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# Prenatal Ultrasound Study of Gender Difference in Urinary Tract Morphology in Normal Fetuses

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**Abstract**

***Objective:*** To compare gender difference on renal pelvic size and urinary bladder volume (BV) in normal male and female fetuses at 37 weeks of gestational age (GA) using ultrasound. ***Methods:*** 414 normal singleton pregnancies of 37 weeks GA were included. In each fetus, antero-posterior (AP) diameter of the renal pelvis and BV was measured. ***Results:*** Male fetuses were found to have greater AP diameter of renal pelvis than female (male: 2.69±0.93 mm and female: 2.46±0.87 mm) ($p<0.05$, independent sample t-test). Female fetuses were found to have a greater BV than male (male: 13.93±8.43 $cm^3$ and female: 17.22±10.22 $cm^3$) ($p<0.05$, independent sample T test). ***Conclusions:*** Gender difference in morphology indicates that the respective urinary tract development is different between male and female fetuses, which probably accounts for gender difference in the urinary tract anomalies detected during neonatal period.

**Key words** Fetus; Gender; Renal pelvic size; Urinary bladder volume

## Introduction

It is well known that certain urinary tract pathologies show sex preponderance during neonatal or infantile period. Male infants show a greater preponderance of hydronephrosis (male:female=5:1), pelviureteric junction obstruction, vesicoureteric reflux (VUR), and urinary tract infection (UTI) in the first year of life.[1-6] Girls show a greater preponderance of VUR[7] and UTI after the first year.[1,8] The difference in the anatomy of the urinary tract between genders has been studied extensively at the postnatal period. Many studies in neonates have shown pelvic ectasia to be more common in boys and frequently affecting the left side[6,9,10] while in Adra's study, the right side was found to be more commonly involved.[11]

Previous literature findings on gender difference in bladder volume are inconclusive. Hakenberg showed that there was no gender difference in bladder volume in a small group of 43 children.[12] In a latter study by Bael et al, no gender difference was found in cystographic bladder capacity.[13] Whereas in a large scale study by Fairhurst, Zerin and Treves of which 1855 subjects less than 14 years old were included, boys were found to have a smaller bladder capacity than girls.[14-16] Bladder emptying is commonly incomplete in infants. O'Donnell reported that larger residual bladder volume was more common in infant boys[17] while Roberts showed that older infant girls had bigger residual bladder volume (2.4 ml) than boys (0.8 ml).[18]

Scarce number of pre natal studies has been carried out to study gender difference in the morphology of urinary tracts in fetuses. Renal pyelectasis was found to be more common in male fetus[10,19,20] but the range of normal value was not described in detail. For gender difference in bladder

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volume, there was only one report by Hedriana showing no gender difference in maximum filling capacity of bladder in a small sample of 11 dead fetuses.[21] To our best knowledge, no similar study has been carried out in live fetuses.

This study sought to investigate gender difference in renal pelvic size and bladder volume based on 414 normal singleton pregnancies at 37 weeks of gestation.

## Methods

Four hundred and fourteen normal singleton pregnancies were included in this study. All the pregnant women were consecutive referrals from the obstetric clinics for a routine antenatal morphology scan at about 20 weeks of gestational age and confirmed to have normal fetal anatomy. Gestational age (GA) of the fetus was determined by date of last menstrual period (LMP). The biparietal diameter, abdominal circumference, and femur length were also measured. The estimated GA from each of the above parameters had to be within 14 days with the estimated GA from LMP, otherwise the subject would be excluded. It is well known that intrauterine growth retardation (IUGR) or potential IUGR cases may be associated with a higher pulsatility index (PI) value in the umbilical artery. Only those cases with PI from 0.43 to 1.42 were included as normal cases.[22] After accurate dating and exclusion of predisposition to intrauterine growth retardation by umbilical artery Doppler, all recruited subjects were asked to return at 37 weeks gestation for a detailed examination of the fetal urinary system including measurement of fetal renal pelvis size and fetal urinary bladder volume. The renal pelvis and bladder volume data were only recorded as single entry for each subject. Multiple measurements for determination of mean value of the urinary bladder volume were not attempted as most fetuses had rapid emptying within a short period of time, making repeated measurements impractical. Postnatal records were retrieved to confirm that there was no evidence of growth restriction or congenital anomalies. Postnatal ultrasound has been performed within three months of birth for all fetuses to ensure no structural uropathy was detected. Also the Maternal Child Health Clinic (MCHC) records were traced to document normal development in the first six months. Informed consent was obtained from all the pregnant women. This study was approved by the institutional review committee of the Chinese University of Hong Kong.

