

## Adverse outcome of pregnancy following air travel: A myth or a concern?

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### Abstract

**Objective:** To assess whether air travel elevates the risk of adverse pregnancy outcomes in essentially healthy women with single non-anomalous fetuses at a gestational age greater than 20 weeks.

**Methods:** A retrospective analysis of air travel during the current pregnancy and pregnancy outcome was undertaken in 992 women admitted for delivery over a 12-month period. The study group of 546 (55%) women, of whom 57% were primigravidae, travelled at least once during pregnancy, and were compared with a control group of 447 women (45%), of whom 54% were primigravidae, who did not travel by air.

**Results:** The primigravidae in the study group showed an increased risk of preterm birth, and this risk was statistically significant between the gestations of 34 and 37 weeks (adjusted odds ratio 1.5, 95% confidence intervals 1.2, 1.8); this risk remained elevated after adjustment for covariates. These women's pregnancies were appreciably shorter than those of primigravidae who did not fly ( $36.1 \pm 0.8$  vs.  $39.2 \pm 2.1$  weeks) and their babies had lower birthweights ( $2684 \pm 481$  vs.  $3481 \pm 703$  g). and were more likely to be admitted to the neonatal intensive care unit. This group of air travellers is unusual for the uncommonly long and frequent duration of air travel, which is not routinely undertaken in most parts of the world. There were no thromboembolic events complicating any pregnancies.

**Conclusions:** Primigravid women who travel by air appear to be at higher risk for preterm birth. Multicentre large studies are required to confirm or refute these findings.

**Key words:** air travel, birthweight, pregnancy, preterm delivery.

### Introduction

Not only is there paucity of literature to verify effects of air flight on pregnancy<sup>1</sup> but to confound matters, it tends to be controversial. The American College of Obstetricians and Gynaecologists (ACOG)<sup>2</sup> currently recommends that pregnant women can safely fly up to 36 weeks of gestation. Contradicting this statement is a study from Finland in 1999<sup>3</sup> that noted a 30% increased risk of spontaneous abortion among flight attendants who worked in early pregnancy. An elegant study, performed in 2004,<sup>1</sup> although on a small cohort of women, concluded that air travel during pregnancy did not seem to pose a significant risk to the pregnancy.

In the Middle East, expatriates from countries such as Asia (Indian subcontinent, Philippines, China) and Africa (Egyptians, Sudanese) form a considerable part of the workforce, along with colleagues from Australia and New Zealand. This eastern region of Saudi Arabia, well established for its universities along with its group of tertiary teaching hospitals, is essentially a university town. An expatriate workforce, with their families, mainly comprise of health-care providers, faculty members of various universities and their respective domestic

maids. This university workforce, along with significant numbers of female nurses and teachers, travel regularly by air and, at times, over long distances.

This study was undertaken as there were no data available from this region addressing the unique conundrum of long and frequent air travel during pregnancy.

### Methods

A retrospective analysis was undertaken in essentially healthy women with single anomalous fetuses, at a gestational age of > 20 weeks, to assess whether air travel elevated the risk of

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adverse pregnancy outcomes. These women attended the antenatal clinics of the university teaching hospitals that are designated tertiary care centres between May 2003 and May 2004. By and large, all pregnant women have their entire antenatal care at these government hospitals. Written consent for this study was obtained from the King Faisal University Ethical Committee, along with informed consent from all patients.

All women admitted for delivery singleton over the specified 12-month period with pregnancies of > 20 weeks gestation were asked if they travelled by air during the current pregnancy. The women who travelled at least once during pregnancy were designated as the study group and were compared with those who did not travel (the control group).

The women were asked if they travelled by air during pregnancy, and if so, to provide details of the gestational age at flight, destination, length of flights and any complications during travel. The study design was based on the protocol of Freeman *et al.*<sup>1</sup> Medical history, obstetric complications and pregnancy outcome information was obtained by chart review, by an investigator who was blinded to flying status. Maternal age, race, parity, chlamydia infection, history of infertility, medications during pregnancy, haematocrit at first prenatal visit and time of delivery, preceding pregnancy complications, gestational age at delivery, history of adverse pregnancy outcome, birthweight, admission to neonatal intensive care unit (NICU).

