# Diagnostic accuracy of mid-trimester antenatal ultrasound for multicystic dysplastic kidneys

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**ABSTRACT**

**Objectives:** To establish the diagnostic accuracy of obstetric ultrasound at a tertiary fetal medicine centre in the prenatal detection of unilateral and bilateral MCDK in fetuses where this condition was suspected; and to undertake a systematic review of the literature on this topic.

**Methods:** Retrospective observational study of all cases with an antenatal diagnosis of either unilateral or bilateral MCDK referred to a regional tertiary fetal medicine unit between 1997 and 2015. Postnatal diagnosis was confirmed by postnatal ultrasound reports or postmortem examination. The accuracy for prenatal ultrasound in the diagnosis of MCDK was calculated. We also performed a review of the literature using a systematic search strategy, regarding the prenatal diagnosis and diagnostic accuracy of MCDK.

**Results:** We included 144 women in the analysis; 37 (25.7%) opted for pregnancy termination (due to unilateral MCDK with additional abnormalities, bilateral suspected MCDK or severe obstructive uropathy). In 126 women all pre- and postnatal data were available, including 104 livebirths; 19 who opted for TOP and where PM was available; and 3 that had an intrauterine fetal death. Two infants died shortly after birth, (due to known bilateral MCDK and known cranial vault defect). The overall number of postnatally confirmed MCDK was 100: of these 98 were diagnosed prenatally (true positive), while 2 were thought to be hydronephrosis prenatally (false negative) and the diagnosis of MCDK was made after birth. In 9 cases the initial antenatal diagnosis of suspected MCDK was revised, either later in pregnancy (n=2) or postnatally (n=7). The overall diagnostic accuracy of MCDK reported in the existing literature was found to range from 53.3 to 100%. MCDK was isolated in the majority of cases, while in 29% of cases was found to be associated with other renal and extra-renal fetal abnormalities.

**Conclusions:** Our study suggests that the diagnostic accuracy for the use of antenatal ultrasound to detect postnatal MCDK was about 91% and can therefore be used to guide antenatal counselling. However, prenatal or postnatal revision of the diagnosis occurs in about 7% of cases and parents should be counselled appropriately.

## INTRODUCTION

Multicystic dysplastic kidney disease (MCDK) is defined as a non-heritable form of renal dysplasia that usually leads in a non-functioning organ due to an abnormal kidney development[1]. Several decades ago Potter et al. suggested that MCDK could be due to a primary failure of renal mesenchyme induction, resolving in the complete absence of nephrons[2]; however, this theory has been challenged because kidneys affected do sometimes contain some recognizable glomeruli and proximal tubules[3]. An alternative view is that disruption of normal nephrogenesis could, at least in part, be explained by impairment of fetal urine flow very early in fetal life, and MCDK is generally attached to an 'atretic', non-patent ureter[4,5].

Antenatally, MCDK is one of the commonest renal anomalies detected on prenatal ultrasound with an incidence between 1 in 1000 to 1 in 4300 live births[6,7]. The classical sonographic appearance is the presence of multiple, hypoechoic, non-communicating cysts with no identifiable normal renal parenchyma[7,8]. Exploration of the renal fossa in some cases reveals no renal artery, renal vein, ureter or cysts, suggesting that renal agenesis and dysplastic kidneys may be at different ends of a spectrum of renal malformation. This is further supported by the finding that, in about 15% of cases with multicystic kidneys, there is contralateral renal agenesis. The condition is usually detected at the mid-trimester scan and although demonstration as early as 15 weeks of gestation has been reported[9], such early detection is unusual: overall detection rates of genitourinary abnormalities during the first trimester of pregnancy are about 34%; the reported detection rates specifically for MCDK are only about 14 %[10,11].