The equipment used was the ATL HDI 5000 (Advanced Technology Laboratories, Bothell, WA) and the Voluson 730 Expert series (GE Medical Systems Kretz Ultrasound, Zipf, Austria) with 3.5 and 5 MHz curvilinear array transducers. All maternal subjects were encouraged to drink (600 ml of water) 20 minutes before the ultrasound examination to ensure they were well hydrated.

Fetal renal pelvic size was recorded by measuring the antero-posterior (AP) diameter of the renal pelvis in the short axis of the renal pelvis within the outline of the kidney (Figure 1). The measurements of the renal pelvic AP diameters were taken with the fetal spine either anterior or posterior. If the fetal lie was oblique or lateral at the initial scan, measurements would be taken at a later time when the fetal lie was in the favourable position. Fetal urinary bladder volume (BV) was calculated by measuring the length (L) of the bladder in the longitudinal scan, the width (W) and the AP diameter or depth (D) in the transverse plane (Figure 2). The ovoid volume formula was used for calculating the volume: BV= 4/3 x $\pi$ x [(L x D x W)/8].[23] To minimise the confounding effect of distended urinary bladder on dilatation of renal pelvis, fetuses who were found to have both dilated renal pelves and distended bladder were rescanned at a later time when the fetal bladder was less distended. To ensure only normal fetuses were recruited, cases with AP diameter of the renal pelvis >7 mm were excluded according to Corteville criteria.[24] All the measurements were made by a single experienced sonographer, who was unaware of the sex of the fetus at the time of the examination and no attempt was made to identify fetus' sex during ultrasound scanning. Standard measurements of biparietal diameter and femur length were also measured to ensure the size of the fetus was within

