ORIGINAL ARTICLE

Evaluation of differences in pregnancy complications and outcomes by fetal gender

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Abstract:
Objective: To assess the effects of fetal gender on obstetric and neonatal outcomes.
Material and Methods: Medical records of obstetric patients admitted at The Aga Khan Hospital for Women Garden, Karachi from January 2020 to December 2021 were reviewed. All patients with singleton pregnancies with either male or female fetuses delivered between 33 to 41 weeks of gestation were included in this study. Patients with congenital anomalies, multiple pregnancies, and previous cesarean delivery were excluded. The patient's age, parity, gestational age, gestational diseases, mode of delivery, neonatal weight, gender and Apgar score were collected on a structured questionnaire. The maternal and neonatal outcomes and their association with fetal gender were measured. The comparisons were made using chi-square or student t-test. The maternal outcomes wererisk of pregnancy-induced hypertension (PIH), gestational diabetes (GDM), breech presentation, fetal growth restriction, placental abruption, previa and mode of delivery. The neonatal outcomes were birth weight, Apgar'sscore, nursery/NICU admission and neonatal death.
Results: A significant association was found between fetal gender and obstetrical risk factors. Pregnancy-induced hypertension was found higher among pregnant women with male fetus 2.7% than female 1.9%, gestational diabetes 8% in male babies and 6.5% in female. Cesarean deliveries were higher in women with male babies 55.4% than 44.5% of female. 5.1% of male neonates were admitted in NICU than females 4.7%.
Conclusion: In our study population the pregnancies with male fetus was found to be associated with higher adverse effects on pregnancy and neonatal outcomes.

Keywords: Fetal gender, pregnancy outcomes, risk factors, gestational diabetes

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Introduction:
Fetal gender has an important role to not only affects the course and complications related to pregnancy but also affects maternal health and well being during and after pregnancy, due to interactions between mother, placenta, and the fetus. The placenta has an active role in maternal and fetal blood circulation and is not only responsible for fetal development but also regulating physiological changes during pregnancy and several related complications due to placental dysfunction.[1] The interplay between the mother and placenta is gender dependent, some pregnancy related complications like gestational diabetes (GDM) and pre-eclampsia showed differences in occurrence which are fetal gender specific.[2]

Gestational diabetes affects pregnant women with poor pancreatic beta-cell function and sub optimal insulin secretion resulting in antepartum hyperglycemia. Fetus not only affects maternal beta-cell function but is also connected with the natural history of maternal diabetes risk after delivery and in the subsequent pregnancy.[3,4]

Fetal gender has a major impact on pregnancy

outcomes which are different between male and female pregnancies.[5] Gender difference has been associated with unfavorable pregnancy outcomes like increased incidence of pre-term birth, pre-term pre-mature rupture of membranes, arrest of labor, cord prolapse, fetal macrosomia and increased frequency of cesarean section for particular sex.[6] In Caucasians, there is an increased risk of preterm delivery before 37-weeks in pregnant women which is gender dependent.[7]

Whereas there is a gender-specific association of better outcomes with lower NICU admission[4] although no difference was found in mortality rate between both genders.[8] It is also suggested that there may be significant fetal gender related differences in electronic fetal monitoring patterns among term pregnancies without evidence of acidemia.[9]

There may be a fetal gender-based difference in pregnancy and neonatal outcomes in pregnancy but why do pregnancies with male babies adversely affect antenatal and course of labor. The answer is hypothetical.

Some studies have found out the association between fetal gender and pregnancy outcome.[5,10] These studies were conducted in western countries where as there are limited reports published in Asia.[11] Although the association between fetal gender and pregnancy outcome are not same in different ethnicity[7] more information is required to be collected in the local context to assess gender-specific pregnancy outcomes in our population.

Thus, the objective of our study is to determine the effect of fetal gender on obstetrics and neonatal outcome in babies delivered at a secondary hospital in Pakistan.

