the 35 – 39 age group, more than twice in the 40 – 44 group and more than seven times among women over 45 (Claramonte Nieto, Meler Barrabes, Garcia Martínez, Gutiérrez Prat, Serra Zantop, 2019). Our study showed that the frequency of cesarean sections in women over 45 has more than doubled compared to the control group. We also found that the number of women who had previous cesarean sections and that gave birth to another child increases after 36 years of age but decreases after 45 years of age, with a statistically significant increase observed in the 36 – 39 age group. A similar trend was seen in the Spanish study (Claramonte et al., 2019).

The most common health problems in pregnant women over 35 years of age are gestational diabetes and PIH (Casteleiro et al., 2019; Claramonte et al., 2019; Kanmaz, İnan, Beyan, Ögür, Budak, 2019). In the study by Claramonte et al, the probability of developing gestational diabetes after the age of 35 was found to increase with maternal age, increasing by almost 40% in the 35 – 39 age group, almost three times in the 40 – 44 age group and almost four times in women over 45. With respect to PIH, the risk in the 36 – 39 age group was similar to that of the control group whereas in the 40 – 44 age group, the risk increases by almost a quarter and is more than three times in the over 45 age group (Claramonte et al., 2019). In our study, a smaller increase in gestational diabetes was observed: in the 40 – 44 age group, the risk increased by half and increased more than two-fold in women over 45. PIH was almost twice as high in the 36 – 39 age group, almost three times as high in the 40 – 44 age group and the highest – at more than six times – in women above 45 years of age compared to the control group.

Intrauterine fetal demise was not statistically significant in our study and was found to occur at similar proportions in studies conducted in Spain and Denmark (Casteleiro et al., 2019; Claramonte et al., 2019; Frederiksen, Ernst, Brix, Lauridsen, Roos, Ramlau-Hansen, Kvist Ekelund, 2018). This could be because studies conducted at single centers have small sample sizes and hence cannot accurately show trends for bigger populations. For example, a study done in United States which included the entire national population reported a nearly 40%-50% increase in stillbirths among women over 40 years of age compared to a younger control group (Dongarwar, Aggarwal, Barning & Salihu, 2020).

The oldest group of women in our study – referred to in the literature as very advanced maternal age (VAMA) – were women over 45 years old and consisted of 32 women. In this group, we observed a higher percentage of pregnancy complications such as diabetes and hypertension, similar to other studies that looked at the same age group (Mehta, Tran, Stewart, Soutter, Nauta, Yoong, 2014; Ogawa, Urayama, Tanigaki, Sago, Sato, Saito, Morisaki, 2017). It has been found that across the world, women over 45 years of age use assisted reproductive technologies (ART) more often, which apart from various methods

of in vitro fertilization also includes artificial insemination or ovulation stimulation stimulation (Wyns, Bergh, Calhaz-Jorge, De Geyter, Kupka, Motrenko, Rugescu, Smeenk, Tandler-Schneider, Vidakovic & Goossens, 2020; Haslinger, Stoiber, Capanna, Schäffer, Zimmermann, Schäffer, 2016). In our study, approximately 30% of the respondents in this age group achieved a pregnancy through in vitro fertilization, which was almost eight times more than in the 35-year-old control group. This is also higher than in a study by Mehta et al. where 10% of women over 45 years of age became pregnant in this way (Mehta et al., 2014).

We found that the percentage of cesarean sections in women over 45 years of age increases significantly. Similar findings were obtained in studies by Carolain et al., Mehta at al. and Ogawa et al., whereas in a study by Rademaker el al., it was higher (Carolain et al., 2013; Mehta at al., 2014; Rademaker, Hukkelhoven, van Pampus, 2021; Ogawa et al., 2017). Apgar scores in the first minutes of life of children born to mothers in this group do not differ significantly from those born to mothers of younger ages. Some studies point to a significantly more frequent need to admit these newborns in intensive care units – we did not include information on this in this study due to a lack of data (Cakmak Celik, Aygun, Kucukoduk, Bek, 2017; Mehta et al., 2014).

A limitation of our study is the lack of data of the prenatal diagnostic and information of sociodemographic data like level of education, employmed and civil status.

Conclusion

Women over 35 years of age are much more likely to be treated for infertility and have complicated obstetric histories due to prior miscarriages. Pregnancy at this age is associated with a risk of complications and health problems such as PIH and gestational diabetes. Children born to mothers over 35 years of age are born in good health.

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