Unilateral MCDK with no associated fetal abnormalities and a normal contralateral kidney is associated with an excellent prognosis; in contrast, bilateral MCDK means that fetal and neonatal renal function is absent, with associated anhydramnios and pulmonary hypoplasia, a condition generally considered incompatible with extra-uterine life[12-14]; this demonstrates the importance of accurate characterisation of MCDK. Although the appearance of MCDK is characteristic, it may be confused with

other renal anomalies, in particular hydronephrosis with calyceal involvement[6,15]. The purpose of this study was to establish the diagnostic accuracy of prenatal ultrasound after initial referral for suspected MCDK using a cohort design in our centre; and by undertaking a review of the literature regarding the prenatal diagnosis and diagnostic accuracy of MCDK.

## METHODS

### *Assessment of our cases*

This is a retrospective study of all cases with an antenatal diagnosis of either unilateral or bilateral MCDK referred to our tertiary fetal medicine unit at St George's hospital, London. All cases were identified from the computerized ultrasound database (Viewpoint, Viewpoint Corporation, GE Healthcare, Austria) over an 18-year period from May 1997 to September 2015. This database includes women identified during routine screening in our local population; as well as referrals from all units within the south west London population. All women identified had the antenatal diagnosis of MCKD confirmed by a senior fetal medicine consultant; the doctors scanning the women were not blinded to the suspected antenatal diagnosis.

The postnatal diagnosis was confirmed by findings documented on postnatal ultrasound or postmortem reports. This information was gathered by reviewing information in case notes, radiology databases and electronically recorded clinic letters, either in our hospital or in the referring unit. In some children no cystic renal tissue was seen on postnatal scan, rather absence of renal tissue. Given the natural history of MCDK, this was interpreted as confirmation of the antenatal diagnosis rather than misdiagnosed renal agenesis. All other postnatal diagnoses were considered as the "gold standard". Clinicians performing postnatal imaging; and those collecting outcome data were not blinded to the antenatal diagnosis of MCKD.

Cases were defined as false negative where a diagnosis of MCDK was established postnatally and where antenatal reports had suspected a renal abnormality; the only exception was when unilateral MCDK was suspected in the contralateral kidney (i.e. there was a right-left error). Finally, in women who opted for a termination of

pregnancy (TOP) but declined post-mortem, it was not possible to establish a postnatal diagnosis.

From these data, the accuracy for the antenatal ultrasound diagnosis of MCDK by ultrasound was calculated.

***Systematic review***

A systematic search strategy was developed and undertaken in PubMed, EMBASE and Scopus to identify citations reporting the diagnostic accuracy of antenatal ultrasound for MCDK. We used medical subject heading (MeSH) terms and key words, and word variants for "Multicistyc dysplastic kindey deasease" and "prenatal diagnosis". The search and selection criteria were restricted to the English language. Reference lists of relevant articles and reviews were hand searched for additional reports. The inclusion criteria were studies reporting data on the prenatal diagnosis and diagnostic accuracy of MCDK. Two authors (CS, ULRM) reviewed all the abstracts independently. Agreement about potential relevance was reached by consensus, and full text copies of those papers were obtained. Two reviewers (CS, ULRM) independently extracted relevant data regarding study characteristics and pregnancy outcome. Inconsistencies were discussed by the reviewers and if needed a third author (ATP) and consensus reached. Only full text articles were considered eligible for the inclusion. Case reports, and conference abstracts were also excluded.

## RESULTS

During the study period 189 patients were seen in the unit for suspected unilateral or bilateral MCDK (Figure 1). In 45 cases no further pregnancy nor postnatal follow up was undertaken and these were excluded from the subsequent analysis; in all but one of these the diagnosis was unilateral suspected MCDK, while in 1 case there was an associated cardiac abnormality but the woman moved abroad. There were no major

differences in maternal and ultrasound characteristics of patients with and without follow-up (Table 1).

