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Clinical Science

Pregnancy Outcome in Women of Advanced Maternal Age: A Cross-Sectional Study in a Turkish Maternity Hospital

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Key words: advanced maternal age; risk factors; prematurity; neonatal morbidity; neonatal mortality.

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Abstract

Background: There is a current trend towards delayed childbearing around the world. This is considered to increase the risk for poor maternal and neonatal outcomes. In this study, we evaluated pregnancy outcomes in women of advanced maternal age in a single maternity hospital in Turkey.

Methods: Medical records of 517 women aged 35 years and older that gave birth between 2009 and 2010 were examined retrospectively. The chi-squared, Mann-Whitney U, and Student t tests were used for statistical analyses.

Results: In total, 462 (89.3%) women aged 39 years or less and 55 (10.6%) women aged 40 years and older were included in the analysis. Cesarean sections, and neonatal mortality were more common in women of advanced maternal age ($p = 0.004$ and $p=0.002$, respectively). Neonatal mortality (OR: 0.1; 95% CI 0.02–1; $p = 0.032$), premature birth (OR: 0.4; 95% CI 0.2–0.8; $p = 0.008$), and low birth weight (LBW) (OR: 0.2; 95% CI 0.1–0.5; $p < 0.001$) were significantly higher in women 40 years and older. Respiratory distress syndrome (RDS) developed in 26% of babies with LBWs. All patients of neonatal death were diagnosed with asphyxiation or RDS.

Conclusions: At the Bolu Izzet Baysal Maternity and Children's Hospital, advanced maternal age was associated with increased adverse fetal and neonatal outcomes.

Introduction

Pregnancies are characterized as high risk when they happen at an early age or advanced age, and in cases of multiparity and short inter-pregnancy intervals. Pregnancies in women of advanced maternal age have become increasingly more common, particularly in developed societies, for reasons that may include higher educational attainment among women, women entering the workforce and developing careers, mental preparation for motherhood, and increased socio-economic status [1, 2]. However, as the age at pregnancy increases, the possibility of becoming pregnant decreases, the pregnancy process becomes more difficult, and the risks of ending with a miscarriage or having babies with anomalies increase [3-5]. High-risk pregnancies are of special importance due to the increased prenatal morbidity and mortality risk for the mother, fetus, and newborn [2, 6].

According to Turkish Population and Health Research (TNSA) 2008 data, the fertility rate in women over 35 years old in Turkey is 4.7%. In addition, pregnancies that happen at over 35 years of age and that have higher pregnancy- and birth-related morbidity and mortality make up 12.2% of pregnancies in Turkey [7]. Age-related medical problems and chronic diseases are observed more frequently in these pregnancies. However, there are also publications indicating that there is no difference in neonatal outcome between older and younger pregnancies [8].

The aim of our study was to examine the effects of advanced maternal age on subsequent

pregnancy outcomes, using medical records from the Bolu Izzet Baysal Maternity and Children's Hospital, Turkey.

Materials and Methods

Setting/population sample

Patient records between January 1, 2009, and December 31, 2010, at Bolu Izzet Baysal Maternity and Children's Hospital were assessed retrospectively with the approval of the local ethics committee. Among the medical records, pregnant women over 35 years of age and their infants were included in the study. Those with files that had incomplete data, and babies born before 24 gestational weeks were excluded. The other 4392 pregnant women and their babies who gave birth within the same period were selected as the comparison group.

Definitions of the measures and variables

The mothers' ages, pregnancy numbers, gestational ages, modes of delivery, birth weights, first and fifth Apgar scores, and Cesarean section indications were assessed from the medical records. The gestational week was determined according to the recordings of the last date of menstruation, if known, and if not, with prenatal ultrasound. The gestational age was decided according to prenatal ultrasound when last date of menstruation and ultrasound were not in agreement. Fetal (intrauterine) death and neonatal (between 0–28 days postnatal) death were recorded. Fifth-minute Apgar scores ≤ 7 were accepted as an asphyctic birth (9). Macrosomia was defined as a birth weight of 4000 g and above, and LBW was defined as less than 2500 g. Newborns with clinical problems were monitored in the neonatal intensive care unit (NICU) until they were clinically stable. RDS was diagnosed in babies according to clinical symptoms (tachypnea, cyanosis, groaning, and intercostal retractions) and radiological symptoms (reticular granularity presence, ventilation of lungs, and deficiencies in compliance and air bronchograms). Serum glucose and calcium levels were studied from babies' blood received within the first 2 h of life.