Material and Methods:

A retrospective medical record review was conducted at The Aga Khan Hospital for Women Garden a secondary care hospital in Karachi, Pakistan. There view included all pregnant womens with singleton pregnancies from January 2020 to December 2021 with either male or female fetuses delivered between 33 to 41 weeks of gestation. Pregnancies with congenital anomalies, intra-uterine death (IUD), multiple pregnancies and patients with previous cesarean section were not included in the study. Patient's age, parity, gestational diseases, gestational age on the date of delivery, mode of delivery, neonatal weight, gender and Apgar's were collected from the medical record on a structured questionnaire. The study was approved by the Ethical review committee of the Aga Khan University Hospital. The study outcomes were increased risk of pregnancy-induced hypertension (PIH), gestational diabetes (GDM), breech, fetal growth restriction, placental abruption, previa, and mode of delivery. The neonatal outcomes were birth weight, Apgar's score, nursery/neonatal intensive care unit (NICU) admission and neonatal death.

The software Excel was used to organize relevant patient data obtained for the study. Data were analyzed after importation into Statistical Package for Social Sciences Software version 19. Descriptive analysis was done by estimating the means and standard deviation of continuous variables and the proportion for categorical variables. We compared maternal and neonatal outcomes concerning the gender of the baby through chi-square or students t-test based on data requirement. A two-sided p-value of 0.05 is considered statistically significant.

Results:

Overall, 3713 singleton pregnancies were included with either male or female fetuses delivered at The Aga Khan Hospital for Women over the study period. Table 1 represents the baseline characteristics of the patients. The mean age of the pregnant women was 28.51 years (SD±4.997). Out of total, majority i.e., 60.9% (n= 2262) of patients were of age 26-34 years, followed by 25.3% (n=941) 17–25 years, and 13.7% (n=510) ≥ 35 years. The mean gestational age of pregnant women was 39.42 weeks (SD±65.3). 93.9% (n=3486) of women were presented with 37-41 gestational weeks followed by 5.8% (n= 217) 33 – 36 gestational

Table 1: Maternal characteristics (N=3713)

Age in years (n=3713)	28.51±4.997
17 - 25	941 (25.3%)
26 - 34	2262 (60.9%)
≥ 35	510 (13.7%)
Parity (n=3710)	1.37±1.506
Primipara	2078 (56%)
Multipara (2 – 4)	1404 (37.8%)
Grand Multipara (≥ 5)	228 (6.1%)
Gestational age in weeks (n=3703)	39.42±65.31
33 – 36 wks	217 (5.8%)
37 – 41 wks	3486 (93.9%)
Body Mass Index (n=3711)	28.06±5.052
< 18.5	48 (1.3%)
18.5 – 22.9	448 (12.1%)
23 – 27.5	1340 (36.1%)
> 27.5	1875 (50.5%)

Table 2: Comparison of Obstetrical risk factors & pregnancy outcomes with fetal gender (N=3713)

Obstetric Risk Factor (n=1118)	**Male**	**Female**	**P-Value**
Pregnancy Induced Hypertension	100 (2.7%)	70 (1.9%)	0.010
Gestational Diabetes	294 (8%)	243 (6.54%)	
Chronic Hypertension	16 (0.4%)	13 (0.3%)	
Fetal Growth Restriction	124 (3.3%)	164 (4.4%)	
Breech	29 (0.78%)	39 (1.0%)	
Placenta Abruption	5 (0.1%)	7 (0.2%)	
Placenta Previa	7 (0.2%)	7 (0.2%)	
Pregnancy Outcome (n=3021)			
Normal Vaginal Delivery	1246 (33.6%)	1329 (35.8%)	0.458
Instrumental Delivery	99 (2.7%)	108 (2.9%)	
Meconium-Stained Liquor	99 (2.7%)	108 (2.9%)	
PPH	20 (0.5%)	12 (0.32%)	
Cesarean Section (n=935)	518(44.4%)	417(44.5%)	
Elective	82 (2.21%)	83 (2.23%)	0.104
Emergency	436 (11.7%)	334 (8.9%)	

Significant p-value <0.05

weeks. The mean parity of women was 1.37 (SD±1.506). The majority i.e., 56% (n= 2078) of women were primiparous, followed by 37.8% (n=1404) multiparous, and 6.1%(n=228) grand Multipara. The mean BMI of patients was 28.06 kg/m^2 (SD ±5.052). 50.5% (n= 1875) of women had BMI >27.5, followed by 36.1% (n=1340) 23–27.5 BMI, 12.1% (n=448) 18.5 – 22.9 BMI, and 1.3% (n=48) had BMI < 18.5.