*Diagnosis*

In 144 cases data were available and these were included in the analysis (Figure 1). The median gestational age (GA) at the time of the initial scan was 22.0 weeks (IQR 21.4-23.7). The median number of follow up scans was 2 (2-3). In 101 (69.4%) there was unilateral suspected MCDK while in 25 (17.4%) there was bilateral suspected MCDK. Associated abnormalities were present in 28 of the 144 cases (21 in the unilateral group and 7 in the bilateral group, Table 2).

*Outcomes*

Of the 144 women, 37 (25.7%) opted for TOP: in 11 women this was due to unilateral suspected MCDK with additional abnormalities conferring a poor prognosis; in 23 there was bilateral suspected MCDK (of these 7 were non-isolated: 4 cases of Meckel Gruber syndrome were found, in 1 case there was VACTERL and in one case mosaic trisomy 13 was found, Table 2), while in the remaining 3 cases the initial diagnosis was a severe obstructive uropathy.

Of the 144 cases, a TOP was performed and no postmortem examination was available in 18; in the remaining 126 cases all pre- and postnatal data were available. This included 104 livebirths; 19 women who opted for TOP and where PM was available (included in the 37, above); and 3 women (2.4%) where an intrauterine fetal death occurred: one for unknown reasons at 36 weeks in a diabetic mother, with a birthweight of 3.5kg; one in a fetus with IUGR at 32 weeks; and one in a fetus with preterm prelabour rupture of the membrane and obstructive uropathy at 31 weeks of gestation. Of the 104 liveborn infants two (1.8%) died shortly after birth: both were expected, where the parents elected to continue with the pregnancy: one with lethal pulmonary hypoplasia secondary to bilateral MCDK and anhydramnios, and one with a cranial vault defect.

*The diagnostic accuracy for MCDK*

Of the 126 cases, the overall number of postnatally confirmed MCDK was 100: of these 98 were diagnosed prenatally (true positive), while 2 were thought to be hydronephrosis prenatally (false negative) and the diagnosis of MCDK was made after birth.

In 9 cases the initial antenatal diagnosis of suspected MCDK was revised (false positive): In 2 of these this was revised later in pregnancy to moderate hydronephrosis during the third trimester of pregnancy and confirmed postnatally; while in the remaining 7 cases the diagnosis was revised postnatally (Table 3, Figure 1 and Figure 2).

The screening characteristics for ultrasound in relation to the diagnosis of MCDK are shown in Table 4. Overall, the diagnostic accuracy for the use of antenatal ultrasound to detect postnatal MCDK was 91.2%.

*Systematic review*

The literature review yielded 252 possible citations. After reviewing title or abstract, 207 were excluded, as they did not meet the selection criteria. The remaining 45 full-text manuscripts were retrieved and a total of 7 eligible studies were included in the systematic review, (Figure 3, Flow chart).

The characteristics of the included studies are presented in Table 5. The overall diagnostic accuracy of MCDK reported ranged widely between 53.3 and 100%. Prenatal diagnosis was made mainly during the third trimester of pregnancy (mean GA was 26 weeks). The condition was isolated in the majority of cases, while in 29% of the cases was found to be associated with other renal or extra-renal anomalies. In total, 653 (77.6%) fetuses were liveborn, 19 (2.3%) suffered an IUD, and 3 (0.4%) fetuses died shortly after birth because of associated abnormalities; while 166 (19.7%) underwent a TOP (Table 5).

## DISCUSSION

The data from this study showed that the antenatal prediction of unilateral or bilateral MCDK appears accurate in about 91.2% of cases. However, in an important number of cases (7.2%) the diagnosis was revised, either later in pregnancy; or postnatally. Although the prognosis was thus largely unaltered, parents should be made aware of this information at the time of the diagnosis at the mid-trimester anomaly scan. Moreover, it needs to be highlighted that in some cases the revised diagnosis of hydronephrosis might be the consequence of the prolonged urinary obstruction in an originally multicystic kidney, making a possible evolution of the disease a revised diagnosis[16]. In addition, our data suggest that, despite the high accuracy of antenatal prediction of MCDK, both follow up antenatal scans and postnatal imaging still needed in infants diagnosed antenatally[17,18].

