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Spontaneous abortion in Astana: Associated factors, 2015-2017

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ABSTRACT

Background

Spontaneous abortion is the most common adverse pregnancy outcome. That is a great challenge for any healthcare facility and population health. The present study is aimed to investigate the associated risk factors of spontaneous abortion against normal delivery in population of Astana and provide reference for policy development of prenatal care.

Methods

A cross-sectional analysis was conducted based on the informational systems of inpatients records (67,759) from 2015 to 2017. This study used records of women with spontaneous abortions and normal delivery pregnancy outcome, older than 18. The prevalence risk ratio was calculated using the Poisson family with equal variances.

Results

The risk of miscarriage for women in age cohort 30-39 was 54% higher than for women in age cohort 19-29 (PRR = 1.54; 95% CI: 0.57 – 0.95). This risk was increasing for women of age older than 40 in comparison with reference group – 272% (PRR = 3.72, 95% CI: 3.22-4.30). The risk of spontaneous abortion was 0.73 times lower for women from rural area than in urban (PRR = 0.73, 95% CI: 0.57 – 0.95). Russian in comparison to Kazakhs had 0.76 lower risk of spontaneous abortion (PRR = 0.76, 95% CI: 0.65-0.90).

Conclusions

Generally, advancing maternal age was increasing the risk of spontaneous abortion. Ethnicity was associated risk factor, but only for Russians and Kazakhs. The residence influenced the

pregnancy outcome. Interventions could be targeted on women from high-risk groups in order to increase the maternity health indicators and population health.

ABBREVIATIONS

WHO World Health Organization

ERI Electronic register of inpatient form

FSHI Fund of Medical Social Health Insurance

CI confidence interval

etc. and so on (*et cetera*)

e.g. for example (*exempli gratia*)

GA Gestational age

hCG human chorionic gonadotropin

i.e. that is (*id est*)

NTD neural tube defect

NCJSC Non-commercial joint-stock company

OR odds ratio

SD standard deviation

vs versus

BACKGROUND

Spontaneous abortion

Spontaneous abortion, or miscarriage, defined as a loss of a pregnancy before fetal viability, from natural causes before the 20th week of gestation.¹ The World Health Organization (WHO) defines spontaneous abortion as expulsion or extraction of an embryo or fetus weighing 500 grams or less. Fetus or embryo is a term used to describe the developmental at less than 10 weeks of gestation.² Spontaneous abortion is classified, according to the gestational period at which it happens. Preclinical (subclinical or unrecognized) spontaneous abortion occurs before or at 5 weeks. Clinical (recognized) spontaneous abortion happens after pregnancy is clinically registered or women realize that she is pregnant. Clinical miscarriages occur at 6 to 20 weeks of gestational age.³ Pregnancy recognition influenced by individual circumstances like a missed menstrual cycle or visit gynecologist due to health problems were mistaken for pregnancy etc.

Spontaneous abortion is known as one of the most common complications of early pregnancy.⁴ The incidence rate of spontaneous abortion among clinical pregnancies approximately is 12–15%, if including early pregnancy losses, it is 17–22%.⁵ The problem of spontaneous abortion rates estimation is a difficulty of subclinical miscarriages identification. Most women do not recognize they had spontaneous abortion or pregnancy. Therefore, studies including preclinical spontaneous abortions yield higher rates (31%).⁶ Approximately

¹ Regan and Rai, 2000

² Johnson et al., n.d.

³ Uptodate.com, 2018

⁴ Regan and Rai, 2000

⁵ García-Enguádanos et al., 2002

⁶ Wilson, 2011

80% of the miscarriages occur during the first trimester, which lasts from early pregnancy through the 13th week of gestation. The frequency of miscarriage occurrence decreases with the increase of gestational period. The overall risk of spontaneous abortion after 15 weeks is low (about 0.6 %) for chromosomally and structurally normal fetuses.⁷

The most common etiological cause of miscarriage is the abnormal fetal karyotype. Approximately 50% of all miscarriages in the first trimester occur due to chromosomal abnormalities. On top of that, the causes of miscarriage may be other environmental toxins, infectious agents, deformations of the female reproductive organs, or chronic diseases of parents. Each of these factors in a certain period of pregnancy to varying degrees affects the incidence of miscarriages.

