Exploring Factors Influencing Kidney Development in Children: A Comprehensive Literature Review

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Abstract

This literature review delves into the intricate factors influencing kidney development in children. The study investigates key determinants such as age, height, gender, weight, and ethnicity, shedding light on their distinct impacts on kidney size. Age emerges as a pivotal factor, with discernible growth patterns before and after 20 months, followed by a stabilization phase. Notably, the initial two years witness a robust correlation between height and kidney length, emphasizing the significance of this developmental phase. In contrast, gender exhibits a minimal role in kidney size variation among children. Research findings indicate no significant differences in kidney lengths between males and females, underlining the limited impact of gender on this aspect of development. While weight is undeniably influential, its correlation with kidney size appears weaker when compared to the robust relationship observed with height. This underscores the complex interplay of various factors in shaping kidney development during childhood. Ethnicity emerges as a potential influencer, introducing variations in kidney size across diverse regions and populations. The call for localized data becomes evident, emphasizing the necessity of considering ethnic nuances in understanding children's kidney growth. In conclusion, this literature review offers a nuanced understanding of the multifaceted factors influencing kidney development in children. The insights gleaned from this exploration hold implications for medical practitioners, researchers, and policymakers, highlighting the need for a comprehensive approach in addressing the complexities of pediatric kidney development.

Keywords: Kidney development, Children, Nutrition.

1. Introduction

The development of kidneys in children is a multifaceted process influenced by a myriad of factors that play pivotal roles in determining kidney size and morphology. Understanding these factors is paramount for healthcare professionals, researchers, and policymakers to ensure comprehensive pediatric care. This literature review embarks on an exploration of the intricate interplay between age, height, gender, weight, and ethnicity in shaping the developmental trajectory of children's kidneys. Age stands out as a fundamental factor influencing kidney development in children. Mohtasib et al.'s (2019) insightful research delineates discernible patterns, showcasing significant changes in kidney growth before and after the critical threshold of 20 months. The subsequent stabilization phase underscores the dynamic nature of this developmental process. Particularly noteworthy is the rapid kidney growth observed during the initial 24 months, followed by a gradual decline.

Beyond this juncture, kidneys exhibit a steady growth rate, highlighting the evolving dynamics throughout childhood. Height emerges as a critical determinant, demonstrating a robust correlation with kidney length during the first two years of a child's life (Oh et al., 2016). This correlation is emblematic of the intricate relationship between somatic growth and kidney development. The initial phases of heightened growth coincide with dynamic changes in kidney dimensions, emphasizing the physiological synchrony during this critical period. The exploration of this relationship contributes to a nuanced understanding of how somatic growth influences organ development during the formative years.

In contrast, gender exhibits a relatively limited impact on kidney size variation among children. Extensive studies by Kim et al. (2013) and Coombs et al. (2019) reveal that, contrary to certain anatomical differences between male and female adults, there are no significant distinctions in kidney lengths between male and female children. This underscores the need for a more nuanced consideration of gender-related factors in the context of pediatric kidney development. Weight, while undeniably influential, introduces a layer of complexity in understanding its correlation with kidney size. Mohtasib et al.'s (2019) findings underscore the significant role of weight in determining kidney dimensions. However, the observed correlation is comparatively weaker than that of height, accentuating the intricate interplay of various factors contributing to pediatric kidney development. The influence of ethnicity on pediatric kidney development introduces a compelling dimension to this exploration. Rongviriyapanich et al. (2020) emphasize that variations in kidney size across different regions and populations underscore the need for localized data. The ethnic nuances in kidney development hint at a complex interplay between genetic factors and environmental influences, necessitating a region-specific approach for a holistic understanding. In conclusion, this literature review sets the stage for a comprehensive exploration of factors influencing kidney development in children.