Women with any prepregnancy complications, such as renal, cardiovascular, pulmonary or immune disease were excluded from the study, as were those with vaginal bleeding, those administered tocolysis for premature labour, and those with fetal or neonatal structural or chromosomal anomalies.

The high incidence of female health-care providers and teachers in this university town assisted with determination of educational and economic status. Smoking and alcohol use were denied by these patients, the former being a social taboo and the latter a religious one. Pregnancies were dated by an early ultrasound confirmation of pregnancy, and this was followed by serial scanning.

### Statistical analysis

Mann-Whitney test compared variables between women who did and did not travel during pregnancy. Chi-squared and Fisher's exact tests were used where appropriate. We estimated the association between air travel and dichotomous birth outcomes (preterm delivery) using logistic regression models.<sup>4</sup> All analyses were stratified by parity and adjusted for maternal age, prepregnancy body mass index (BMI, kg/m<sup>2</sup>), social status of mother and sex of the baby.

The association between air travel and birthweight was examined by fitting linear regression models using covariates<sup>4</sup> as defined. The association between air travel and low birthweight at term was estimated restricting analysis to births occurring from 37 weeks onward. To assess<sup>1</sup> whether longer flights have a heavier statistical impact than shorter flight, and whether the time of gestation when flight occurs impacts the outcome, a weighted average gestational age at flight was

created,<sup>1</sup> (duration of 1st flight \* gestational age + duration 2nd flight \* gestational age, etc/total hours airborne). To assess whether time of gestation when flight occurs impacts the outcome, a variable of cumulative hours airborne by all patients at each trimester of pregnancy was calculated.<sup>1</sup>

A composite adverse pregnancy outcome variable was also used to increase the power to detect a significant adverse effect of air travelling. The composite variable<sup>1</sup> consisted of the summation of stillbirth, 5-min Apgar score, delivery at < 37 weeks, pre-eclampsia, and birthweight < 10th centile. Linear and logistic regression analysis was used to control for confounding variables. A two-tailed  $P < 0.05$  or an odds ratio with 95% confidence interval (CI) not inclusive of unity was considered statistically significant.<sup>1</sup>

The odds ratio (OR) of adverse birth outcomes associated with air travel was estimated. We adjusted for covariates<sup>4</sup> and stratified on parity. Logistic regression analysis was performed, taking into account maternal race and other demographic variables.

### Results

Nine hundred and ninety-two consecutive singleton pregnancies of > 20 weeks gestation, admitted for delivery over the specified 12-month period, were studied. The women studied were essentially healthy with mean (SD) age 23.8 (2.9) years; range, 16–49 years.

The study group (group A) of 546 (55%) of women travelled at least once during pregnancy, and consisted of 312 (57%) primigravidae (A1) and 234 (43%) multiparae (A2). The control group (group B) consisted of 447 (45%) women who did not air travel, and was made up of 241 (54%) primigravidae (B1) and 206 (46%) multiparae (B2).

The women in the study group (A) flew for the first time in their pregnancy at a gestational age of  $11.2 \pm 2.2$  weeks (mean  $\pm$  standard deviation), with average flights lasting  $7.8 \pm 1.2$  hr, and a median of 7 flights (range 1–18). Control group B consisted of 447 women (45%) who did not travel by air; 241 (54%) of this group were primigravidae (B1).

The characteristics of the women in the two groups are shown in Table 1. Women who travelled by air were significantly more likely to be expatriates, rather than Saudi nationals. Haematocrit at delivery did not vary appreciably between the study and control groups. Haematocrit levels both initial and at delivery remained similar between groups. No other variables differed significantly between the two groups. There was no occurrence of thromboembolism or neonatal death in either group.