Risk factors

According to the studies numerous risk factors are associated with increased risk of pregnancy loss, but most reported are advancing maternal age, recurrent spontaneous abortions and maternal smoking, and caffeine consumption.⁸

Maternal age

Advancing maternal age is the risk factor of miscarriage for both chromosomally normal and abnormal fetuses. In the research associated with over 1 million clinically registered pregnancies, the overall risk of spontaneous abortion was increasing with age of women. At age of 35-year rate elevated by 9 to 17 percent, the age of 40 it was up to 40 percent and for women who were 45 years and elder it increased up to 80 percent.⁹

⁷ Huang et al., 2005

⁸ Andersen, 2000

⁹ Regan and Rai, 2000

Recurrent spontaneous abortion

Recurrent miscarriage is defined as two or more spontaneous losses.¹⁰ Recurrent spontaneous abortion or previous miscarriage is an important predictor of a pregnancy outcome. The risk for women to have a spontaneous abortion after previous one miscarriage is 12 percent, after suffering two miscarriage the risk rises to 29 percent, after three – 36 percent.¹¹ In comparison to those who had recurrent miscarriages, women with previous successful pregnancies represented lower occurrence of spontaneous abortion (5%)¹²

Tobacco smoking

In general, in Kazakhstan, there is a very high prevalence of smoking - 65.3% among men and 9.3% among women. Despite these indicators, a small proportion of these women in Kazakhstan smoke during pregnancy, as this is hampered by social norms and cultural characteristics of the country.¹³ Nevertheless, smoking is an aggravating factor for the outcome of pregnancy. The relative risks of miscarriage range from 1.2 to 3.4. Also, detrimental to a woman's pregnancy outcome is a smoking partner.¹⁴¹⁵ It has been scientifically proven that many constituent components of cigarettes are interrelated with the abortive outcome of pregnancy and increase the risk of miscarriages. Nicotine causes vascular spasms, which can be expressed in placental pathologies.¹⁶

Caffeine consumption

¹⁰ Van den Berg et al., 2012

¹¹ Risk factors for miscarriage identified, 2007

¹² Coste, Job-Spira & Fernandez, 1991

¹³ Gilmore et al., 2004

¹⁴ Barger, 1991

¹⁵ Lehtovirta & Forss, 1978

¹⁶ BRENT & BECKMAN, 1994

Caffeine increases the risk of spontaneous abortion by half if the daily dose is 500 milligrams.¹⁷ Caffeine is a substance present in many beverages of daily consumption. Basically, it is consumed through coffee with an average concentration of 107 milligrams per cup. In smaller concentrations, it can be found in tea, effervescent beverages, like cola, and in some pharmacological preparations.¹⁸

There are other risk factors that influence the pregnancy outcomes like drugs, alcohol, folate intake, previous induced abortions, uterine anatomic defects, menstrual disorders, etc.¹⁹

Outcome of spontaneous abortion

Every spontaneous abortion experience is different for women. Women who suffered several miscarriages could react in different ways for each episode. The spontaneous abortion could result in depression, anxiety and stress. Recurrent spontaneous abortion aggravates those emotional effects and could result in adverse psychological states²⁰. Not only mental health is influenced. With each incidence of miscarriage risk for next normal deliveries are decreasing. Risks are increasing with each spontaneous abortion occurred and decrease the possibility for next normal delivery, moreover recurrent spontaneous abortions could lead to infertility.²¹

In Kazakhstan there are no statistics provided for spontaneous abortion prevalence or incidence from 2003. Moreover, there were no studies conducted on women of fertile age regarding the risk factors associated with spontaneous abortion.

¹⁷ Fenster, Eskenazi, Windham & Swan, 1991

¹⁸ García-Enguñdanos, Calle, Valero, Luna & Domínguez-Rojas, 2002

¹⁹ Ibid.

²⁰ Bellieni and Buonocore, 2013

²¹ nhs.uk, 2018

AIMS

The overall objective of this thesis was to identify risk factors and risk groups of spontaneous abortion among women in Astana.

- The specific aims of the study included:
- To compare the occurrence of spontaneous abortion vs. normal delivery among women of different age categories in Astana
- To compare the occurrence of spontaneous abortion vs. normal delivery among women of living in urban area of Astana and rural area.
- To compare the occurrence of spontaneous abortion vs. normal delivery among women with different ethnicities in Astana.
- To compare the occurrence of spontaneous abortion vs. normal delivery among women with different occupation status in Astana.
- To compare the occurrence of spontaneous abortion vs. normal delivery among women in Astana depending of the period of pregnancy registered.
- To provide useful information for surveillance and intervention based on identified high risk groups

MATERIALS AND METHODS

Study design and settings

The study was conducted via cross-sectional study design based on secondary data obtained from the informational systems "Electronic register of inpatient form" (ERIF) and

“The register of pregnant women and women of childbearing age” (RPWWCA). The ERIF was developed in 2013 and RPWWCA was developed in 2014.²²²³ Both informational systems have unified data entry via parameters listed in user guides. Those user guides are developed and legislatively approved by the Ministry of Health (MOH). the Informational systems are stored and analyzed in SQL servers at Republican Center of Electronic Healthcare. Data access was approved by NCJSC “Fund of Medical Social Health Insurance”.

