International Journal of Scientific Reports
Sekhavat L et al. Int J Sci Rep. 2024 Sep;10(9):315-319
http://www.sci-rep.com
pISSN 2454-2156 | eISSN 2454-2164
DOI: https://dx.doi.org/10.18203/issn.2454-2156.IntJSciRep20242368

Original Research Article

Influence of preconception paternal age on the spontaneous abortion: a retrospective study

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Received: 14 June 2024
Accepted: 15 July 2024

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ABSTRACT

Background: Due to the frequency of chromosomal abnormalities in sperm with increasing male age, the effect of increasing father's age as a cause of miscarriage is plausible, but there are still not enough studies available. The purpose of this study is to evaluate the effect of paternal age on spontaneous abortion.
Method: In a retrospective study conducted on the files in the archives of Shahid Sadoughi Hospital in Yazd from 2020 to 2021, we reviewed the cases of 824 nulliparous pregnant women without systemic diseases or any risk for abortion. All women were under 35 years old with singleton pregnancies and aborted their babies before 20 weeks. Information collected included paternal age and paternal BMI.
Results: A total of 104 cases were included in this study. In 10 cases, paternal ages were <20 in 15 cases, paternal ages were 20–30 in 35 cases, paternal ages were 31–40 and in 44 cases, paternal ages were >40 years. There was a significantly higher rate of abortion among paternal ages >40 years.
Conclusions: Our study demonstrates that paternal age has an impact on abortion. The incidence of abortion increases among older fathers.

Keywords: Gestational age, Nulliparous pregnant, Paternal age, Abortion

INTRODUCTION

Due to the frequency of chromosomal abnormalities in sperm with increasing male age, the effect of increasing father's age as a cause of miscarriage is plausible. However, there are still not enough studies available. In recent years, a growing body of literature has examined the influence of maternal age on adverse fetal birth outcomes.[1-3] The effect of maternal aging on chromosomal anomalies is well-known, and these anomalies play a role in the etiology of spontaneous abortion.[4,5] Recently, the average paternal age at the time of having a first child has been increasing.

From 1972 to 2015, data from the National Vital Statistics System showed that the mean paternal age in the US increased from 27.4 to 30.9 years.[6] Increased life expectancy, advanced age of marriage, and various socio-economic factors have led couples to start their families at a later age.[7] Most analyses show that advanced age of the male partners is associated with lower pregnancy rates, a higher risk of early spontaneous pregnancy loss, and may increase the occurrence of stillbirth or preterm birth.[8,9] In 2018, Oldereid et al evaluated the influence of paternal factors on a broad spectrum of perinatal and pediatric outcomes, finding associations between advanced paternal age and adverse outcomes in the offspring.[10] The age of the father and the mutation rate in the offspring are strongly related, possibly due to the larger number of germline divisions that have occurred in older males.[11]

Recent studies show that the sperms of older men are associated with increased chromosomal abnormalities.[12] Older fathers transmit these genetic and chromosomal defects to their offspring, increasing the incidence of

miscarriages. Moreover, advanced paternal age significantly increases the risk of chromosomal aneuploidy in embryos.[13] Moreover, recent studies report that women over 35 years of age are more likely to conceive a non-viable embryo, which can be a result of aberrant fertilization and/or impaired division of embryonic cells during preimplantation development.[8,14]

These genetic abnormalities in the fetus may originate in older mothers who have senescent eggs that have lost their DNA integrity, thus directly reflecting the effect of maternal age on increased miscarriage. Aged sperm cells, which carry 50% of the embryo's genetic material, can also be the cause of some of these DNA errors and miscarriages.[15,16]A new systematic review finds that advanced paternal age beyond 40 years is significantly associated with an increased risk of spontaneous miscarriage when adjusted for maternal age, especially in the first trimester of pregnancy.

Authors reported that if the father's age exceeded 45 years, the risk of pregnancy loss before 20 weeks increased by 43%, and before 13 weeks, it increased by 74%. Investigating the effect of paternal age on the risk of miscarriage is challenging. This study was designed to evaluate the influence of paternal age on the risk of spontaneous abortion under consistent maternal conditions.