Table 2 summarizes the comparison between the obstetrical risk factors and pregnancy outcomes with fetal gender. A significant association was found between fetal gender and obstetric risk factors (p-value=0.01). PIH was found to be higher among pregnant women with male fetuses in comparison to females (2.7% vs. 1.9%), similarly GDM (8% vs. 6.5%), and chronic hypertension (0.4% vs. 0.3%). However, fetal growth restriction (FGR) was found to be more in women with female fetuses than males (4.4% vs. 3.3%), similarly breech (1.0% vs. 0.78%), and in placental abruption (0.2% vs. 0.1%).

No significant association was found between fetal gender and pregnancy outcome (p-value=0.46), although post-partum hemorrhage (PPH) was found to be more in women with male fetuses than females (0.5% vs. 0.32%).

More women who had normal vaginal delivery (NVD) were pregnant with female fetuses than males (35.8% vs. 33.6%), similarly instrumental delivery (2.9% vs. 2.7%), and meconium-stained liquor (MSL) (2.9% vs. 2.7%).

25.2% (935/3713) babies were delivered by cesarean section (CS), among them 518(55.4%) were male and 417(44.5%) females. Elective surgeries 4.4% (n=165) were performed bit more in female fetuses than males and it was done quite higher in pregnant women with female fetuses than males (n=83, 2.23% vs. n=82, 2.21%). 20.7% (n=770) women had undergone an emergency section among them majority of pregnant women were with male fetuses than female (11.7% vs. 8.9%) (P-value= 0.10).

Regarding reasons for cesarean sections (CS) among pregnant women, 324/3717 of women had CS because of non-progress of labor, amongst them most women were with male fetuses in comparison to female (5.27% vs. 3.44%), and similarly in non-reassuring Cardiotocograph (CTG) (4.03%, vs. 3.20%).

Cesarean section due to malpresentation was found to be higher in women with female fetuses than males (1.80% vs. 1.56%), similarly for

Table 3: Comparison of Neonatal Outcomes with fetal gender (N=3713)

Neonatal Outcome (N=3711)	Male	Female	P-Value
Gender (n=3711)	1858 (50%)	1853 (49.9%)	
Birth Weight (n=3711)	(Mean±SD 3.27±0.446)		
≤ 2.5kg	220 (5.9%)	*277 (7.5%)*	0.000
2.6 – 3.5kg	1427(38.4%)	*1445(38.9%)*	
≥ 3.5kg	211 (5.7%)	*131 (3.52%)*	
APGAR Score (n=8)			
< 7 in 5min	1 (0.02%)	*4 (0.10%)*	1.000
7 in 5min	0 (0%)	*3 (0.08%)*	
Admission to Nursery /NICU (n=364)	190 (5.11%)	*174 (4.7%)*	
Neonatal Deaths (n=3)	2 (0.05%)	*1 (0.02%)*	

Significant p-value <0.05

CS on maternal request (1.1% vs. 0.1%).

Table 3 summarizes the comparison of neonatal outcomes with fetal gender. Out of the total 3,713 women who delivered at the hospital, 50% (n=1858) delivered male, and 49% (n=1853) female babies. The mean birth weight of neonates was 3.27kg (SD±0.446). A significant correlation was found between birth weight and fetal gender (p-value=0.00). Majority of women delivered female babies with birth weight (BW) 2.6–3.5kg in comparison to males (38.9% vs. 38.4%), similarly for BW≤2.5kg (7.5% vs. 5.9%), and for birth weight≥3.5kg (3.52% vs. 5.7%).

No significant association was found between Apgar score and fetal gender (p-value=1.00), although more female neonates were born at Apgar score <7 in 5min in comparison to male (0.10% vs. 0.02%), similarly at apgar score 7 in 5min (0.08% vs. 0%).

9.8%(364/3713) of neonates were admitted to neonatal intensive care (NICU), majority of them were male than female (5.1% vs. 4.7%). Only 3-neonatal deaths were reported out of which 0.05% (n=2) were male and 0.02% (n=1) female neonate.

216/3713 neonates were admitted to the Neonatal Intensive Care Unit (NICU) for presumed sepsis , among them majority were male neonates in comparison to females (3.28% vs. 2.53%). Also, more male neonates were admitted with low birth weight (LBW) to NICU than female (1.13% vs. 0.9%), similarly for neonatal jaundice (NNJ) (1.07% vs. 0.91%), transient tachypnea of newborn (TTN) (0.67% vs. 0.56%), and respiratory distress syndrome (RDS) (0.35% vs. 0.26%). However, more female neonates were admitted to NICU with meconium aspiration syndrome (MAS) in comparison to males (0.56% vs. 0.48).