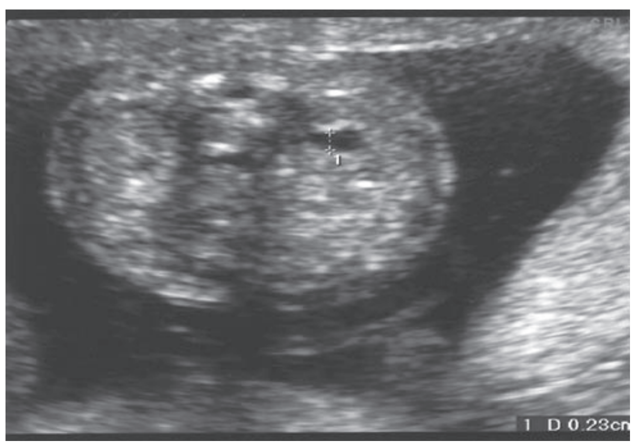


**Figure 1** Prenatal ultrasound study showing measurement of AP diameter of the renal pelvis in the transverse view.

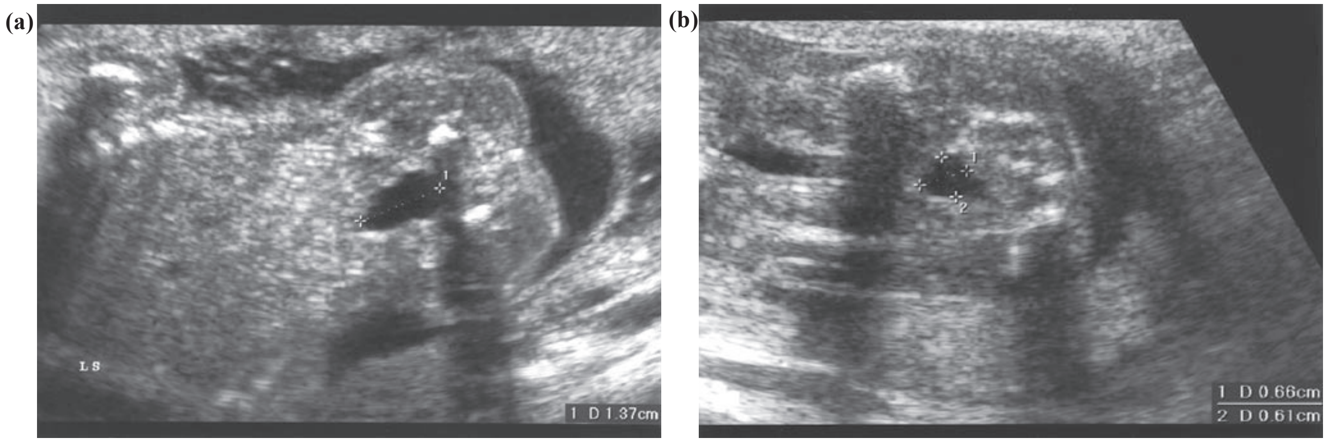


**Figure 2** Fetal bladder volume measurement (a) longitudinal view, (b) transverse view. The ovoid volume fomula is used for calculating the volume: BV= 4/3 x π x [(L x D x W)/8], where BV=bladder volume, L=length of bladder in longitudinal scan, W=width and D=depth in the transverse scan.

2 weeks from the expected size of a fetus at 37 weeks. The intra-observer variability was tested in a randomly selected sample of 40 fetuses. In each case, the AP diameter and BV were measured three times and the error was calculated in the method according to Moore.[25] The error in three measurements was calculated by comparing each single measurement with the average of the three measurements.

Paired t-test was used for comparing the right and left renal pelvic diameter. Independent sample t-test was used for testing the difference in AP diameter of fetal renal pelvis and BV between sexes. Statistical significance was set at p value $<0.05$ and results were expressed as the mean ±standard deviation (SD).

## Results

The mean maternal age was 29.91±5.11 years old. Four hundred and fourteen fetuses with gestational age of 37 weeks were measured. There were 207 male fetuses and 207 female fetuses. No attempt had been made to select an equal number for both sexes and equal incidence of gender was fortuitous. All fetuses had their biparietal diameter and femur length measurement within two weeks of the calculated gestation and none of the recruited subjects showed evidence of intrauterine growth retardation. There was no significant difference of fetal sizes between the two gender groups. All fetuses were found to have normal development in the first six months after birth by either paediatricians or MCHC doctors and no structural uropathy detected from our postnatal ultrasound. No subject was found to have aneuploidy clinically. The intra-observer variability of measurements of renal pelvis and bladder volume was 1.9±0.29% and 2.2±0.35% respectively.

### *Renal Pelvic Size*

The maximum AP diameter of the renal pelvis on either right or left sides of all fetuses ranged from 0.1 to 6.3 mm. There was no statistically significant difference between right and left side in either sex ($p>0.05$). Therefore in the following analysis, only data on the right side was used.

The distribution of sizes of renal pelves in both sexes is given in Figure 3. Male fetuses were found to have a greater AP diameter of the renal pelvis than females (2.69 vs 2.46 mm, $p<0.05$, independent sample T test) (Figure 3).

### *Bladder Volume*

The overall BV ranged from 0.83 to 49.73 $cm^3$. The distribution of size of BV of both sexes is given in Figure 4. In male fetuses, the mean BV was 13.93±8.43 $cm^3$. In females the mean BV was 17.22±10.22 $cm^3$ ($p<0.05$, independent sample T test). Therefore the female fetuses had a significant larger bladder volume than male.