Chromosomal abnormalities and syndromes were found in approximately 7% of pregnancies referred with suspected MCDK, and this is in line with the prevalence reported in the current literature[19,20]. The presence of other associated malformations was found in almost 1 in 5 cases with MCDK. This is similar to the study by Eckoldt et al.[21], who reported 23.4% of fetuses with MCKD had associated extra-renal malformations of other organ systems. The frequency of women who underwent a TOP for lethal abnormalities in addition to those that end in an IUD/NND because of renal complications was 25%, similar to the prevalence in previous reports 30%[22] (Table 5). This association with anomalies highlights the need for detailed antenatal assessment for co-existing renal or extra-renal anomalies. This, more than any other factor, will alter antenatal counselling – at one end of the spectrum an isolated unilateral MCKD with a normal contralateral kidney conferring an excellent prognosis and at the other, lethal multi-organ syndromes or chromosomal abnormalities that are incompatible with life. Hence, referral to a tertiary centre should always be considered unless a high level of local expertise is available.

A previous study of 85 cases of antenatally diagnosed MCDK suggested that prenatal ultrasound is associated with a sensitivity of 53%. Our data suggest a diagnostic accuracy of 92.3%, and one possible explanation for this difference could be the improvement during the last 10 years of the level of the operator skills in fetal medicine and better ultrasound technology available nowadays. Nevertheless, we cannot exclude the possibility of missed diagnoses or referral bias as contributing to

this difference, thought this is unlikely due to the structured referral pathways in the entire region for both fetal medicine and nephrology services.

The strengths of our study are the large number of included cases, detailed antenatal assessment in a specialist fetal medicine centre and postnatal assessment using a unified protocol. However, our study has certain limitations. Firstly, we assumed that postnatal imaging is the gold standard by which renal tract anomalies can be diagnosed. Given the larger object of interest and clearer views postnatally we think this is a reasonable assumption[23]. Secondly, we had a loss-to-follow up rate of 23.8% and this may have biased the data we are able to report. Nevertheless, maternal and scan characteristics for the cases lost to follow-up were similar to those with follow up, suggesting a random (rather than systematic) loss; thus we have no reason to suspect that these data would vary greatly. Finally, because we are a tertiary referral centre that serves a large number of hospitals in London, we have no information on cases where MCDK was diagnosed postnatally but had not been suspected antenatally. While this prevents us from being able to properly calculate the number of false negative cases and specificity, we can still calculate diagnostic accuracy data on those with an antenatal diagnosis. We believe that the characteristic appearance and reported high detection rates of renal anomalies makes significant under-diagnosis unlikely.

## CONCLUSION

Our data show that antenatal diagnosis of MCDK is accurate when compared against postnatal imaging and can therefore be used to guide antenatal counselling. The overall diagnostic accuracy of antenatal diagnosis of MCDK was 91.2%. In about 19.4% of cases MCDK was associated with renal and extra-renal abnormalities highlighting the need for expert evaluation. In 7.2% of cases the initial diagnosis was revised, either pre- or postnatally; hydronephrosis was the common differential diagnosis. Thus, parents should be counselled that there is a small risk of revision of diagnosis, but that – in unilateral disease – this should not alter postnatal outcome. In view of our findings it seems reasonable to recommend detailed anatomical assessment at initial diagnosis; a repeat ultrasound in later pregnancy; and postnatal diagnostic work-up.