Discussion:

The study showed a significant association between fetal gender and obstetric risk factors. GDM and hypertensive disorder of pregnancy PIH/Pre-eclampsia were higher in women with male fetuses as compared to women having female. The placental abruption among pregnant women showed no significant difference with the female and male fetus. Breech presentation was found more in women with female fetuses than in male, similarly, FGR was found more in women with female fetuses than males. More female babies were delivered by normal vaginal delivery (NVD) than males, and most male babies were born by cesarean sections (CS) in comparison to females. A significant correlation was found between birth weight and fetal gender, also no significant difference was found between apgar score and fetal gender. However, more male babies were admitted to NICU/nursery due to low birth weight (LBW) than females.

It is increasingly emerging that pregnancy with a male fetus is associated with poorer maternal beta-cell function, increased risk of GDM and chances of developing type-II diabetes. Studies on the association between abnormal carbohydrate metabolism and fetal gender have conflicting results.[5] GDM was 1.5% higher in women with male fetuses than women having female. A meta-analysis of 20-studies showed that women with male fetus were at an increased risk for GDM compared with women with female (RR=1.04; 95%, CI=1.02, 1.06) overall p=0.045.[12] Another study showed that GDM was significantly higher among male bearing women than with female babies (p< 0.001).[13]

Hypertensive disorders of pregnancy PIH/Pre-eclampsia are major complications of pregnancy

and associated with maternal and fetal morbidity and mortality in our study, it was found to be 0.8% higher among pregnant women with a male baby in comparison to women with a female. A meta-analysis also found an association of gestational hypertension with male fetal sex dominance.[1] Whereas another study found no statistically significant difference in gestational hypertension between women with a male and female fetus.[6] A study reported that pregnant women with a male fetus with hypertensive disorder of pregnancy/pre-eclampsia showed a reduction in microvascular vasodilatation, however, no such differences were observed in women with the female fetus.[14]

The placental abruption among pregnant women showed no significant difference in the female fetus than male in our study. Another study also found that women with male fetuses had no significantly higher risk of placental abruption in the male and female fetuses.[15] Although there is a theoretically higher risk of placental abruption in women with male fetuses due to deficient anchor in the matrix tissue and poor placental vascularization.[16,17]

Breech presentation was found 0.22% more in women with female fetuses than male in our study. These results are comparable with a study which showed that non-cephalic presentation was more evident in women with a female baby than male,[1] another study also reported that breech presentation was 4.4% in women with a female baby than 3.7% with a male.[18]

Fetal growth restriction (FGR) is due to maternal and fetal disorders associated with birth weight less than the 10th percentile for the gestational age. It was found 1.1% more in women with female fetuses than in male. This is comparable to the results of a study that showed pregnancies with female fetuses have an increased rate of fetal growth restriction by 1.9% as compared to male by 1.5%.[6] Another study showed fetal growth restriction was more in female babies as compared to males[11] Hormonal, physiological, or genetic factors are often considered to be responsible for fetal growth restriction.

In our study female babies were delivered by normal vaginal delivery (NVD) 2.2% more than male, this is supported by a study that showed more female babies were delivered by NVD in women with female fetuses than women with male.[11] Another study showed that female babies were more likely to be born by NVD 52.3% than male 47.7%.[19]

The instrumental deliveries were found to be 0.2% higher among female fetuses than male, this finding is not supported by other studies. A study showed more male babies 1.9% delivered by instrumental delivery as compared to females 1.4%.[13] Another study also confirmed this finding and showed that more male babies required instrumental delivery than female.[19]

10.9% of male babies were born by cesarean sections (CS) as compared to female babies. This is comparable to the study which showed male babies were born by cesarean delivery more as compared to female.[19]

There was no significant difference found for elective cesarean in male and female babies 2.21% and 2.23%, but the emergency cesarean section was performed 2.8% more on patients with male babies in comparison to female. Another study showed that emergency cesareans were more in male than in female babies.[13]

