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Review article

Evaluation of fetal kidney growth using ultrasound: A systematic review

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ABSTRACT

Purpose: To determine the role of ultrasound imaging in evaluating fetal kidney growth.
Methods: MEDLINE, CINAHL and EMBASE databases were electronically searched for studies between 1996 and January 2017 and limited to English language. Studies were included if they reported on an ultrasound technique to assess fetal kidney growth and they were not a case report or case series. There was independent selection of studies by two reviewers in consensus with one other reviewer. Data were extracted by one reviewer in consensus with two other reviewers.
Results: A total of 1785 articles were identified. The full text of 39 of these were assessed for eligibility for inclusion. Twenty-eight studies were then included in the review. Standard two dimensional (2D) fetal renal measurements are easy to perform, however, this review identified that most studies had some methodological limitations. The disadvantage with 2D and three dimensional (3D) fetal renal volumes are that they include the entire kidney and good reproducibility of 3D volumes has not yet been demonstrated. Currently there is limited research on fetal kidney growth in the setting of abnormal fetal growth. Research focussing directly on fetal kidney parenchyma and blood flow is scarce.
Conclusions: Some nomograms of 2D and 3D fetal kidney size and volume have been developed. Kidney length is the most popular single fetal kidney measurement; however, it does not seem to be a good indicator of growth. In IUGR fetuses, kidney length remained similar to appropriately grown fetuses whereas AP and TS dimensions were significantly decreased. New ultrasound techniques focusing on the parenchyma of the kidney and perfusion to the kidney should be explored as they may provide more meaningful information on kidney development in the fetus and future kidney function.

1. Introduction

It is well established that an adverse intrauterine environment can affect fetal kidney development resulting in possible hypertension and chronic kidney disease later in life [1,2]. Intrauterine growth restriction (IUGR) can result in significant reductions in nephron number [3] which may ultimately result in decreased renal function [4]. Although most studies concentrate on IUGR and low birth weight infants, overgrowth or large for gestational age (LGA) are also emerging as factors that can disrupt normal fetal kidney development and increase risks for hypertension and chronic kidney disease [5]. The normal development of the fetal kidneys can be crucial to an individual's long-term health outcomes.

The human kidney develops through three successive embryonic stages. Transient development and regression of the primary (pronephros) and secondary (mesonephros) fetal kidneys occurs between day 23 and day 112 [6]. These primitive fetal kidneys have no impact on fetal renal function. The definitive, tertiary fetal kidney is the metanephros and this is the permanent functional kidney. It begins developing on day 30 leading to the formation of nephrons − the functional units within the kidney [6,7]. Fetal kidneys are unlike most other organs in that the maximum cell proliferation occurs in the third trimester. Nephrogenesis continues up until 34–36 weeks gestation with approximately 60% of nephrons formed in the third trimester [8].

Assessment of the fetal kidneys is an essential part of an obstetric ultrasound. Accurate information regarding kidney size is crucial to

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identifying kidney abnormalities and detecting changes in fetal kidney growth. Ultrasound imaging is safe, cost effective and widely available to evaluate fetal kidney size, echotexture and perfusion. A variety of two and three-dimensional ultrasound techniques have emerged and advanced to evaluate kidney development. The aim of this review was to systematically review the literature to determine what role ultrasound plays in evaluating fetal kidney growth. Current ultrasound imaging techniques and accuracy will be reviewed.

2. Method

A systematic review of observational studies was conducted using a protocol designed *a priori* and following the PRISMA guidelines for systematic reviews. Author SB developed and conducted the search strategy using medical subject headings (MeSH) and keywords and this was reviewed by author YK (Appendix A). MEDLINE (ovid); CINAHL and EMBASE electronic databases were electronically searched in August 2016 and again in January 2017; for publications from the year 1996 onwards. The literature search was limited to the English language. The reference lists of relevant articles were hand-searched for additional relevant studies.

Human observational ultrasound studies that were not a case report or case series were included. Only studies reporting on an ultrasound technique assessing fetal kidney growth were included. Studies that only assessed fetal pelvic renal dilatation were excluded.

Only studies published from the last 20 years (from 1996) were included as it was felt that the significant advances in ultrasound techniques and improvements in diagnosis and definition in prenatal imaging made these older studies less relevant. Also excluded were unpublished studies, non-peer-reviewed, conference abstracts, letters to the editor and opinion articles. If data from a single study population was reported more than once, the publication containing the most complete information was included.

Study selection was performed in two sequential steps, firstly assessing articles by title and abstract and secondly by full text of the article. Two reviewers (SB and YK) independently screened the titles and abstracts of all identified citations and potentially eligible studies were selected. The full text of these potentially eligible studies was screened by the same two reviewers. Any discrepancies between the reviewers were resolved by consultation with a third reviewer (DW).

