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Review Article

Interfering Factors in the Growth of the Pediatric Population after Kidney Transplantation

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Abstract

Growth failure is a marked feature in children with CKD. Kidney transplantation (KTx) is the therapeutic option that provides the greatest benefits to the pediatric population.

Considering the importance of this subject, a systematic search of the literature was carried out on the principal databases from January 2015 to December 2020. The following descriptors in health science (DECs) from the VHL portal (library virtual health) were applied: pediatric kidney transplantation (PKTx), growth and development.

It was found that among the etiologies, congenital abnormalities of the kidneys and urinary tract (CAKUT) were the main causes of loss of renal function. The highest mean age was 15.52 ± 1.8 years. The type of donor was reported in only 3 studies, in 1 of which the living donor was predominant. The immunosuppression (ISS) schemes after PKTx were similar in the studies, the triple scheme with corticoid, calcineurin inhibitor and anti-proliferative being used in most of them. The use of GH did not occur in 4 of the 9 studies.

We could conclude that weight and height gain after PKTx is an important outcome to be evaluated. In underdeveloped or developing countries where, in addition to chronic disease, we find nutritional and economic precariousness, it is very important to know the factors that greatly contribute to the impairment of height and weight gain of these patients. Controlled and randomized studies that find answers for the control of pediatric patients after PKTx and that can be applied in our country are desired.

Keywords: children; adolescents; growth; kidney transplantation

1. Introduction

Chronic kidney disease (CKD) is responsible for high rates of morbidity and mortality in the general population. In pediatric patients, mineral and bone metabolism disorders with evolution to skeletal deformities, fractures and growth retardation are more pronounced [1]. Growth failure in particular is a hallmark of children with CKD. Although the prognosis for the height of these patients has improved considerably in recent decades, approximately 40% of these patients will require RRT before puberty and will continue with reduced thin height into adulthood (<-2 SD) [2-9]. The risk of stunting is more severe the younger the child, and short stature is associated with a higher risk of hospitalization and higher mortality [1-3,10,11].

The prevalence of stunting in pediatric patients with CKD on conservative treatment was previously described in the *Noth American Pediatric Renal Trials and Collaborative Studies* (NAPRTCS) registry report from 1994 to 2007, in which the height of more than one-third of patients was below the 3rd percentile [12]. A 2014 study with 800 children with CKD (median estimated glomerular filtration rate (eGFR) = 50 ml / min / 1.73 m^2), included in the CkiD study, revealed a reduction in the prevalence of stunting, since

that only 12% of patients had severe short stature. Interestingly, this study also demonstrated that for every 10 ml/min/1.73m^2 reduction in eGFR there was a decrease in mean height of 0.14 standard deviation [13].

Records provided evidence that growth retardation is highly prevalent at the start of dialysis treatment. The 2011 NAPRTCS showed a mean height standard deviation equal to -1.60, with those younger than 2 years being the most affected: -2.59 [14]. Likewise, the *International Pediatric Dialysis Network* demonstrated a mean height standard deviation of -2.25 in its cohort of 2,800 children who had started treatment with chronic peritoneal dialysis. However, the height of patients at the time of transplantation, according to the NAPRTCS, improved substantially over time, with a mean standard deviation of height equaling -2.4 in 1987 to -1.17 in 2013. Final height of transplant recipients also increased from an average of -1.93 in the 1987 to 1991 cohort to -0.89 in the 2007 to 2013 cohort [7].

The pathogenesis of short stature in CKD is multifactorial. A broad spectrum of concomitant complications such as poor nutritional intake, metabolic acidosis and electrolyte changes, as well as growth hormone insensitivity associated with CKD, must be considered. Inadequate calorie and protein intake can have important adverse effects on growth and development, especially in infants with severe CKD, in whom height loss may be greater than 2 standard deviations in the first 6 months of life, when growth is accelerated [15]. Malnutrition can be the result of altered taste, elevated levels of cytokines that affect satiety, possible gastroesophageal reflux, and increased intra-abdominal pressure that accompanies peritoneal dialysis [9].

Disturbances in the growth hormone–insulin growth factor-1 (IGF-1) axis also contribute to the genesis of reduced growth associated with CKD (10). An important advance in driving the growth of children with CKD was the introduction of recombinant human growth hormone (rhGH), which improves the growth of these children [11].