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**Figure Legends**

**Figure 1. Details on the population analysed in the study.**

**Figure 2. A and B prenatal features of hydronephrosis; C and D prenatal features of MCDK.**

**Figure 3. Folow chart of the included studies in the sytematic review.**

**Table 1:** Maternal and scan characteristics of patients with and without follow-up; figures are median (IQR); mean (±standard deviation) or n (%) as indicated.

| | **Patients with follow-up data (n 144 )** | **Patients lost at follow-up (n 45 )** |
|---|---|---|
| Gravida | 2 (±1.55) | 2 (±2.04) |
| Parity | 1 (0-2) | 1(1-2) |
| BMI | 24.6 (±4.6) | 25.3 (±5.2) |
| Number of prenatal scan | 2(2-3) | 2 (1-2) |
| Mean GA at diagnosis | 21.4 (20.5-22.6) | 21.8 (20.4-25.8) |
| Number of TOP/IUD/NND | 38 (26.3%) | NA |
| Side of MCDK | -Left MCDK 55 (38.2%)<br>-Right MCDK 47 (32.6%)<br>-Bilateral MCDK 25 (17.4%) | -Left MCDK 18 (40%)<br>-Right MCDK 27 (60%)<br>-Bilateral MCDK 0 (0%) |
| Associated anomalies | 28 (19.4%) | 1 (2.2%) |

BMI: body mass index; TOP: termination of pregnancy; IUD: intrauterine death; NND: neonatal death; MCDK: multicystic dysplastic kidneys

**Table 2.** Individual characteristics, ultrasound findings and post-natal diagnosis of fetuses with non-isolated MCDK
**NOTE TO EDITOR: THIS COULD BE AN ONLINE ONLY TABLE**

| Case (n) | Pregnancy | GA at scan (weeks) | MCDK | Associated prenatal findings | Outcome | GA outcomes | Associated postnatal findings |
|---|---|---|---|---|---|---|---|
| 1 | Singleton | 21+6 | Left MCDK | None | Livebirth | 36+0 | 17q12 micro deletion |
| 2 | Singleton | 21+0 | Left MCDK | None | Livebirth | 38+4 | Right hydronephrosis |
| 3 | Singleton | 21+6 | Right MCDK | None | Livebirth | 39+3 | Left duplex kidney |
| 4 | Singleton | 21+1 | Left MCDK | None | Livebirth | 41+3 | Left hydronephrosis |
| 5 | Singleton | 23+6 | Right MCDK | None | Livebirth | 39+5 | Left hydronephrosis |
| 6 | Singleton | 23+0 | Right MCDK | None | Livebirth | N/A | Right ureterocele |
| 7 | Singleton | 23+0 | Right MCDK | None | Livebirth | 38+4 | Left hydronephrosis |
| 8 | Singleton | 19+3 | Right MCDK | Suspected duodenal obstruction/atresia | Livebirth | 38+0 | Duodenal atresia |
| 9 | Singleton | 19+5 | Left MCDK | Polyhydramnios | Livebirth | 39+4 | Fetal macrosomia |
| 10 | Singleton | 21+2 | Left MCDK | SGA | IUD | 32+0 | SGA |
| 11 | Singleton | 22+0 | Left MCDK | Anencephaly | NND | NA | No PM assessment |

