

## **Problems of Older Maternal Age and Pregnancy Outcome**

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**Objective:** To examine pregnancy outcome at age 40 and older.

**Setting:** King Fahd University Hospital, Al-Khobar.

**Methods:** The study population consisted of women who delivered at age 40 or over between January 1995 and December 2002. The control population was women who delivered between age 20 and 29 years during this 8 year period.

**Results:** Thirty one thousand and eight hundred women delivered during the study period. One thousand two hundred and seventy two (4%) women were age 40 or older, of which 1202 (3.7%) were included this study, of these 254 (21%) were nullipara. The cesarean delivery rate for these patients was 42.0%, while multipara women it was 26.0%. In the control group cesarean rate was 19.5% for nullipara and 12.8% for multipara women. In the older age group the operative vaginal delivery rate was 11.2% for nullipara and 4.6% for multipara women compared to 5.3% and 2.0% respectively among the younger group. The following rates were significantly higher among older nulliparas: asphyxia 5%, growth retardation 2%, malpresentation 7% and gestational diabetes 6% compared with younger nullipara controls (2.5, 1, 2.5, 1.8% respectively). There was similar significant increase among older multipara compared with younger multipara controls. Birth weight of infants delivered by older nullipara women were significantly lower than that among younger nullipara controls ( $P<.01$ ). However, mean birth weight in the group of older multipara was no different than that of younger multipara controls. Gestational age at delivery was significantly lower among older nullipara, compared with younger nullipara controls ( $P<.01$ ), and similarly lower among older multipara, compared with multipara controls.

**Conclusion:** Women aged 40 or over have a higher risk of operative delivery than younger nullipara women. Rates for birth asphyxia, growth restriction, malpresentation and gestational diabetes were significantly higher among older nullipara respectively compared with younger nullipara controls. There were similar significant increases among older multipara compared with younger multipara controls. Birth weight of infants delivered by older nullipara women were significantly lower than younger nullipara controls ( $P<.01$ ). Gestational

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***Bahrain med Bull 2004;26(4):***

Historically, women who desired to become pregnant after the age of 35, often were discouraged from considering pregnancy because of the increase in both maternal and perinatal morbidity and mortality<sup>1-3</sup>. The increased incidence of underlying medical diseases, decreased cardiovascular reserve, and diminished ability to adapt to physical stress that may accompany aging could combine to increase perinatal and maternal morbidity or even mortality. However, medical literature on this topic is composed largely of reports of studies involving small population of patients, with the majority of patients being multiparous, or reports of data collected over many years and in the setting of changing practice patterns<sup>4</sup>. In recent years, it was noted that when patients of advanced maternal age were followed and delivered their infants in a modern tertiary care center, no increase in adverse outcome was noted<sup>5-10</sup>.

This controversy encouraged to compare the obstetric and maternal outcome of patients age 40 or over with those with a control group of patients aged 20-29 years who delivered during the same period.

## **METHODS**

This is a retrospective cohort study of 1202 essentially healthy women.

The patients were divided into Saudi Arabs and Asians or non-Saudi. This was done as the majority of patients are locals. King Fahd University teaching hospital is a tertiary referral hospital for the Eastern Province of Saudi Arabia and serves a clinically diverse population. During these years, senior obstetric nurses working exclusively in the labor room entered information on all deliveries into labor room registers.

The population was mixed of Arabs and Asians consisted essentially of healthy women who delivered infants of 500 gm or more at the age of 40 years or over between January 1995 and December 2002. These women had no known chronic medical condition. Seventy women above 40 years of age were excluded from this study, as they had chronic medical condition.

A control group of patients was obtained by retrieving records of delivered patients who were 20-29 years of age on the day of delivery, during this study period. These women had no known chronic medical condition.

Each of these groups was divided into nullipara and multipara subgroup. Ethical Committee approval was obtained prior to this study.

Statistical Analysis: As racial differences existed we calculated adjusted odds ratio (ORS) comparing deliveries of women aged 40 years or older with deliveries of women aged 20-29 stratified by parity. SAS software (SAS Institute Cary, NC) was used. The statistical protocol of Gilbert et al was adopted for this study<sup>11</sup>. All analyses of pregnancy outcomes was risk adjusted for race to remove the effect that this factor has on outcome.