A data extraction sheet was developed. Only pre-specified outcomes of interest in the review were collected. Review author SB extracted the data from the studies and the second review author YK checked the extracted data. Any disagreements were resolved by discussion with a third reviewer (DW). Fig. 1 outlines study selection process. A narrative synthesis, including tables, was done on the extracted data to explain and summarise the characteristics and findings of the included studies.

3. Results

A total of 1785 articles were identified and after review of the title and abstract, the full text of 39 of these were assessed for eligibility for inclusion (Fig. 1). Four papers from the Generation R study reported the same renal data [9–12] and therefore these data were only considered once using the paper by Verburg et al. [9] as it contained the most relevant and complete data assessing fetal kidney measurements. Finally, 28 studies were reviewed.

Relevant characteristics of these included studies are presented in Tables 1–3. Most studies were prospective in design with only 2 of the 28 studies retrospective [13,14]. A cross-sectional design was utilised by 21 studies while 7 studies had a longitudinal design. Selected studies were divided into three groups depending on the ultrasound technique used to assess the kidneys. Some studies reported on more than one ultrasound technique (Tables 1–3).

Generally, the study time and duration, how participants were recruited and missing participants and data was poorly reported.

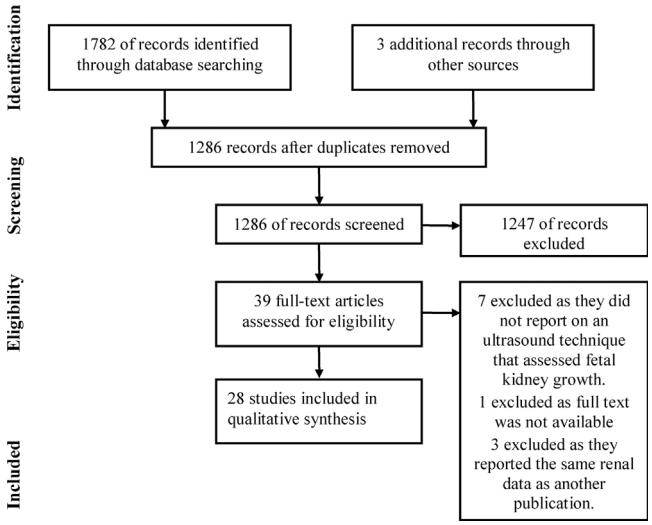

Fig. 1. Study selection process.

Calculation of estimated gestational age (GA) was most commonly achieved using the last normal menstrual period (LNMP) correlated with a first or early second trimester ultrasound (18 studies) [13–30]. Six studies used ultrasound dating only [9,31–35], one used only an accurate LNMP [36] and three did not report how GA was determined [37–39].

Overall ultrasound features of the studies and measurement methods were well described. Most studies focussed on the mid-second trimester to third trimester [9,13,14,16,18–31,33–35,37–39], as imaging the fetal kidneys well under 20 weeks can be difficult [33,40]. The three studies that reported data below 14 weeks GA used transvaginal scanning [15,17,36]. The GA range assessed was very variable between studies. Two studies showed only a snap shot in time with a GA range of 15 days (around 34 weeks) [34] and 4 weeks (28–32 weeks) [9]. One study measured the fetal kidneys at 23 weeks and again at 32 weeks [18]. Studies covering the longest GA ranges were Chitty and Altman [20] 16–42 weeks, van Vuuren et al. [32] 16–42 weeks and Hsieh et al. [25] 15–40 weeks. The GA range was unclear in one study [23].

3.1. Differences between right and left kidneys and gender

Overall the evidence strongly supported no significant difference between right and left fetal kidney size (17 of the 18 studies) for all ultrasound measurements regardless of the technique used [13,15,16,17,19,23–26,28–33,35,38]. Six of the seven studies that examined gender differences found no significant difference between fetal kidney measurements [17–19,23,29,30]. Only one study demonstrated a difference in size between right and left kidneys and males and females [9]. This was a large study, however, it had a small four-week gestational window (28.4–32.6 weeks) when each fetus was measured once. The study revealed right kidneys had a larger transverse and antero-posterior dimension when compared to left kidneys, resulting in larger calculated renal volumes. No difference, however, was found between kidney lengths. All kidney measurements were smaller in females than males [9].

3.2. Standard two dimensional (2D) measurements

Nineteen studies reported on a standard two-dimensional (2D) ultrasound measurement [9,13,15–23,29,31,32,34,36–39]. Standard two-dimensional (2D) measurements of the fetal kidneys was the earliest and simplest method utilised to assess kidney size at different gestational ages [41,42]. Most reviewed studies involved a low risk, uncomplicated pregnancy to obtain normal fetal kidney nomograms