| | | | | | | | |
|---|---|---|---|---|---|---|---|
| | | | | | | | available |
| 12 | Singleton | 13+2 | Bilateral MCDK | Ecephalocele, polydactyly | Termination | 13+6 | Meckel-Gruber syndrome |
| 13 | Singleton | 13+0 | Bilateral MCDK | Ecephalocele | Termination | 13+2 | Meckel-Gruber syndrome |
| 14 | Singleton | 19+3 | Bilateral MCDK | Ecephalocele, anhydramnios | Termination | 20+0 | Meckel-Gruber syndrome |
| 15 | Singleton | 21+3 | Bilateral MCDK | Ecephalocele, anhydramnios | Termination | 22+0 | Meckel-Gruber syndrome |
| 16 | Singleton | 21+4 | Bilateral MCDK | Tetralogy of Fallot and lumbar scoliosis | Termination | 22+1 | Vacterl syndrome |
| 17 | Singleton | 18+0 | Left MCDK | Right kidney agenesis | Termination | 18+2 | Vacterl syndrome |
| 18 | Singleton | 17+0 | Bilateral MCDK | 2 vessel cord | Termination | 17+0 | Vacterl syndrome |
| 19 | Singleton | 21+1 | Right MCDK | Tetralogy of Fallot, bilateral talipes | Termination | 23+5 | 22q11deletion |
| 20 | Singleton | 20+4 | Left MCDK | Major cardiac abnormality | Termination | 21+0 | Mitral atresia, agenesis of the right kidney, small bilateral cervical ribs |
| 21 | Singleton | 15+4 | Left MCDK | Agenesis of the right kidney | Termination | NA | Left MCDK and agenesis of the right kidney |
| 22 | Singleton | 22+5 | Left MCDK | Major cardiac | Termination | 23+0 | Double outlet |

| | | | | | | | |
|---|---|---|---|---|---|---|---|
| | | | | abnormality | | | right ventricle, VSD, pulmonary stenosis, small mitral valve |
| 23 | Singleton | 16+4 | Bilateral MCDK | Mosaic trisomy 13 | Termination | 17+6 | Mosaic trisomy 13 |
| 24 | Singleton | 20+2 | Left MCDK | Kyphoscoliosis and lumbar spina bifida | Termination | NA | No PM assessment available |
| 25 | Singleton | 20+4 | Left MCDK | Ascites and anhydramnios | Termination | 21+0 | No PM assessment available |
| 26 | Singleton | 22+4 | Right MCDK | Agenesis of the left kidney | Termination | NA | No PM assessment available |
| 27 | Singleton | 21+5 | Left MCDK | Agenesis of the right kidney | Termination | NA | No PM assessment available |
| 28 | Singleton | 20+5 | Right MCDK | Agenesis of the left kidney | Termination | 21+3 | No PM assessment available |

IUD: intrauterine death; NND: neonatal death; MCDK: multicystic dysplastic kidneys; IUGR: intrauterine fetal growth restriction; PM: post-mortem

**Table 3:** Individual characteristics, ultrasound findings and post-natal diagnosis of fetuses with a postnatal revision of the MCDK diagnosis
**NOTE TO EDITOR: THIS COULD BE AN ONLINE ONLY TABLE**

| Case (n) | Pregnancy | GA at scan (weeks) | MCDK | Associated prenatal findings | Outcome | GA outcomes | Postnatal findings |
|---|---|---|---|---|---|---|---|
| 1 | Singleton | 19+0 | Right MCDK | None | Livebirth | 41+0 | Single cyst right kidney |
| 2 | Singleton | 20+4 | Right MCDK | None | Livebirth | 39+1 | Bilateral dysplastic kidneys |
| 3 | Singleton | 21+1 | Left MCDK | None | Livebirth | 41+3 | Left reflux |
| 4 | Singleton | 21+0 | Right MCDK | None | Livebirth | 41+4 | Right duplex Kidney |
| 5 | Singleton | 21+3 | Left MCDK | None | Livebirth | 38+1 | Adult type polycystic disease with infantile onset |
| 6 | Singleton | 24+0 | Right MCDK | None | Livebirth | 38+2 | Right hydronephrosis, ureterocoele |
| 7 | Singleton | 32+6 | Right MCDK | None | Livebirth | 39+2 | Right Duplex kidney |

MCDK: multicystic dysplastic kidneys

**Table 4.** Overall predictive accuracy of ultrasound in detecting MCDK (95% Confidence intervals).

| | **Sensitivity** | **Specificity** | **PPV** | **NPV** |
|---|---|---|---|---|
| **MCDK** | 98.00% (92.96-99.76) | 65.38 % (44.33-82.79) | 91.59% (84.63-96.08) | 89.47% (66.86-98.70) |