## Discussion

A number of urinary tract pathologies shows sex preponderance during neonatal period. There were previous studies on gender difference in the anatomy of urinary tract, trying to explain the reason of sex predisposition. Some authors suggested that pelvic dilatation in fetus was

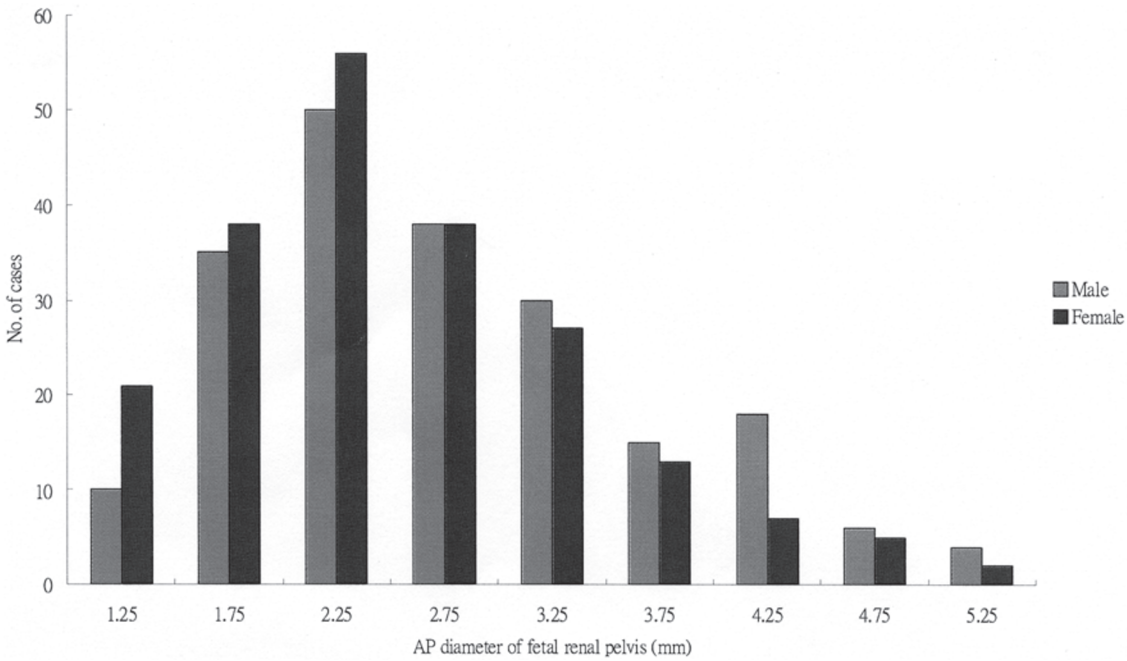


**Figure 3** Distribution of the AP diameter of right renal pelvis in 207 male and 207 female fetuses.

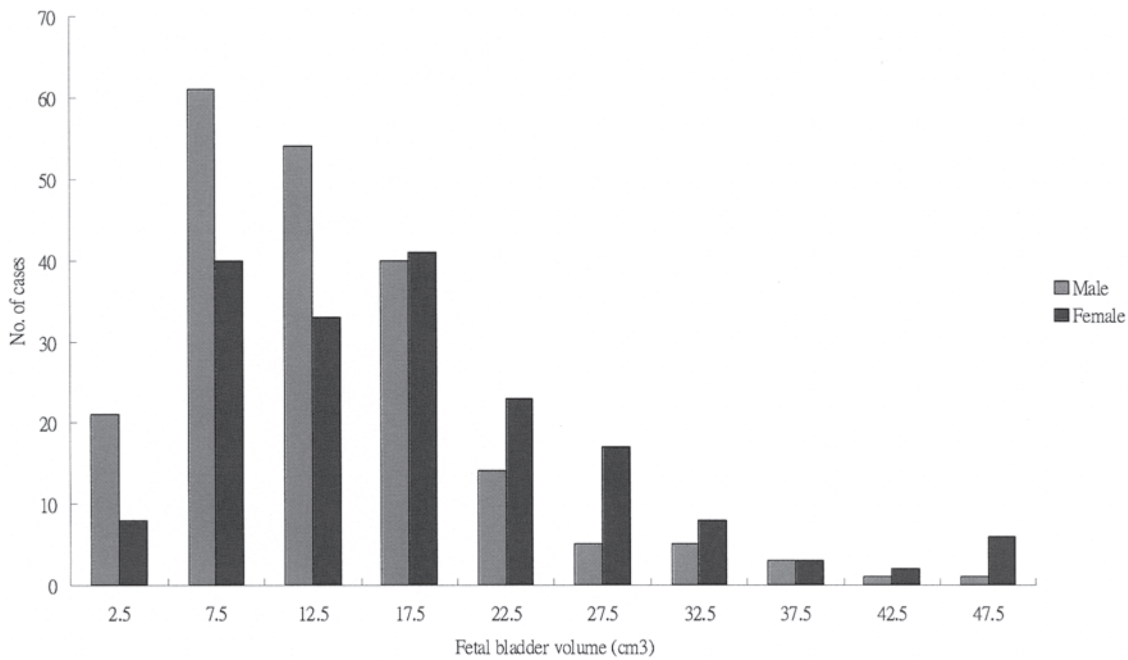


**Figure 4** The distribution of BV in 414 fetuses.

principally the reflection of urinary tract obstruction[9] and the grade of antenatal renal pelvic dilatation (AP diameter >7 mm) was significantly associated with hydronephrosis confirmed at the post natal stage, which require close monitoring and sometimes active treatment.[26,27] However, underlying factors contributing to gender difference in the incidence of the above abnormalities are still unknown.

Findings of this study confirmed there was significant gender difference in fetal renal pelvic size and urinary bladder volume based on a large sample of fetuses at late gestation. From the results, normal male fetuses had a larger renal pelvis at baseline. It seems logical that when considering making a diagnosis of fetal hydronephrosis, a higher cut-off value should be allowed in male fetuses while a lower threshold of suspicion should be considered in female fetuses. Scottand and Renwick reported that though there was infrequent association of antenatal renal dilatation with the presence of VUR, if VUR did occur, it was more common to detect renal dilatation in male fetuses. In female fetuses, VUR could not be excluded even when the renal pelvis was only minimally dilated.[4]

Our findings on gender difference in fetal bladder volume agreed with the observation made in older children that boys had a smaller bladder volume than girls.[14-16] The difference in size of urinary bladder between genders therefore was likely to be predetermined during the fetal life. Gender difference of urinary tract morphology implies that the underlying development is probably different between male and female fetuses. This is in agreement with the histological study by Sebe et al who has found that the morphological characteristics of female adult external urinary sphincter are already evident in early fetal development and do not evolve during postnatal growth or by the influence of sex hormones.