Among primigravidae, air flight during pregnancy was associated with an increased risk of preterm births at < 37 and > 34 weeks of gestation (Table 2) (adjusted odds ratio (OR) 1.5; 95% CIs 1.2, 1.8) and this remained elevated after adjustment for covariates. Among these women, gestational age at delivery was appreciably lower ( $36.1 \pm 0.8$  weeks) with lower birthweights ( $2684 \pm 481$  g) when compared with the controls ( $39.2 \pm 2.1$  weeks;  $3481 \pm 703$  g). There was a consequent increase in admissions to the neonatal intensive care

**Table 1** Demographic characteristics of 992 women in relation to air travel during pregnancy

Variable	Group A (Air travel – Yes) ( <i>n</i> = 546)	Group B (Air travel – No) ( <i>n</i> = 446)	<i>P</i> value
Maternal age	22.3 ± 5.6	23.1 ± 5.4	NS
Primigravids	312 (57%)	241 (54%)	NS
Race			
Expatriates	399 (73%)	210 (47%)	< 0.01
Saudi nationals	147 (27%)	237 (53%)	< 0.01
Socioeconomic status			
High	292 (53%)	200 (48%)	NS
Middle	167 (31%)	155 (35%)	NS
Low	87 (16%)	92 (21%)	NS
Education			
Higher education	371 (68%)	277 (62%)	NS
Secondary school or less	174 (32%)	125 (28%)	NS
Gestational age at initial haematocrit (weeks)	10.6 ± 4.0	10.8 ± 2.6	NS
Haematocrit at delivery (%)	34.5 ± 2.6	34.8 ± 2.8	NS

Data presented as percentage or mean ± SD.

NS, not significant.

**Table 2** Ante-intra-post partum variables in relation to air travel during pregnancy study group A (air travel – yes) and control group B (air travel – no). Data presented as percentages

Variables	Primigravidae			Multigravidae		
	Group A1 ( <i>n</i> = 312)	Group B1 ( <i>n</i> = 234)	Adjusted OR (95% CI)	Group A2 ( <i>n</i> = 241)	Group B2 ( <i>n</i> = 212)	Adjusted OR (95% CI)
Pre-eclampsia	5	6.4	0.91 (0.44, 1.72)	4.5	6.4	1.19 (0.62, 2.10)
Vaginal bleeding	2.6	3.3	1.24 (0.59, 2.11)	2.9	3.6	1.27 (0.58, 2.18)
Birth < 34 week	5.2	2.3	2.01 (0.59, 6.12)	3.4	2.2	1.52 (0.69, 3.15)
Birth > 34 < 37 weeks	14.4	9.1	*1.5 (1.2, 1.8)	8.2	7.8	1.02 (0.58, 2.18)
Birthweight < 10th centile	2.1	1.4	1.24 (0.49, 2.7)	1.1	1.8	2.17 (1.21, 4.58)
Caesarean section	18	17.8	1.32 (0.58, 3.01)	17.2	18.1	1.46 (0.72, 3.09)
Admission to NICU	4.9	2.8	1.27 (0.58, 2.18)	2.2	3.1	1.25 (0.80, 1.95)
Stillbirth	NIL	NIL	–	NIL	NIL	–
Neonatal death	NIL	NIL	–	NIL	NIL	–

Air travel – yes (group A):

A1 Gestational age at delivery (mean ± SD) = 36.1 ± 0.8 weeks and birthweight 2684 ± 481 g; A2 Gestational age at delivery (mean ± SD) = 39.2 ± 2.1 weeks and birthweight 3481 ± 703 g.

Air travel – no (group B):

B1 Gestational age at delivery (mean ± SD) = 39.1 ± 1.1 weeks and birthweight 3407 ± 700 g; B2 Gestational age at delivery (mean ± SD) = 39.4 ± 1.4 weeks and birthweight 3502 ± 400 g.