2. Review Content

2.1 The Kidney Anatomy

The kidney is a bean-shaped organ with a medial concavity and lateral convexity. There are two kidneys bilaterally, situated retroperitoneally behind the peritoneum, which separates the inner abdominal wall from other abdominal organs (Vasković, 2022). In the supine position, kidneys are located between the T12 and L3 transverse processes. The right kidney is lower due to the presence of the liver above it, and the left kidney is more medial, longer, and slender compared to the right one. The upper and lower parts of the kidneys are called poles. On the medial side, there is a deep concavity called the hilum, where the renal artery, renal vein, and ureter connect. Inside the kidney, after a vertical bisection, the renal hilum forms the renal sinus. The kidney's structure consists of the cortex, the outer part surrounding the medulla, and the medulla, the inner part. The renal medulla has triangular-shaped structures called renal pyramids, separated by extensions of the renal cortex called renal columns. The base of the renal pyramid faces the cortex, while the apex faces the renal sinus. The apex is called the renal papilla, connecting with minor renal calyces to receive urine from the papillary foramina, which open at the renal papilla. Minor renal calyces join to form major renal calyces, eventually forming the renal pelvis as the superior end of the ureter (Drake, et al., 2019).

2.2 Nephrogenesis

Kidney formation begins in the embryonic stage from the mesodermal layer. Nephrogenesis has three phases: pronephros, mesonephros, and metanephros. Pronephros, the first generation of the kidney, consists of nephrotomes, aggregations of nephrogenic cells. This stage occurs in the early fourth week of gestation. Pronephros undergoes rudimentation and regression by the end of the fourth week, giving rise to the

mesonephric duct. The ureteric bud branches from the distal part of the mesonephric duct/Wolffian duct to the metanephric mesenchyme to form the metanephros in the fifth week of gestation (Soriano, et al., 2021). The ureteric bud expands to form the renal pelvis and ureter. Eventually, it will branch into major calyces by the sixth week of gestation. Each major calyx stimulates to divide and form new buds in the seventh week. From major calyces, they develop into minor calyces. The formation of the collecting tubules continues until they merge with the renal pyramid. Nephrons start producing urine by the 12th week of gestation. Nephrogenesis continues until around 35-36 weeks of gestation (Soriano, et al., 2021). After birth, the kidneys keep growing based on size increments.

2.3 Postnatal Kidney Growth

Kidney formation stops at 36 weeks of gestation, and the final number of nephrons in the kidneys is established at birth (Murawski, et al., 2010). The number of nephrons varies between 200,000 to 2.7 million in each kidney at birth. Kidney growth continues after 34 weeks of gestation, through the maturation of existing nephrons rather than the formation of new ones (Stewart & Marks, 2022). According to the diagnostic ultrasound manual, the age of the child affects the size of the kidneys. At birth, the normal kidney length is about 4.5 cm, increasing to 6 cm at 1 year, 8 cm at 5 years, and 10 cm at 10 years old (Cochlin & Robinson, 2011).

2.4 Kidney Disorders Affecting Morphology and Size in Children

Normal-sized kidneys indicate a healthy child. Besides being of normal size, kidneys can also shrink or swell. Changes in kidney size can lead to various diseases affecting the body. Therefore, it is essential to evaluate a child's kidney size early on.

- Kidney agenesis is a condition where a baby lacks one or both kidneys (CDC, 2021). Incidence: Unilateral kidney agenesis occurs in 1 in 1,000 births, while bilateral kidney agenesis is 1 in 3,000 to 4,000 pregnancies (Jelin, 2021).
- Kidney hypoplasia is a congenital disorder where the kidneys are small due to incomplete development (CDC, 2021). Incidence: Relatively common, with one in 400 babies born experiencing kidney hypoplasia (Cain, et al., 2010).
- Ectopic kidneys are those located outside their normal position (NIDDK, 2019). Incidence: Approximately 1 in 1,000-5,000 births (Kidney Care UK, 2021).
- Horseshoe kidney is a condition where both kidneys fuse, resembling a horseshoe rather than the typical bean shape (Cleveland Clinic, 2022). Epidemiology: Around 1 in 400-1,600 births have this condition, with a prevalence of 0.25% in the general population (Pawar, et al., 2018).
- Hydronephrosis is the enlargement or swelling of the kidneys due to the accumulation of urine (NHS, 2021). Ultrasonography reveals a large hypoechoic area branching and connecting in the renal calyx region (Koratala, 2019).
- Kidney cysts are fluid-filled sacs formed within the kidneys (Radiology Info, 2022). The most common type is simple kidney cysts, which develop with age and usually occur in adults (Garfield & Leslie, 2023). However, they are rare in children, with the incidence of simple kidney cysts in children being less than 1% (Bellagha, et al., 2013).
- Kidney Abscess. A kidney abscess is a rare complication of pyelonephritis. Ultrasound examination reveals a clear mass with low echogenicity and a thick wall (Bellagha, et al., 2013).
- Urolithiasis is the macroscopic formation of deposits or stones in the kidneys, usually composed of calcium oxalate or calcium phosphate. In children, this condition is relatively common, with an epidemiology of 2-3%, and a recurrence rate ranging from 6.5-54% (Ricardo, 2017).