Subject selection information

All records of women with registered pregnancies that occurred between January the 1st of 2015 and December the 31st of 2017 in Astana were eligible for inclusion. Women under 18 years old were excluded from the analysis and were not approved for display due to ethical issues. Patients with normal deliveries and spontaneous abortion were included for analysis.

Data entry and cleaning

The data was provided in Russian and translated to English language in Excel. Two databases contained different variables, but unified IDs of patients. In order to merge two databases, the SQL phpMyAdmin free software tool written in PHP was used. Then the data was exported and analyzed in STATA 12 software. The data cleaning and entry lasted one month. Records containing missing values were dropped. Moreover, outlier and range technique were used for data cleaning.

²² Ministry of Health, 2014

²³ Minister of Health, 2015

Data analysis

The results of the study were analyzed using STATA 12 software. As the first step, the univariate analysis was conducted to characterize the results. In the next step, we performed a bivariate analysis. It was done to identify a statistically significant difference of factors and pregnancy outcome by Chi-square test for categorical variables and t-test for continuous variables. Hereafter, to indicate significant associations ($p < 0.25$) between risk factors and pregnancy outcome simple bivariate Poisson regression with robust equal variances was used. Finally, multivariate Poisson regression with robust equal variances with the outcome of spontaneous abortion vs. normal deliveries was used to identify the adjusted prevalence risk ratios. The Poisson regression is used for analysis of the cross-sectional study, as it provides correct estimates of the prevalence ratio and considered to be the better alternative rather than logistic regression.²⁴

Variables

The provided data from databases of inpatients were divided into categories and composed following parameters: 1) pregnancy outcome (spontaneous abortion vs. normal delivery); 2) maternal age categories (19-29 years, 30-39 years, 40+ years); 3) occupation (housewives, working and students); 4) ethnicity of patients (Kazakh, Russians and others); 5) residency (urban vs. rural); pregnancy period registered (trimester when women registered her pregnancy for the first time), year of admission (2015, 2016, 2017). According to the user guides of informational systems ERIF and RPWWCA, spontaneous abortion was a natural

²⁴ Blizzard and Hosmer, 2018

abortion with ICD10 code O 00.02 – O 00.03 occurring from early pregnancy to 22nd week of gestation. Normal delivery was a natural delivery without complications occurring from 37th to 41st weeks of gestation.²⁵

Ethical considerations

The ethical approval for the study was obtained from the Institutional Review Board of the Nazarbayev University School of Medicine. The research did not put at risk the participants and did not contain any identifiable information. The study concentrated on the information related to pregnancy outcomes.

RESULTS

In total, 119,184 records were extracted from the database. After excluding records with missing values (51,425 records), 67,759 records were enrolled in the analysis. Table 1 shows the sociodemographic characteristics of the sample from Astana city.

Table1. Demographic, socioeconomic and reproductive characteristics, by pregnancy outcome

²⁵ Minister of Health, 2015

	Spontaneous abortion	Normal delivery	Overall
Number of participants	2,376	65,383	67,759
Age category (%)			
19-29 years	46.97	60.72	60.24
29-39 years	45.12	36.42	36.72
40+ years	7.91	2.86	3.04
Mean (SD)	30 (0.12)	29 (0.02)	29 (0.02)
Residency (%)			
Urban	97.64	96.79	96.82
Rural	2.36	3.21	3.18
Occupancy (%)			
Housewives	56.40	64.09	63.82
Working	42.42	34.05	34.34
Student	1.18	1.87	1.84
Ethnicity (%)			
Kazakhs	86.32	84.86	84.91
Russians	6.61	7.79	7.75
Others	7.07	7.34	7.33
Period of pregnancy registered (%)			
1st trimester	91.37	58.20	59.36
2nd trimester	8.63	31.74	30.93
3rd trimester	0.00	10.06	9.71
Year (%)			
2015	30.56	36.38	36.18
2016	35.69	37.82	37.75
2017	33.75	25.79	25.07