\*Significant determinants/elevated risks.

unit; however, the risk was not significantly elevated. Among the primigravidae who travelled by air, regression analysis showed a definite relationship between gestational age at delivery and gestational age at first air travel ( $r = 0.002$ ,  $P = 0.01$ ) and also total hours airborne ( $r = 0.012$ ,  $P = 0.01$ ). In the multigravidae who travelled by air (study group A2) no such relationship was noted between gestational age at delivery and gestational age at first air travel ( $r = 0.006$ ,  $P = 0.82$ ) or total hours spent airborne ( $r = 0.029$ ,  $P = 0.68$ ).

A whole group analysis revealed that air flight during pregnancy was associated with an increased risk of preterm

births at < 37 and > 34 weeks of gestation (Table 3). Among these women, gestational age at delivery was appreciably lower with lower birthweights. Although the risk factor decreased regression analysis showed a definite relationship between gestational age at delivery and gestational age at first air travel ( $r = 0.004$ ,  $P = 0.05$ ) and also total hours airborne ( $r = 0.012$ ,  $P = 0.05$ ).

It was reassuring that between those who did or did not travel by air, there were no differences or elevated risks of rates of vaginal bleeding, pre-eclampsia, Caesarean birth or birth asphyxia/neonatal death.

**Table 3** Group analysis in relation to air travel during pregnancy: study group A (air travel – yes) and control group B (air travel – no)

Variables	Group A ( <i>n</i> = 546) %	Group B ( <i>n</i> = 446) %	Adjusted OR (95% CI)
Pre-eclampsia	9.5	10.9	1.29 (0.69, 2.4)
Vaginal bleeding	5.9	6.5	1.20 (0.64, 2.24)
Birth < 34 week	7.7	5.6	1.25 (0.8, 1.95)
Birth > 34 < 37 weeks**	23.5	16.0	2.21(1.08, 4.52)
Birth weight < 10th centile	3.5	2.9	1.57 (0.78, 3.18)
Caesarean section	35.8	35.3	1.53 (0.70, 3.35)
Admission to NICU	7.7	5.3	2.35 (1.26, 4.44)
Stillbirth	NIL	NIL	–
Neonatal death	NIL	NIL	–

\*\*Significant determinants/elevated risks.

Air travel – yes (group A): gestational age at delivery (mean  $\pm$  SD) = 36.95  $\pm$  0.8 weeks and birthweight 3045  $\pm$  200 g.

Air travel – no (group B): gestational age at delivery (mean  $\pm$  SD) = 39.1  $\pm$  1.1 weeks and birthweight 3491  $\pm$  10 g.

Because of the presence of significant differences in the racial distribution of the study population, regression analysis was performed<sup>1</sup> to determine whether the lack of a significant association between air travelling and composite adverse pregnancy outcomes persisted after correcting for maternal age, race, parity and trimester of air travel. No individual variable was significantly or independently associated with adverse neonatal outcome.

## Discussion

In our study, primigravidae who travelled by air were at increased risk for preterm delivery with corresponding lower birthweights (Table 2). Risk estimates remained elevated even after adjusting for several factors that might potentially affect both preterm delivery and birth outcome. Among primigravidae who travelled by air, regression analysis showed a definite relationship between gestational age at delivery and gestational age at first air travel ( $r = 0.002$ ,  $P = 0.01$ ) and also total hours airborne ( $r = 0.012$ ,  $P = 0.01$ ). The risk factor appeared to persist (Table 3), even on whole group analysis of the data.

The primigravidae who did travel by air, did so early in pregnancy (first flight taken at 11.2  $\pm$  2.2 weeks), with long (average flights lasting 7.8  $\pm$  1.2 hr) and frequent flights (median 7 flights, range 1–18) during their pregnancy. Foreign workers, especially primigravidae, who are often not conversant with the surrounding lifestyle, find the strict codes (e.g. of dressing and lifestyle) challenging, especially during months of intense heat, and elect to travel frequently. The multigravidae have often lived in these regions for some time and are comparatively more settled. Their air travel tended to be later in pregnancy (first flight 13.8  $\pm$  1.8 weeks) with a lesser number of shorter flights (5.6  $\pm$  3.6 hr; median 4 flights.) and, thus, less stress.