METHODS

A retrospective study was conducted using files from the archives of Shahid Sadoughi Hospital in Yazd, covering the period from May 2020 to April 2021. We reviewed the cases of 824 nulliparous pregnant women without systemic diseases or any risk factors for abortion. All women were under 35 years old, with singleton pregnancies, and experienced abortions before 20 weeks of gestation. Information collected included demographic characteristics and pregnancy complications, such as diabetes mellitus and hypertensive disorders. Women with known clinical disease histories or those who underwent in vitro fertilization were excluded. Data analysis was performed using SPSS 20.A sample size of 900 was determined, assuming a confidence interval of 95% and 80% power. The Pearson chi-square test assessed differences among categorized paternal ages, and the McNemar test determined independence between groups. A p-value of less than 0.05 was considered statistically significant.

The study is retrospective, and information was obtained from archived files at the hospital. Prior to conducting the study, permission to use the files was obtained from the hospital's ethics committee. The funding for this research was provided by study authors.

RESULTS

In this retrospective study, we evaluated a total of 104 nulliparous mothers with singleton pregnancies that ended in abortion before 20 weeks of gestation. The comparison of maternal sociodemographic characteristics between paternal age groups is presented in Table 1. The comparison of paternal sociodemographic characteristics between paternal age groups is presented in Table 2.

Table 1: Comparison of maternal sociodemographic characteristics between paternal age.

Maternal characteristics	Paternal age <20 years	Paternal age 20-30 years	Paternal age 31-40 years	Paternal age >40 year	P value
	n=10	n=15	n=35	n=44	
Age (in years), N (%)					
<20	8 (80)	4 (27)	6 (17)	1 (2)	
21-30	2 (20)	10 (67)	19 (54)	36 (82)	0.1
31-35	0 (0)	1 (6)	10 (29)	7 (16)	
Body mass index(kg/m^2), N (%)					
<18.5	3 (30)	2 (13)	4 (11)	5 (11)	
1.8-25	5 (50)	12 (80)	28 (80)	30 (68)	0.2
>25	2 (20)	1 (7)	3 (9)	9 (21)	
Employment, N (%)					
Yes	2 (20)	9 (60)	16 (46)	20 (45)	0.09
No	8 (80)	6 (40)	19 (54)	24 (55)	
Educational level					
< 12	4 (40)	10 (67)	32 (91)	31 (70)	0.1
>12	6 (60)	5 (33)	3 (9)	13 (30)	
Prenatal care					
Adequate	7 (70)	14 (93)	27 (77)	33 (75)	0.07
Inadequate	3 (30)	1 (6)	8 (23)	11 (25)	

Table 2: Comparison of paternal sociodemographic characteristics between paternal age.

Paternal characteristics	Paternal age <20 years	Paternal age 20-30 years	Paternal age 31-40 years	Paternal age >40 year	P value
	n=10	n=15	n=35	n=44	
Body mass index(kg/m2), N (%)					
<18.5	0	1 (6)	0	1 (2)	
1.8-25	9 (90)	14 (93)	29 (83)	24 (55)	0.3
>25	1 (10)	0	6 (17)	10 (23)	
Employment, N (%)					
Yes	6 (60)	11 (73)	28 (80)	35 (80)	0.1
No	4 (40)	4 (27)	7 (20)	9 (20)	
Educational level, N (%)					
<12	6 (60)	6 (40)	12 (34)	15 (34)	0.07
>12	4 (40)	9 (60)	23 (66)	29 (66)	
Smoker, N (%)					
Yes	2 (20)	10 (67)	22 (63)	26 (59)	0.1
No	8 (80)	5 (33)	13 (37)	18 (41)	

Table 3: Comparison of gestational age of abortion in various paternal age groups.