- Nephrocalcinosis involves an increase in calcium levels in the kidneys (Fulop & Batuman, 2021). Ultrasound findings show increased echogenicity in the medullary pyramids with acoustic shadows or artifacts in the kidney medulla (Bellagha, et al., 2013).
- Kidney tumors can be benign or malignant. Wilms tumor (nephroblastoma) is the most common tumor in children, usually occurring between the ages of 3-5 years. Typically, a solid kidney mass with large and heterogeneous characteristics is observed, with low echogenicity of the tumor (Bellagha, et al., 2013).

2.5 The Influence of Nutrition and Protein on Kidney Development in Children

Protein intake during the growth and development stages of infants may be associated with the size and function of the kidneys. Data indicates that infants receiving additional protein intake tend to have larger kidney sizes compared to those not receiving additional protein. However, it is still unknown whether there is a relationship between protein intake and kidney size growth in later childhood. Based on a study conducted by Voortman et al. (2015), research was carried out on 2968 six-year-old children. The results of the study state that there is no significant relationship between total protein intake and factors such as gender, birth weight, gestational age, ethnicity, or kidney volume. On the other hand, protein intake was found to be associated with the development of kidney function. However, no correlation was found regarding its relationship with the growth of kidney size. Interestingly, even in the absence of a connection between protein intake and kidney size, no differences were observed for animal and plant protein intake.

2.6 Factors Influencing the Size of Children's Kidneys

2.6.1 Age
According to Mohtasib et al. (2019), age significantly influences kidney length. Kidney length undergoes changes before and after 20 months of age. Rapid kidney growth occurs in the first 24 months, but this growth gradually slows down after reaching 24 months. Subsequently, the kidneys grow at a constant rate.

2.6.2 Height
Numerous studies have found a strong correlation between height and kidney length in children. The explanation for this lies in the rapid increase in height during the first 2 years, closely linked to the increase in kidney length. In other words, height and kidney length increase simultaneously, demonstrating a cause-and-effect relationship (Oh et al., 2016).

2.6.3 Gender
In many studies, gender has been found not to significantly influence kidney length in children. This is due to the lack of significant differences in kidney length between males and females. According to Kim et al. (2013), gender is not a significant independent variable, and the difference in kidney size between males and females is minimal, indicating a weak relationship. Similarly, Coombs et al. (2019) found that kidney length is not associated with gender, whether left or right kidney.

2.6.4 Weight
Similar to height, weight information is obtained through anamnesis or measurements before performing ultrasound examinations. Several research findings suggest that weight can influence a child's kidney length, although this influence is generally weaker than that of height. For instance, in a study by Mohtasib et al. (2019), the correlation coefficient between weight and right kidney length is 0.714, and for the left kidney, it is 0.708.

2.6.5 Ethnicity

Ethnicity can potentially affect the growth of children's kidney size. Kidney size may vary between regions or populations, requiring information and data from the local area (Rongviriyapanich et al., 2020). Since kidney size growth is also influenced by a child's overall body growth, research results from other countries may not be strong evidence for universality. Studies on normal kidney sizes in children from various countries have yielded different results (Arooj et al., 2011).