Not surprisingly, such complications were noted more frequently among expatriates travelling to and fro from far lands such as New Zealand/Australia/Philippines to the Saudi Arabian kingdom.

On long commercial flights,<sup>3–5</sup> travelling at 39 000–41 000 ft, cabin pressure is maintained at the equivalent of an altitude pressure of 8000 ft, while at 32 000 ft (for shorter flights), cabin pressure is set at an equivalent of 6000 ft. The conditions at a cabin pressure of 8000 ft will create a more hypoxic environment than those at 6000 ft. At 6000 ft oxygen consumption in pregnant women is 13% (L/min) lower than at sea level, in comparison with non-pregnant women for whom the decrease is only 3% lower. These changes are associated with a decrease in partial oxygen pressure, which should not affect normal pregnant women. However, a study from Finland in 1999<sup>3</sup> detected a 30% increased risk of spontaneous abortion among healthy flight attendants who worked during early pregnancy compared with those who did not.

In a recent elegant study of 118 women who travelled by air, the authors<sup>1</sup> concluded that air travel during pregnancy does not seem to pose a significant risk to the pregnancy. In this study,<sup>1</sup> the first flight was taken at a later gestational age than our primigravidae (13.3  $\pm$  7.6 vs. 11.2  $\pm$  2.2 weeks), and the average flight lasted for an appreciably shorter duration (4  $\pm$  2 vs. 7.8  $\pm$  1.2 hr).

When we adjusted for factors such as age, socioeconomic status, the associations between air travel and preterm delivery decreased in magnitude, indicating that these factors may explain some of the association. However, significant associations still remained.

A potential confounding variable in the study is the significant racial difference in women who did and did not travel. However, the higher rate of expatriate women who travelled compared to the resident Saudi Arabian population did not reflect a sociodemographic difference between the two groups (Table 1) as there was no significant difference regarding education and economic status between the study and control groups.

Logistic regression analysis was performed taking into account maternal race as well as other variables such as demographic, and there was a lack of significant associations between air travel and adverse pregnancy outcomes such as pre-eclampsia or rates of vaginal bleeding.

Although there was an increase in admissions to the neonatal intensive care unit, among the babies of the primigravidae, in the study group as a direct result of preterm delivery (Table 2), there were no instances of neonatal complications such as respiratory distress syndrome or intraventricular haemorrhage. Although preterm, these births occurred at a mean of  $36.1 \pm 0.8$  weeks, with a fairly reassuring birthweight of  $2684 \pm 481$  g. This could possibly account for the lack of serious complications.

One of the major strengths of this study is that our data on gestational age were reliable, and this increased the accuracy of determination of preterm births and allowed appropriate adjustment for gestational age when looking for effects on birthweight. A constraint of the study was that smoking and alcohol consumption, important variables, were not disclosed factually. We were unable to evaluate whether air travel influences miscarriages rates by virtue of the study design. We cannot exclude the possibility that some pregnancies followed a period of undisclosed infertility or chlamydia infection. Both these factors can contribute towards preterm labour.<sup>28</sup>

There is paucity of data addressing the issue of air travel and pregnancy outcome. Such research is vital, in defining new strategies for preventing adverse birth outcomes. The sample size is relatively larger than other such studies.<sup>1</sup>

## Conclusions

This research defined the relationship between air travel and a possible elevated risk of preterm delivery among primigravidae, which needs further validation. The unusual factor

is the very long and frequent duration of air travel in the study population, which is not routinely undertaken in most parts of the world, appears to have been a contributory factor. It is essential that any possibility of risk be defined to create awareness among researchers, so that future large multicentric studies may be undertaken not only to confirm or refute these findings, but also for physicians to counsel patients on the safety of frequent and long hours of air travel during pregnancy.

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