## RESULTS

During the 8-year study period 31,800 women delivered; and out of that 1272 (4%) were age 40 years or older; and eventually 1202 (3.7%) women were admitted into the study.

The control population (age 20-29) was composed of 19,080 women (60% of the 31,800 women that delivered). Nine thousand three hundred and forty-nine (49%) of them were primipara and 9731 (51%) multipara.

**Table 1. Demographic and Gestational characteristics**

	Nulliparous		Multiparous	
	≥40 yrs. n= 254	20-29 yrs. n= 9349	≥40 yrs. n= 948	20-29 yrs. n= 9731
Maternal race				
Saudi Arabs	38	68	74	59
Asians	61	32	26	31
Delivery mode (%)				
Cesarean	*42.0	19.5	*26.0	
Forceps}	*4.5	2.1	1.2	0.8
Vacuum}	6.7	6.0	3.4	1.2
Mean Gestational Age (weeks)				
Singletons	*38.1 ± 0.4	39.6 ± 0.5	*38.4 ± 0.2	39.4 ± 0.5
Twins (n=7)	36.2 ± 0.1	NIL	36.1 ± 0.2	NIL
Triplets (n=1)	2015 ± 2	NIL	NIL	NIL
Mean birth weight (gms)				
Singletons	3214 ± 8	3312 ± 21	3381 ± 2	3386 ± 3
Twins	2252 ± 4	NIL	2352 ± 5	NIL
Triplets	2015	NIL	NIL	NIL
Deliveries (n)				
Singletons	254	9349	948	9731
Twins	7	NIL	3	
Triplets	1			

Data are presented as % or mean ± standard error  
\*P<0.05 for nulliparous and multiparous groups.

Of the 1202 women aged 40 years and above 254(21%) were nullipara, and 948 (82%) were multipara. The cesarean delivery rate for these nullipara patients was 42.0% and 25.6% for multipara women. In the control group cesarean rate was 19.5% for nullipara and 12.8% for multipara women. In the older group, the operative vaginal delivery rate was 11.2% for nullipara and 4.6% for multipara women compared to 5.3% and 2.0% respectively among the younger group. Cesarean and operative vaginal delivery (forceps and vacuum) rates were significantly higher in the older nullipara and multipara group compared with the younger control group.

Three patients received blood transfusion after cesarean delivery, 2 for post-partum hemorrhage and one for placenta praevia. These complications occurred among the older pregnant women.

Mean ( $\pm$  standard error) birth weight of infants delivered by older nullipara women  $3101 \pm 89$  was significantly lower than that among younger nullipara controls  $3281 \pm 29$ . However, mean birth weight in the group of older multipara was no different than that of younger multipara controls. Gestational age at delivery was significantly lower among older nullipara ( $38.1 \pm 0.4$  weeks), compared with younger nullipara controls ( $39.6 \pm 0.5$  weeks), and similarly lower among older multipara, compared with multipara controls.

There were no significant racial differences among the Saudi and non-Saudi (Asian) women under study.

Multiple pregnancies were limited to the older group and were all (8/8), delivered by cesarean section. The cesarean delivery was not related to prior parity within this cohort. The multiple pregnancies were delivered prematurely, the majority, electively at  $36.2$  weeks  $\pm 0.1$  weeks. One patient required the delivery of twins at 34.3 weeks for acute onset of severe pre-eclampsia. The triplets had elective cesarean at 34.1 weeks. There was no incidence of respiratory distress syndrome in any infant.

In the control Group two patients with singleton pregnancies were delivered prematurely at 34.4 and 35.2 weeks respectively for severe pre-eclampsia. Two patients carrying singleton pregnancies experienced premature rupture of membranes at 34 and 36 respectively, and were hospitalized till delivery. The neonates had no complications.

There were no maternal deaths in both the study and control groups. Also, there were no cases of congenital anomalies.

Table 2 depicts that there were statistically significant increase in the rates of most complications of pregnancies among the nullipara age 40 or older compared with the other groups. These increases were seen in both maternal medical complications and complications of labor.