Socio-demographic characteristics

The mean age (SD) for the whole sample was 29 years (0.02) overall, 30 years (0.12) in women with spontaneous abortions and 29 years (0.02) in women with normal deliveries. The overall difference in pregnancy outcomes was different between age categories. It is well seen that the difference is increasing with advancing maternal age. As the place of interest was the urban city, the percentage of rural residents was small (3.18 %). Overall, two-thirds of all

respondents were housewives and non-working women, only one-third were working or individuals on own labor and 1.84 percent from all records were students. According to pregnancy outcome, the difference was varying from one current occupancy to another. In case of normal deliveries, the proportion was almost the same with overall proportions. But this proportions changed a lot in case of spontaneous abortions. Women who were housewives accounted for more than half of all participants, working woman accounted for approximately 40 percent, and students took only 1 percent. Regarding ethnicity, most of the participants were Kazakhs (85%), Russians were 7% and for others 7%. Approximately 90% of all spontaneous abortions were experienced by women who registered their pregnancy in the 1st trimester with the proportion being lower in women who experienced normal deliveries (58.2%).

Factors associated with spontaneous abortion

Table 2 shows the prevalence risk ratio (PRR) of spontaneous abortion vs. normal deliveries, using the generalized linear model with equal variances. Bivariate analysis of comparison among all variables revealed that almost all the variables had the strong association with spontaneous abortion and normal delivery. The likelihood of spontaneous abortion among residents of rural area was 0.73 times lower than in residents of the urban area (PRR = 0.73, 95% CI: 0.57 – 0.95). The inverse association of advancing maternal age and risk of spontaneous abortion versus normal delivery was found. In the age category of 30 - 39 years the likelihood of spontaneous abortion increased to 54% (PRR = 1.54, 95% CI: 1.42 – 1.67) in comparison to age category 19 – 29 years. The likelihood increases dramatically for the age category of women 40 years older (PRR = 2.72, 95% CI: 3.22 – 4.30) in comparison to

reference group. The likelihood risk of spontaneous abortion among housewives represent the protective effect compared with working women (PRR = 1.09, 95% CI: 1.01 – 1.19).

As for effects of ethnicity on spontaneous abortion, the risk was reduced in Russians (PRR = 0.76, 95% CI: 0.65 – 0.90) compared with Kazakhs. Women who register their pregnancy in the second trimester (0.18, 95% CI: 0.15 – 0.20) represent decreased risk of spontaneous abortion in comparison of women who are registering in the first trimester. There was a remarkable increasing risk of spontaneous abortion with the later year (2017) of admission, compared with women admitted earlier in 2015 (PRR = 1.56, 95% CI: 1.41 – 1.72). Significant trends were found in residence, advancing maternal age, current occupation, ethnicity, the period of pregnancy registered and year of admission (all p-values are significant).

Table2. The prevalence risk ratio of spontaneous abortion associated different factors

Status	Prevalence risk ratio (PRR)	p-value	95% Confidence Interval
Residence (%)			
Urban (ref.)	1.00		
Rural	0.73	0.02*	0.57 - 0.95
Age category (%)			
19-29 years (ref.)	1.00		
30-39 years	1.54	< 0.01*	1.42 - 1.67
40+ years	3.72	< 0.01*	3.22 - 4.30
Current occupation (%)			
Housewife (ref.)	1.00		
Working	1.09	0.028*	1.01 - 1.19
Student	0.83	0.329	0.58 - 1.20
Ethnicity (%)			
Kazakh	1.00		
Russian	0.76	0.001*	0.65 - 0.90
Others	0.95	0.534	0.82 - 1.11
Period of pregnancy registered (%)			
1st trimester (ref.)	1.00		
2nd trimester	0.18	< 0.01*	0.15 - 0.20
3rd trimester	0.00	< 0.01*	0.00
Year of admission (%)			
2015 (ref.)	1.00		
2016	1.05	0.308	0.95 - 1.16
2017	1.56	< 0.01*	1.41 - 1.72

DISCUSSION

This study utilized the database from the governmental informational systems, investigating possible risk factors associated with spontaneous abortion among women in Astana. A clear effect of higher women age on the risk of spontaneous abortion, rather than of youngers. The prevalence risk ratio was increasing from one age category to another. This finding was consistent with results of international studies of risk factors associated to spontaneous abortion. In European study²⁶ represented increasing risks of spontaneous abortion with advancing maternal age. Moreover, they included age of the partner, which was identified as risk factor, too. If we compare this study to the research conducted in France in 1988, we could see that the risk of miscarriage in Astana is much higher than it was in France (COR for age cohort from 30-34 = 1.32; 95% CI: 0.87 – 2.02)²⁷.