Statistical Analyses

The records of patients were entered into a database prepared with the SPSS software (ver. 15.0 for Windows; SPSS Inc., Chicago, IL). The results are provided as averages (standard deviation). The chi-squared test, Mann-Whitney U-test, and Student's t-test were used to assess results, and p values < 0.05 were considered to indicate statistical significance.

Results

Characteristics of the study population

In total, 4909 births occurred in the study period. Of these, 517 (10.5%) of the women aged 35 years and older who gave birth were of advanced age. A comparison of the advanced maternal age and under 35 years of maternal age groups is presented in Table 1. A total of 40 (7.7%) of the pregnant women were nulliparous while 477 (92.2%) were multiparous. There was a significant difference in numbers observed in women of advanced maternal age compared to women aged 35 years or less in parity (p<0.0001), mode of delivery (p=0.004) and neonatal mortality (p=0.002) only.

Table 1: Characteristics of the study population.

Specifications		Advanced maternal age (>35 years) (n:514)	Normal maternal age (<35 years) (n:4392)	p value
Parity * (Min-max)		2.8 ± 1.1 (1-8)	1.3 ± 0.8	<0.001
Gestational age (weeks)* (Min-max)		38.1 ± 1.9 (24–43)	38 ± 0.8	0.28
Birth weight (g)* (Min-max)		3259 ± 603 (600–5120)	3263 ± 510	0.85
Apgar 1* (Min-max)		8.7 ± 1.3 (3–10)	8.8 ± 0.9	0.73
Apgar 5* (Min-max)		9.7 ± 1.2 (5–10)	9.8 ± 0.8	0.64
Asphyxiation**		16 (3.1)	85 (1.9)	0.079
Mode of delivery**	Cesarean	280 (54.1)	2082 (47.4)	0.004
	Vaginal	237 (45.8)	2310 (52.6)	
Gender**	Female	258 (49.9)	2174 (49.5)	0.86
	Male	259 (50)	2218 (50.5)	
Mortality**	Fetal mortality	6 (1.1)	31 (0.7)	0.25
	Neonatal mortality	5 (0.9)	7 (0.1)	0.002

*: Mean±SD, **: n (%)

Main findings

Of the mothers, 462 (89.3%) of them were 35-39 years old while 55 (10.6%) were 40 years and older (Table 2). Neonatal mortality was determined in 3 (0.6%) of the babies born to mothers 35-39 years old and in 2 (3.6%) of those 40 years and older.

Table 2: Comparison of babies born to mothers 40 years and older versus women aged 35-39 years.

Specification (%)	n	35-39 years old (*n* = 462)	40 years and older *n* = 55)	OR	95% CI	p value
Fetal mortality		4 (0.9)	2 (3.6)	4.3	0.7–24.1	0.070
Neonatal mortality		3 (0.6)	2 (3.6)	0.1	0.02–1	0.032
Prematurity		82 (17.7)	18 (32.7)	0.4	0.2–0.8	0.008
LBW		34 (7.4)	12 (21.8)	0.2	0.1–0.5	<0.001
Asphyxiation		12 (2.6)	4 (7.3)	0.3	0.1–1	0.058
Admittance to neonatal intensive care unit		64 (13.9)	8 (14.5)	0.9	0.4–2	0.88
Additional admittance diagnosis		51 (11)	9 (16.4)	0.6	0.2–1.3	0.24

Premature birth was determined in 82 (17.7%) of the babies born to mothers 35-39 years old and in 18 (32.7%) of the over-40 group. LBW was determined in 34 (7.4%) of the babies born to mothers 35-39 years old and in 12 (21.8%) of the over-40 group. These differences were statistically significant (OR: 0.1; 95% CI 0.02–1; p = 0.032, OR: 0.4; 95% CI

0.2–0.8; p = 0.008, and OR: 0.2; 95% CI 0.1–0.5; p < 0.001, respectively). Fetal mortality occurred in 4 (0.9%) mothers 35-39 years old and in 2 (3.6%) of the 40 and over years group. Asphyxiation occurred in 12 (2.6%) babies born to mothers 35-39 years old and in 4 (7.3%) mothers 40 years and older. These differences were not statistically significant (OR: 4.3; 95% CI 0.7–24.1; p = 0.07, and OR: 0.3; 95% CI 0.1–1.1; p = 0.058, respectively).