Table 2. Ante partum and Intrapartum Complications

Diagnosis	Nulliparous (%)		*Adjustment OR (95% CI)	Multiparous (%)		OR (95%CI)
	≥40 y (s)	20-29 y(c)		≥40 y	20-29 y	
Gestational Diabetes	6.4	1.8	4.7 (3.7,6.0)	7.0	2.0	4.1(3.2,4.8)
Malpresentation	6.9	2.5	2.7 (1.6,2.9)	11	3.7	2.4(1.8,2.4)
Obstructed Labour	8.9	3.8	1.3 (1.1,1.6)	0.9	0.3	1.5(1.3,1.8)
Abnormal Forces Labor	12.6	10.8	1.3 (1.2,1.4)	5.8	2.7	1.4(1.3,1.5)
Prolonged Labor	3.2	2.5	1.2 (1.1,1.4)	0.9	0.6	1.2(1.1,1.8)
Cephalo-fetal disproportion	10.6	5.8	1.4 (1.2,1.6)	2.8	1.6	1.6(1.4,1.7)
Preeclampsia	6.4	3.8	1.8 (1.6,2.1)	2.7	1.0	3.1(2.8,3.2)
Chronic Hypertension	1.5	0.3	4.7 (3.7,6.0)	1.9	0.3	8.9(7.8,0.2)
Placenta Previa	0.11	0.03	10.5 (3.4,6.0)	0.19	0.04	2.4(1.2,3.6)
Prematurity	13.1	8.1	1.7 (1.6,1.8)	11.1	9.3	1.2(1.2,1.4)
Post term delivery	5.2	10.1	0.4 (0.3,0.5)	5.4	10.1	0.45(0.3,0.6)
Intrauterine Growth Retard	2.1	1.2	1.6 (1.3,2.1)	1.4	1.0	1.4(1.2,1.4)

\*Adjusted for race

OR: Odds ratio; CI: Confidence interred

The incidence of pre-eclampsia was appreciably greater in women older than aged  $\geq 40$  years.

Among the study group women of older women aged  $\geq 40$  years all 13.4% of diabetic patients required insulin; and were all gestational diabetics. In comparison, gestational diabetes was noted in only 3.8% of the young women, who was well controlled by diet modification.

The rate of birth trauma was less in the older nullipara group of patients, compared with the control patients, probably because of the increased cesarean delivery rate in the older group. Neonatal death rate was increased among the older multipara patients compared to the nullipara aged  $\geq 40$  years and the control group.

Table 3. Neonatal Complications

Diagnosis	Nulliparous (%)		*Adjusted OR	Multiparous(%) * Adjusted OR		
	≥40 y (s)	20-29 y (c)	(95%CI)	≥ 40 y (s)	20-29 y (c)	(95%CI)
Birth Trauma	4.2	5.1	1.7 (0.7,1.8)	2.8	3.0	1.8(1.2,2.1)
Birth Asphyxia	2.1	2.5	2.1 (1.6,2.9)	1.9	1.7	1.4(1.1,1.8)
Intra ventricular hemorrhage	0.1	0.1	1.3 (1.1,1.6)	0.9	0.03	1.5(1.3,1.8)
Neonatal death	0.2	0.17	1.6 (0.6,2.1)*	0.4	0.2	1.9(1.3,2.1)

\*Adjusted for race

OR: Odds ratio; CI: Confidence intervals

## DISCUSSION

The maternal and neonatal outcome in pregnant women aged 40 years and above were compared with those of young women aged 20-29 years. Although intuitively and factually, it was felt that the younger women would rate favorable outcome measures, as our study population, “a healthy one” with no chronic medical illnesses, we were curious to see how acute the comparison would be<sup>5-10</sup>.

Operative delivery: As depicted in Table 1, the elderly primigravidas are at high risk for some form of operative delivery (cesarean delivery 42.0%, operative vaginal delivery 11.2%), compared with younger women in the control group (cesarean delivery 19.5%, operative vaginal delivery, 5.3%). The multipara women in the study group also had significant increase in rates of operative deliveries compared with younger controls. This significantly increased operative delivery rate especially cesarean deliveries may be explained by factors such as: (1) Increased incidence of ante-partum complications (Table 2), and the high risk nature of these pregnancies. The increased incidence of mal-presentations among the older nullipara patients, also contributed to the increase in cesarean delivery rates in this group.

Multiple gestation was observed among the older patients exclusively, which could be the outcome of assisted reproduction or as a sequela of aging.