According to the study, it was found that the risk of spontaneous abortion in women from the urban area was higher than from rural. Interestingly, this finding contradicts several researches done in this area. For example, in China women from rural area had higher risks for miscarriage than women from urban (Adjusted OR = 1.68, 95% CI: 1.54 – 1.84)²⁸. Other studies underlined the accessibility of healthcare for the population. Inconsistency of the study in comparison of rural vs. urban areas could be that Astana is the urban city by itself. According to the socio-geographical law, people living in the districts of Astana are urban living population. When, people registered outside of those three districts (Yesil, Almaty nd Saryarka) counted rural area population. In spite of registry as rural area population, those women have the same access to healthcare facilities. Thus, for better exploration of those risk

²⁶ De La Rochebrochard and Thonneau, 2002

²⁷ Coste, Job-Spira and Fernandez, 1991

²⁸ Zheng et al., 2017

factor further research conducted in other Kazakhstan regions with greater proportion of urban vs. rural population is needed.

Working women had slightly higher risk of spontaneous abortion when compared to housewives or non-workings. This risk factor was consistent with French study, where non-working status acted as protective factor against spontaneous abortion.²⁹ This prevalence risk ratio of spontaneous abortion among working women could be highly associated with stress that women are exposed on work.

The ethnicity also was an associated risk factor, Russian women had decreased risks of spontaneous abortion compared with Kazakhs. In the Post-Soviet countries such research of associated factors with spontaneous abortion were not found. Therefore, it was hard to compare ethnicity relation.

The risk factor of spontaneous abortion associated with the period of pregnancy registered was protective from miscarriages in the second trimester. So, it decreased only in women who registered their pregnancy in the second trimester when compared to women who registered in the first trimester. This association could be explained by several factors. Firstly, spontaneous abortion known to occur almost in 80% of cases in the first trimester. And the second reason, could be for less admissions to hospital regarding the pregnancy for women, who have less concerns or reasons to worry. In other words, women who have no problems with her pregnancy tend to register her pregnancy later and if her pregnancy goes beyond the period when her fetus could not survive (more than 20 weeks).

²⁹ De La Rochebrochard and Thonneau, 2002

The association of higher risk of spontaneous abortion was explored in the year of admission. The risk of miscarriage increased twice in 2017 when compared to 2015. This risk factor is hard to explain because no clinical protocols regarding the spontaneous abortion were found. This increasing risk could explain that the prevalence and risk of spontaneous abortion is increasing in Astana. However, the controversial fact that the prevalence risk ratio of spontaneous abortion in 2016 was insignificant did not allow to conclude so.

Strengths and Limitations

This study has several strengths to admit. The database was provided by the governmental company and used in the analysis for policy development. The significant number of records used in the analysis. Thus, it was possible to provide estimates with significant power due to large sample size and big number of spontaneous abortion cases. Secondly, this is the first study conducted in Kazakhstan among women of fertile age. This study could help to identify the high-risk groups for spontaneous abortion and provide the surveillance and intervention in time. Therefore, as the consequence, the maternity health would be protected and represent higher indicators of population health.

Limitation of the study is the cross-sectional study design. It was hard to determine whether the outcome followed exposure or exposure resulted from the outcome. It was suitable to use cross-sectional design as spontaneous abortion known to be non-rare pregnancy outcome – one in five pregnancies. It is impossible to measure the incidence of the spontaneous abortion with this study design. As we dropped almost 40% of records due to missing data, it was certain that those databases need more work to be done on data entry. Possible biases

as there is no information by whom and when the data entry was done. Data entry should be carried out during the patient visit. However, some hospitals do the data entry by patient history once in a month. Also, one of the biggest problems of spontaneous abortion registry is its underreporting. Women confuse it with abnormal menstrual period or hormonal abnormalities. The recommendation could be to develop the policy on prenatal care. To conduct and provide possibilities for screenings once in half a year. This screening will include the ultrasound checkup of women. Especially women of high-risk groups (elder women, 30+ years).

CONCLUSION

This study is analysis of associated risk factors with spontaneous abortion, revealing that spontaneous abortion is the most common adverse pregnancy outcome. The highly associated risk factors were: advancing maternal age, urban area residence, working current occupancy, and Kazakhs ethnicity. It provides important evidence about high-risk groups for accurate prenatal care policy development. Women working with higher ages from urban area need more attention, surveillance and treatment in time. In addition, further studies are needed to conduct such researches across the Kazakhstan and compare those risk factors with more detailed variables like recurrent spontaneous abortions, partners age and etc.

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