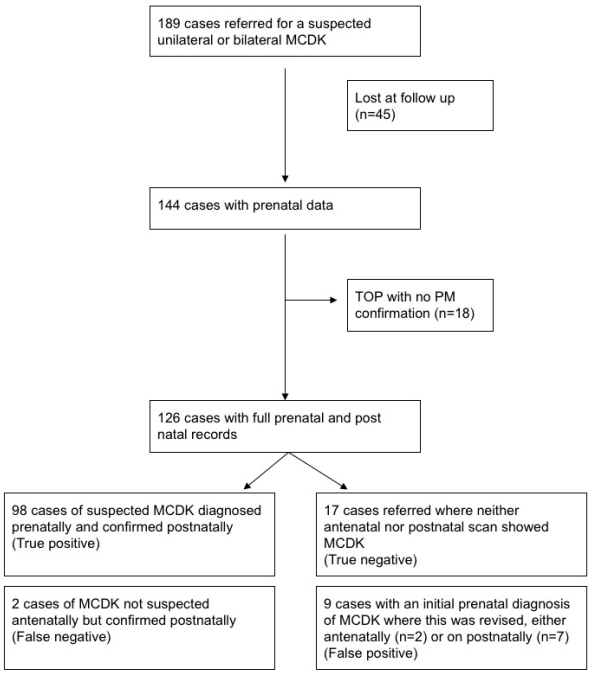
MCDK: multicystic dysplastic kidneys; PPV: positive predictive value; NPV: negative predictive value

Table 5. General characteristics of the 7 studies reporting prenatal detection of MCDK included in the systematic review
**NOTE TO EDITOR: THIS COULD BE AN ONLINE ONLY TABLE**

| First author | Study design | MCDK | Mean GA at scan (weeks) | Associated prenatal findings (n, %) | Prenatal diagnostic accuracy (n, %) | Outcomes (n, %) |
|---|---|---|---|---|---|---|
| Winding L et al. (2014) | Multicentre retrospective study | 601 | 21 | 157 (26.1%) | 527/601 (87.7%) | 446 (74%): livebirths<br>14 (2%): IUD<br>141 (23%): TOP |
| Moralıoglu S. et al. (2013) | Retrospective study | 68 | NA | 15 (22%) | 64/68 (94.1%) | 68 (100%): livebirths |
| Eckoldt F. et al. (2004) | Retrospective study | 107 | NA | 60 (56%) | 56/107 (53.3%) | 70 (82.4%): livebirths<br>3 (3.5%) IUD<br>12 (14.1%): TOP |
| Chang LW. et al. (2002) | Retrospective study | 28 | 27 | 7 (25%) | 28/28 (100%) | 16 (57.1%): livebirths<br>2 (7.1%): IUD<br>10 (35.8%): TOP |
| Van Eijk L. et al. (2002) | Retrospective study | 38 | NA | 10 (26.3%) | 38/38 (100%) | 30 (100%). livebirths |
| Avni EF. et al. (1987) | Retrospective study | 13 | 28 | NA | 13/13 (100%) | 13 (100%) |
| Rizzo N. et al. (1987) | Retrospective study | 16 | 27 | 5 (41.7%) | 12/12 (75%) | 10 (62.4%): livebirths<br>3 (18.8%): NND<br>3 (18.8%): TOP |
| ***Total*** | | 871 | 25.8 | 254 | 738 | 653 (77.6%): livebirths<br>19 (2.3%): IUD<br>3 (0.4%): NND<br>166 (19.7%): TOP |

IUD: intrauterine death; NND: neonatal death; MCDK: multicystic dysplastic kidneys; TOP termination of pregnanacy