[28] The gender difference in anatomical development of urinary tract likely accounts for clinical observation of different incidence of urinary tract anomalies between genders. However, whether an intrinsic smaller bladder volume and more easily dilatable renal pelvis are significant anatomical risk factors for the different pathological conditions warrants further detailed case controlled studies. Under normal circumstances, the renal pelvis size was not affected by the size of the kidneys. Furthermore, as all the fetal subjects were scanned at 37 weeks of gestation and they were confirmed to have normal growth development after birth. We believed that the comparison between genders was unbiased in this selected group of subjects.

## Limitation of This Study

There are several limitations in this study. There was known association of distended fetal bladder and transiently dilated renal pelves.[29-31] This was taken into consideration when both a dilated fetal pelvis and a distended fetal bladder were encountered; we would rescan the maternal subject at a later time when the fetal pelvis was less distended. Our result also confirmed that the renal pelvis measurement was not confounded by bladder volume as the male fetuses were found to have larger renal pelvis size but a smaller bladder volume. Furthermore, as bladder filling was a dynamic process, the fetal bladder volume varies with time. However, this factor could be diluted with statistical analysis of a reasonably big sample of subjects of different sexes.

We quoted the intra-observer variability so as to prove that the error in measurement in this study was within an acceptable range. If error was too great, then the measurement had no clinical significance. One limitation of this study was that we had not provided inter-observer error because the ultrasound parameters of each fetus were measured once by a single observer only.

Finally with the recent advances in ultrasound scanning, three-dimensional ultrasound assessment of fetal bladder volume should be a more accurate assessment of bladder volume[32]; however this option was not available in our center when this study was started.

## Conclusion

Male fetuses have larger renal pelvic AP diameters and smaller bladder volumes than female. This gender difference in morphology indicates that the respective urinary tract development may be different between male and female fetuses, which likely accounts for gender difference in the urinary tract anomalies detected during neonatal period.

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