Gestational age	Paternal age <20 years	Paternal age 20-30 years	Paternal age 31-40 years	Paternal age >40 year	P value
	n=10 (%)	n=15 (%)	n=35 (%)	n=44 (%)	
<12 weeks	7 (70)	10 (67)	21 (60)	25 (57)	0.3
12–15 weeks	1 (10)	2 (13)	9 (26)	10 (23)	
>15-20 weeks	2 (20)	3 (20)	5 (14)	9 (20)	0.07

In 10 cases, paternal ages were <20 years; in 15 cases, paternal ages were 20–30 years; in 35 cases, paternal ages were 31–40 years; and in 44 cases, paternal ages were >40 years. There was a significantly higher rate of abortion among paternal ages >40 years. After adjusting for the mother's age, the risk of spontaneous abortion associated with paternal age was 1.4 times higher for ages 31-40 years and 1.8 times higher for ages >40 years compared to fathers under 30 years old. The highest rates of abortion were observed among infants with fathers aged >40 years, while the smallest rates were among fathers aged <20 years.

Smoking status did not significantly affect the rate of abortion in this study. Table 3 shows the gestational age at the time of abortion in relation to paternal age. Although the difference between the ages of abortions in the paternal age groups was not significant, the second trimester abortion.

Table 3 shows the gestational age at the time of abortion in relation to paternal age. Although the difference in abortion rates among paternal age groups was not statistically significant, the results indicate a higher ratio of second-trimester abortions in fathers over 40 years old.

DISCUSSION

This study reveals a paternal age effect on pregnancy loss before 20 weeks of gestation. Specifically, pregnancies with paternal ages over 40 are associated with a higher incidence of miscarriage. Paternal ages 40 to 45 years old showed a 22% higher likelihood of stillbirth compared to fathers aged 25 to 29 years. Additionally, pregnancies with paternal ages over 40 years old had 28% more miscarriages compared to those with paternal ages under 30 years old.

Previous studies confirm these findings of increased risk of adverse birth outcomes among older fathers.[8,9,16,17] A systematic review and meta-analysis by du Fossé et al combined data from various studies, demonstrating significant paternal age effects in age categories 40–44 and ≥45, thereby increasing statistical power. Individual studies often had limited sample sizes in advanced age groups, similar to our study.

While many risk estimates in these categories were not statistically significant alone, pooling effect measures across studies provided clearer insights.[16] We evaluated the methods used to adjust for maternal age in the included studies. Most studies carefully adjusted for maternal age by either matching cases and controls or treating maternal age as a continuous variable using orthogonal coding.[8,18] In our retrospective study, we used a maternal age cutoff of 35 years and excluded mothers over this age. Muncey et al reported an association between increasing paternal age and higher rates of miscarriage, possibly linked to paternal sperm DNA damage. They found that sperm DNA fragmentation

index (DFI) and DNA damage doubled between ages 20 and 60 years.[15] However, their study also showed that the odds of chromosomal abnormality-related miscarriage were higher among the youngest fathers (20–24 years old) compared to those aged 25–29 years. In this study, there was no statistically significant effect of paternal age ≥30 years on the risk of chromosomal aberrations-related miscarriages.[12] Contrary, Zhiyuan et al, in their study reported that there was no statistically significant effect of paternal age≥30 years on the risk of chromosomal aberrations-related miscarriages.[7] There was no statistically significant effect of paternal age ≥30 years on the risk of chromosomal aberrations-related miscarriages. Similar to our findings, previous research consistently associates advanced paternal age with an increased risk of spontaneous abortion.[7,8,18-20] Kleinhaus et al specifically reported a significant association between increasing paternal age and spontaneous abortion.[19]

In contrast to our results, Erdogan et al recently found no association between paternal age and increased miscarriage rates. Their study focused on couples undergoing in vitro fertilization, highlighting the specificity of their findings.[21]

CONCLUSION

This study underscores the significant impact of paternal age on pregnancy outcomes, particularly miscarriage rates. Delaying fatherhood may elevate the risk of miscarriages, especially before 12 weeks of gestation. Additionally, our study found no significant effect of paternal smoking on miscarriage rates.

Funding: No funding sources
Conflict of interest: None declared
Ethical approval: The study was approved by the Institutional Ethics Committee

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Cite this article as: Sekhavat L, Tabatabaie RS. Influence of preconception paternal age on the spontaneous abortion: a retrospective study. Int J Sci Rep 2024;10(9):315-9.