**Figure1: Details on the population analysed in the study**



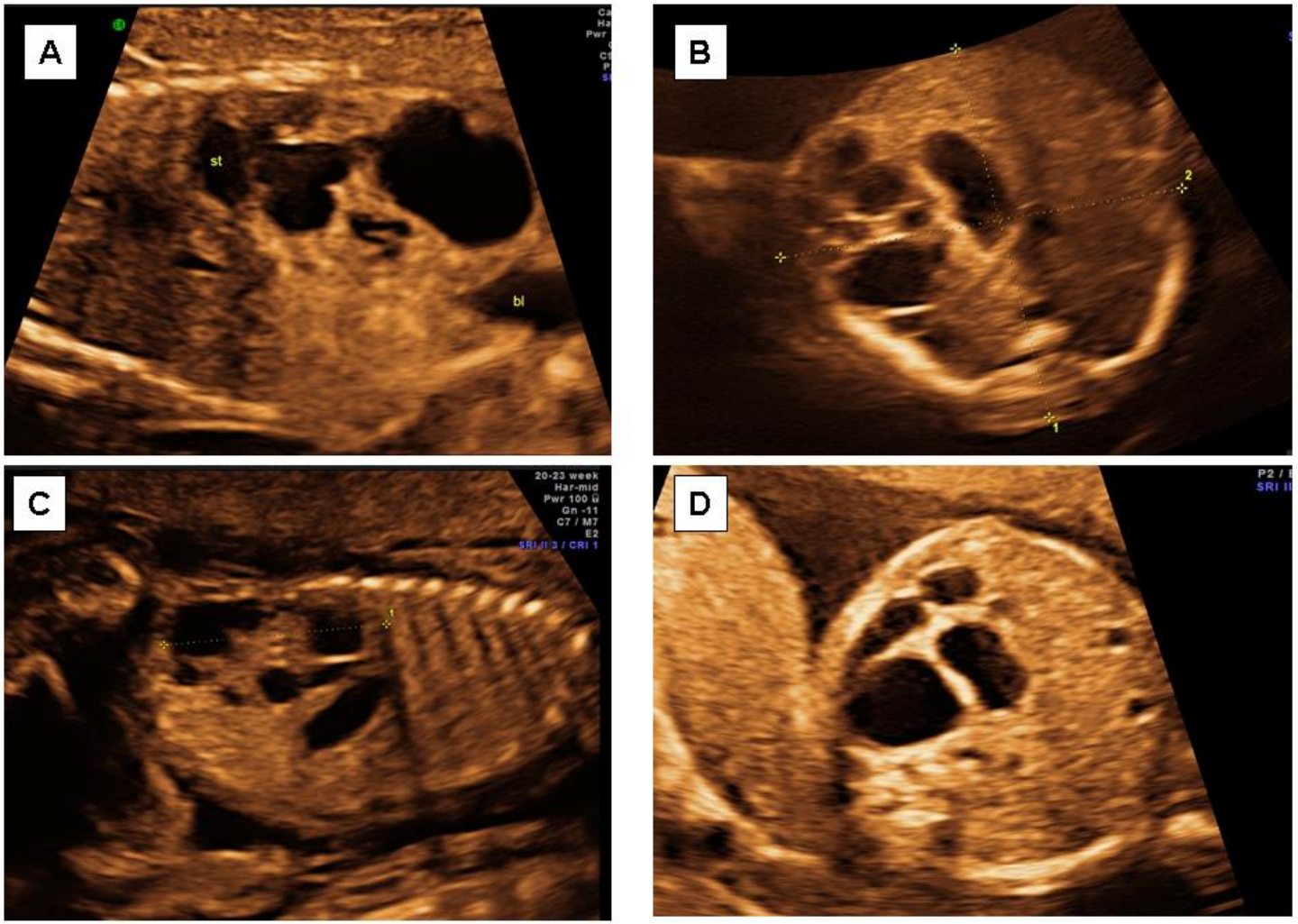



**Figure 2. A and B prenatal features of hydronephrosis; C and D prenatal features of MCDK**

**Figure 3.** Flow chart of the included studies in the systematic review