### Complications of Pregnancy

Gestational Diabetes was increased dramatically in the study group (Table 2) both in nullipara and multipara patients (5 and 3.5 fold respectively), compared to the control group, which suggests that maternal age rather than parity is involved in the

increase in this disease. An analogous increase in the rate of gestational diabetes with increasing maternal age was reported by Mestman<sup>13</sup>. In that series, the incidence of gestational diabetes was reported to be 3.7% in women younger than 20 years and 13.8 % in women >30 years. In the current series, 13.4 % of women in the study group had gestational diabetes, controlled by Insulin. Gilbert et al reported pregnancy outcomes in 24,032 cases above 40 years quoted the incidence of gestational diabetes as 14.8%<sup>11</sup>. Paulson et al discussing pregnancy in the 6<sup>th</sup> decade reported that 12.5% of women had gestational diabetes mellitus controlled by diet and only 2.5% had their diabetes controlled by insulin<sup>5</sup>. The above figures suggest that the trend towards higher rates of gestational diabetes with age continues after 50 years of age representing 3-4 fold increase in incidence compared to younger women<sup>2</sup>.

**Pre-eclampsia:** In a recent series reported in 2002<sup>2</sup>, the incidence of pregnancy induced hypertension (PIH) was 9.6% in women older than 40 years compared to 2.7% in younger gravidas 20-30 years of age. The observed rate of 6.4% among the elder primigravidas in the current study represents an almost 3 fold increase compared with younger gravidas (Table 2). Gilbert et al had similar results<sup>12</sup>. Pre-eclampsia is also more common among primigravidas as was noted in all 3 studies (Present one, Mestman and Gilbert et al<sup>11,13</sup>).

Intrauterine Growth Retardation was observed in older patients who had almost 2 fold chance of having fetal growth retardation, compared to the younger gravidas. This could be attributed substantially to the increased incidence of hypertension and pre-eclampsia in these women (Table 2).

Placenta Previa was 5 fold increase in the incidence of placenta previa in the older nullipara women, compared with the corresponding younger patients. Multiparity has long been known to increase the risk of placenta previa, and our data along with that of Gilbert et al supports this<sup>5</sup>.

Singleton infants (Table 1) born to both the study and control groups of multipara patients had similar mean birth weight suggesting that maternal age may not affect birth weight as much as other factors. The older nullipara patients were associated with the lowest birth weights and the highest cesarean delivery rates.

Mean gestational age for the study population at delivery was statistically lower than that for the control population, even when parity was taken into account. The cause may relate to underlying maternal or fetal problems such as diabetes, pregnancy induced hypertension, fetal distress.

The rate of birth trauma was decreased in the older nullipara group of patients, compared with the control patients, probably because of the increased cesarean delivery rate in the older group. Among the mature primi gravidas, there was 1.5 fold increase in birth asphyxia and an almost 2 fold increase in intraventricular hemorrhage compared to the younger women. . These results are consistent with

those reported in the older literature that cited increases in perinatal morbidity and mortality<sup>1-4</sup>. In spite of these complications, the majority of neonatal outcomes were good with no increase in neonatal death among the older nullipara patients, and a slight increase in these rates among the older multipara patients, compared with the controls. There were no infant deaths in either group.

The fact that many of the outcome rates in this study are similar to those found in studies involving smaller and a few larger populations suggests that there was a reasonable degree of reliability<sup>12</sup>. One of the limitations of the study is that the data was taken from labour room registry and that the quality of diagnosis reporting could vary. Although most of the data such as birth weight, gestational age are reliable, other more obscure outcomes may be missed. However, major outcomes such as cesarean or operative vaginal delivery are likely to be recorded correctly. A computerized data base is in the process of being established in this big teaching hospital.

## CONCLUSION

**Women aged 40 or over have a higher risk of operative delivery than younger nullipara women. Rates for birth asphyxia, growth restriction, malpresentation and gestational diabetes were significantly higher among the older nullipara respectively compared with younger nullipara controls. There were similar significant increases among older multipara compared with younger multipara controls. Birth weight of infants delivered by older nullipara women were significantly lower than that among younger nullipara controls (P<.01). Gestational age at delivery was significantly lower among older nullipara, compared with younger nullipara controls (P<.01), and similarly lower among older multipara, compared with multipara controls. Additional work is needed in the area of complications of pregnancy in older women and birth outcomes so that better management protocols may be developed.**

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