3. Conclusion

In conclusion, this comprehensive review illuminates the dynamic interplay of age, height, gender, weight, and ethnicity in shaping pediatric kidney development. Age and height emerge as pivotal determinants, with age delineating distinct growth patterns and height exhibiting a robust correlation with kidney length. Gender's impact is limited, while weight's influence is significant yet complex, with a weaker correlation than height. Ethnic nuances add complexity, emphasizing the need for localized data. This synthesis provides critical insights for optimizing pediatric care, guiding future research, and informing targeted public health strategies.

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References

- Arooj, A., Lam, J., Yeoh, J. W. & Supriyanto, E., 2011. Comparison of Renal Size among Different Ethnicities. INTERNATIONAL JOURNAL OF BIOLOGY AND BIOMEDICAL ENGINEERING, 5(4), pp. 221-229.
- Bellagha, I. et al., 2013. Urinary tract and retroperitoneum in paediatric ultrasound. In: M. Lauckner, ed. Manual of diagnostic ultrasound. Slovenia: World Health Organization, pp. 289-314.
- CDC, 2021. Center for Disease Control and Prevention. [Online] Available at: https://www.cdc.gov/ncbddd/birthdefects/surveillancemanual/quick-reference- handbook/renal-agenesis-hypoplasia.html
- Cochlin, D. L. L. & Robinson, M., 2011. Kidneys and ureters. In: H. Lutz & E. Buscarini, eds. WHO manual of diagnostic ultrasound. Malta: WHO Library Cataloguing, pp. 267-319.
- Drake, R. L., Vogl, A. W. & Mitchell, A. W. M., 2019. Gray Dasar-Dasar Anatomi. 2 ed. Singapura: Elsevier Singapore Pte. Ltd.
- Fulop, T. & Batuman, V., 2021. Nephrocalcinosis. [Online] Available at: https://emedicine.medscape.com/article/243911-overview [Accessed 18 September 2023].
- Jelin, A., 2021. Renal agenesis. SMFM CONSULT SERIES, 225(5), pp. 28-29.
- Kidney Care UK, 2021. info Kid. [Online] Available at: https://www.infokid.org.uk/sites/default/files/topics/infoKID%20Ectopic%20we bformat.pdf [Accessed 29 Juli 2022].
- Koratala, A., 2019. The Ultrasound Mimics of Hydronephrosis. [Online] Available at: https://www.renalfellow.org/2019/05/10/the-ultrasound-mimics- of-

hydronephrosis/#:~:text=On%20the%20sonogram%2C%20hydronephrosis%20appears,in%20the%20renal%20collecting%20system. [Accessed 19 September 2023].

- Mohtasib, R. S. et al., 2019. Sonographic measurements for kidney length in normal Saudi children: correlation with other body parameters. Annals of Saudi Medicine, 39(3), pp. 143-154.
- Oh, M. S. et al., 2016. Sonographic Growth Charts for Kidney Length in Normal Korean Children: a Procpective Observational Study. J Korean Med Sci, 31(7), pp. 1089-1093.
- Pawar, A. S. et al., 2018. Incidence and characteristics of kidney stones in patients with horseshoe kidney: A systematic review and meta-analysis. Urol Ann., 10(1), pp. 87-93.
- Ricardo, A., 2017. Gambaran Klinis dan Tata Kelola Batu Saluran Kemih pada Bayi dan Anak-anak. Jurnal Kedokteran Meditek, 22(58).
- Rongviriyapanich, C. et al., 2020. Sonographic renal length and volume of normal Thai children versus their Chinese and Western counterparts. Clinical and Experimental Pediatrics, 63(12), pp. 491-498.
- Soriano, R. M., Penfold, D. & Leslie, S. W., 2021. Anatomy, Abdomen and Pelvis, Kidneys. Treasure Island: StatPearls Publishing.
- Stewart, D. J. & Marks, S. D., 2022. Renal Development and Dysfunction. In: D. T. Wilcox & D. F. M. Thomas, eds. Essentials of Pediatric Urology. Florida: CRC Press, pp. 13-22.
- Vasković, J., 2022. KenHub. [Online] Available at: https://www.kenhub.com/en/library/anatomy/kidneys [Accessed 12 Juni 2022].