Indication for Cesarean section

Over half (54.7%) of the babies born were delivered by Cesarean section. Previous Cesarean section (*n* = 125, 24.1%) was the most common indication for undergoing another Cesarean section, followed by pre-eclampsia and eclampsia (*n* = 32, 6.1%), cephalopelvic disproportion (*n* = 23, 4.4%), breech presentation (*n* = 14, 2.7%), and fetal distress (*n* = 10, 1.9%).

Additional admittance diagnosis

Sixty patients had an additional admittance diagnosis (Table 3). Of them, 43 (8.3%) were tracked due to neonatal jaundice, 12 (2.3%) due to RDS, 8 (1.5%) due to transient tachypnea of newborns, 5 (0.9%) due to sepsis, 3 (0.5%) due to meconium aspiration syndrome, and 1 (0.1%) due to cleft palate-lip. RDS was detected in 12 (26%) of the babies with LBWs. Of the infants hospitalized, polycythemia was detected in 4 (0.7%), hypocalcemia in 7 (1.3%), and hypoglycemia in 11 (2.1%). Five (0.9%) live-born babies were lost during the neonatal period due to asphyxiation. One (0.1%) of them was mature and four (0.7%) were advanced premature babies.

Table 3: Additional admittance diagnoses of the babies.

Additional diagnoses	*n* (%)	Neonatal death (*n*)
Cleft palate-lip	1 (0.1)	-
Meconium aspiration syndrome	3 (0.5)	-
Sepsis	5 (0.9)	-
Transient tachypnea of newborn	8 (1.5)	-
Respiratory distress syndrome	12 (2.3)	5
Neonatal jaundice	43 (8.3)	-

Discussion

Lower numbers of babies and an increase in late pregnancies has increased in countries with higher incomes in recent years. By 2004, advanced maternal age in the UK had increased to more than twice the rate in the 1990s and reached 18.2% of all pregnancies [10]. According to TNSA 2008 data, women of advanced maternal age made up 12.2% of all pregnancies in Turkey [7]. Advanced maternal age was reported to be 7.8% in Çetinoğlu et al. [11] and 12.6% in Jolly et al. [12]. In the present study, advanced maternal age accounted for 10.5% of all pregnancies.

Advanced maternal age has been associated with adverse pregnancy outcome including preterm birth, hypertension, pre-eclampsia, hypertension, intrauterine growth restriction, and placental abruption also increase [13]. Şekeroğlu et al. [14] reported a premature birth rate of 23.6%. We found an elevated rate of preterm births (19.3%). Premature births increase in proportion to increased pregnancy age [15]. Similar findings were obtained in the current study.

Chronic medical problems, decreased cardiovascular reserves, and a decreased ability to adapt to physical stresses in connection with these factors are considered to be fundamental factors that increase morbidity and mortality [16]. The intrauterine fetal mortality ratio increases in advanced-age pregnancies for different reasons. The reason for observing fetal mortality more frequently is the chromosomal and structural anomalies observed at advanced ages [4]. In Tough et al. [17], fetal mortality was 0.9% for these kinds of pregnancies. The risk of fetal mortality increases in direct proportion to age in pregnancy. In a previous study, the ratio of fetal mortality was 0.4% in advanced maternal age and 3.5% in very advanced maternal age [18]. Fetal mortality did not increase with age in our study population, consistent with Cnattingius et al. [19].

The ratio of births with LBW has also increased. Çetinoğlu et al. [11] reported that 11.4% of babies are born at a LBW. The rate of 8.8% detected in our study may be due to the fact that these pregnant women were followed more closely at our hospital. LBW increased with age in our study population, consistent with the literature [20].