Regarding reasons of CS, its rate was 1.83% high due to non-progress of labor (NPOL) in women with male babies than female followed by non-reassuring CTG which were 0.83% more in women with male babies than females. Malpresentation was found to be 0.24% higher in women with female fetuses than males. These findings are supported by a study that showed that cesareans due to NPOL were higher in mothers with male babies than female.[20] and 1.1% more male babies were delivered by cesarean due to fetal distress than female. Another study showed that CS due to NPOL were more in male fetuses as compared to females while cesarean due to breech/malpresentation was more in female babies 4.4% than in males 3.7%.[18]

Regarding neonatal outcome, a significant correlation was found between birth weight and fetal gender (P-value =0.00). 1.6% more female babies were born with birth weight ≤ 2.5kg in comparison to male. While the babies delivered with birth weight >3.5kg were 2.2% more male as compared to female babies. The LBW was 1.2% more common in females than in males and large for dates babies were 1.18% more commonly males than females babies.[11]

There was no significant association found between apgar score and fetal gender (P-value=1.00) although more female babies 0.1% were born with apgar score <7 in 5 minutes in comparison to male 0.02%. Similarly, 0.08% of female babies were born with an Apgar score of 7 in 5 minutes in comparison to male 0%. The above findings were supported by a study in which no difference was found in apgar score <7 in 5 min in male and female babies.[18]

Despite no significant difference in apgar score at birth between male and female babies, NICU admissions were 0.4% higher in male babies than females. This is supported by a study in which 1.2% of more male neonates were admitted in NICU more as compared to females.[18] Another study also showed a higher percentage of male babies' admission in NICU as compared to females.[21]

In the present study 3-neonatal deaths were reported, out of which 0.05% were male and 0.02% female babies, other studies have also reported perinatal deaths were more common in male infants as compared to females.[11,22]

Regarding reasons of admission in NICU/nursery 0.23% more male babies were admitted due to LBW than female babies although the findings are not supported by other studies which showed that more female babies were admitted in NICU due to FGR than male.[6] NICU admission due to presumed sepsis was 0.75% more among male neonates than females this is supported by a study that this was more in male babies than females[6] although the percentage is quite high as compared to the present study. In male babies' NNJ was 0.17% higher than females, this is comparable to the results of another study which showed that more male neonates needed NICU admission than female.[6] Female babies were admitted due to MAS more 0.56% than male 0.48%, and this is supported by another study in which more female babies were admitted than male.[6] Neonatal admission due to TTN and RDS were higher in male babies at 0.67% and 0.35% than female's 0.56% and 0.26% respectively. A study that supported these findings showed that RDS was more common in male neonates than female.[23]

Based on fetal gender there are differences in pregnancy and neonatal outcomes. Certain obstetric conditions like PIH, GDM are more predictable depending on fetal gender. The risk of mortality and morbidity has been gender-specific and hormonal factors from fetuses have also an impact on pregnancy outcomes which are different in pregnancies with male or female babies.

Our study specifies that male babies are associated with increased morbidity and adverse perinatal outcomes. Although there are gender-dependent differences in pregnancy and neonatal outcomes, it is unclear whether individualized care to pregnant women should be planned according to gender or not.

There are certain limitations of our study, this is a retrospective review of medical records based on delivery records at a secondary obstetric center. Our sample excluded certain higher-risk pregnancies that were not managed at our site and referred to the tertiary center due to limited resources. Our study only analyzed the association between fetal gender and adverse pregnancy outcomes but did not find out the causes of this association. The strength of our study is that it is one of the few studies in Asia and to the best of our knowledge, the first study in Pakistan to assess the effects of fetal gender and pregnancy outcome.

Conclusion:

Our study finding supports the rising concept of

different maternal, fetal, and placental responses according to sexual dimorphism. Fetal gender act as an independent factor that influences pregnancy and neonatal outcome due to which male babies need more obstetrics and neonatal intervention than female babies so fetal gender should be considered as a risk factor when assessing pregnancy complications, but the question remains how parents are counselled about intrapartum and neonatal events when there is insufficient evidence available at present to alter intra-partum management based on gender and their impact.

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Role and contribution of authors:

Arshia Javed, collected the data, references and did the initial writeup.

Ghulam Kubra Rind, collected the data, did the interpretation of data and helped in result writing.

Nadia Mohammad, collected the data, references and helped in introduction, discussion and result writing.

Irfan Sheikh, critically review the article and advised useful changes.

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