In addition to doctor and patient concerns over increased medical problems during pregnancy in advanced-age mothers, decreases in myometrial function and increases fetal distress with increasing age are considered to be fundamental factors that increase the incidence of birth by Cesarean sections [21]. Cesarean sections were used in 35.2% of cases in Yogev et al. [20] and in 65.4% of cases in Çetinoğlu et al. [11]. In our study, 54.1% of the births were delivered by Cesarean sections. Cesarean sections in the advanced maternal age group (p = 0.004). The high ratio of Cesarean sections in our study was attributed to the fact that Cesarean sections are generally performed in this population at our hospital.

Özçelik et al. [22] found that a previous Cesarean section was the most frequent indication for having a Cesarean section. This was also the most frequent indication in our study. The high ratio was attributed to the hospital having a high primary Cesarean section rate in general. Other indications included preeclampsia-eclampsia, cephalopelvic disproportion and breech presentation.

The risk of fetal anomalies increases in advanced maternal age. Fetal anomalies were detected in 3.8% of the cases in Şekeroğlu et al. [14].

Çetinoğlu et al. [11], however, found no congenital malformation in their evaluation. We detected fetal anomalies at 0.1% in our study. One reason why few fetal abnormalities were identified in our study could be that miscarriages were caused by the chromosomal abnormalities that are frequently encountered in such pregnancies [17].

One of the most significant outcomes in this kind of pregnancy is that asphyxiation, which can affect the individual's entire life negatively, has increased. On the other hand, Wang et al. [23] found out that asphyxiation did not increase with increasing age. While asphyxiation was confirmed in 0.4% of babies born to advanced-age mothers in Akyol et al. [18], it was detected in 4.2% of babies born to mothers of very advanced maternal age [18]. In our study, birth asphyxia did not increase in parallel with age.

Along with the increase in maternal and perinatal problems in advanced-age pregnancies, the ratio of admittance of newborn babies to ICUs also increases for different reasons. The mortality rates of babies can be significantly decreased with the care provided in these units. In Şekeroğlu et al. [14], 9.7% of newborn babies were admitted to ICUs. In our study, 13.9% of the babies were admitted to NICUs for various reasons. Admittance to ICUs increases in direct proportion to perinatal problems that increase with the age of pregnancy. About 6% and 11%, and 7.4% and 8.7%, of babies born to mothers of advanced maternal age and very advanced maternal age were reported in Akyol et al. [18] and Yogev et al. [20], respectively. In our study, the increase in the mother's age was not directly proportional with hospitalizations in the NICU, as in Yogev et al. [20]. One reason for this may be that the rates of premature birth and LBW we identified for the neonates were below the levels in the literature.

It is widely accepted that RDS is the most important perinatal morbidity and mortality factor in newborns. Prematurity and LBW is the most important factors increasing the frequency of RDS. RDS has been observed in 5.8% [24] and 23.3% [25] of babies with LBW. In the present study, RDS was confirmed in 26% of babies born with a LBW.

Jacobson et al. [15] reported that in addition to giving birth to babies with LBW, neonatal mortality also increased along with the mother's age. Similar findings were obtained in the current study. Yogev et al. [20] reported 0.6% neonatal deaths in advanced-age mothers and 0.7% of very-advanced-age pregnancies. The neonatal mortality ratio, which was 0.9% in advanced-age pregnancies in our study, increased to 3.6% as the mother's age increased ($p = 0.032$). All of the babies that died during the neonatal period in our study were diagnosed with asphyxiation and RDS; this shows that perinatal follow-up of these babies should be rigorous.

The possibility of developing hypoglycemia and hypocalcemia is very high in babies with LBW and babies that are born prematurely, because they have low glycogen and calcium depots. Hypoglycemia has been reported at 25%, hypocalcemia at 20%, and polycythemia at 8% for premature babies and babies with LBW [26, 27]. Erdem et al. [28] reported that hypoglycemia was detected in 9.7%, hypocalcemia in 17.7%, and polycythemia in 1.6% of premature and low-weight babies. Our low ratios were attributed to the small numbers of samples.

The limitations to this study other than the small sample size need to be addressed, including that confounders were not adjusted for in the analyses which is a major limitation.

In conclusion, despite technological developments, the rates of perinatal morbidity and mortality remain high in advanced maternal age. We believe that by explaining the risks of advanced maternal pregnancies, we can decrease these health problems. We also recommend that the babies are delivered and followed up in centers that have sufficient experience and appropriate equipment to decrease these morbidity and mortality rates.

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