Height deficit is commonly observed at all levels of CKD in children [7] and leads to a worsening in the quality of life and self-esteem of these patients. In adult life, short stature is correlated with difficulties in interpersonal and professional relationships [9], generating psychosocial repercussions for these patients.

As aforementioned, kidney transplantation (KTx) is currently the therapeutic option that provides the greatest benefits to the pediatric population, however, despite the advantages associated with this therapy, the final height reached by most recipients is not the calculated target height [10]. This discrepancy is correlated with several factors, including: age of the child at the time of KTx, duration of renal replacement therapy (RRT), use of corticosteroids and immunosuppressants (ISS), patient's history of prematurity, cause of CKD, graft function, donor type, insulin-like growth factor type 1 (IGF1) axis abnormalities, and nutritional status, among others [16].

Studies on the growth of pediatric patients with CKD evaluated after KTx are limited to small populations, especially in developing or underdeveloped countries [17]. This makes it difficult to identify which factors would be more related to this stunting. Knowing the experience and results of other transplant centers on the growth of children after KTx is important for the implementation of measures to mitigate the factors that interfere in the process and seek a better outcome for these patients. In this scope, this study aims to make a systematic review of the factors that interfere with the growth of the pediatric population after KTx.

2. Methods

A systematic literature search was carried out in the CAPES, PubMed, Cochrane Library and Scielo databases. The following health science descriptors (DECs) from the VHL portal (virtual health library) were used: *kidney pediatric transplant, growth and development*. The population was restricted to pediatric patients under the age of 18 years. We decided to use only articles in English, Spanish and Portuguese and the publication date was set for the period from January 2015 to December 2020.

Initially, 20 articles were found and nine articles met the criteria for this review. These articles were evaluated using the *Critical Appraisal Skills Programmer* (CASP) [18]. The level of evidence of the articles was evaluated using the *Grading of Recommendations Assessment, Development and Evaluation scale.* (GRADE) [19]. In the article selection process, 20 studies were evaluated based on the criteria described above. Of these, eleven studies were excluded, one of them was duplicated in the database, five articles covered a population over 18 years of age, three articles did not assess the height of the patients and two articles were outside the predetermined period, being final nine selected articles. The way in which the selection was developed is summarized in Figure 1. It is, therefore, an integrative review of the literature on the subject.

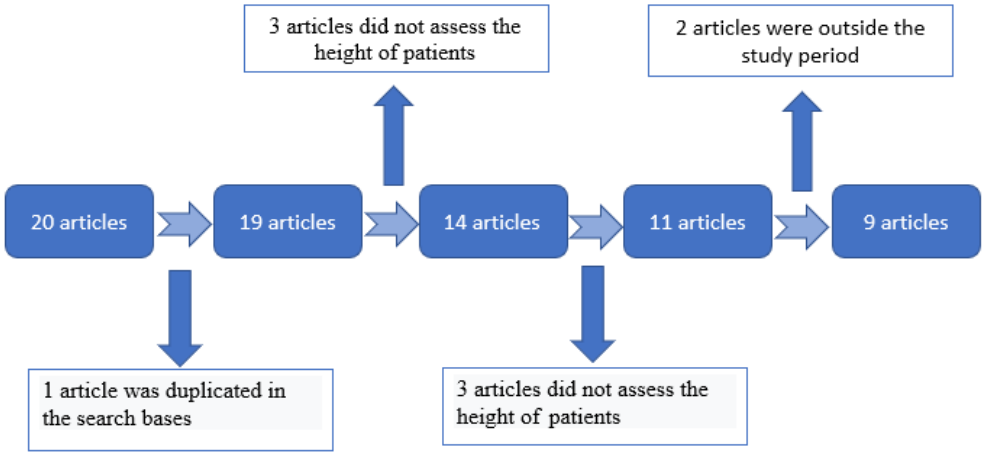

Figure 1: Article selection process

3. Outcome measures

Factors that interfered with post-transplant linear growth, as indicated by a change in the standardized Z-score of height from baseline, were the primary outcomes evaluated. Secondary outcomes were patient and graft survival, renal graft function (expressed as eGFR), and adverse events. These data were present in clinical trials, longitudinal studies and literature review.

4. Results

The nine articles that met the inclusion criteria and were used to carry out this literature review are summarized in Tables 1 and 2. The characteristics and results of these studies were listed as follows: sample size, follow-up time, gender, race and age of participants, CKD etiology, type of RRT, donor, immunosuppression, height variation, GH use, outcomes and biases [7,16]. The methods used in these studies were quite diverse, with seven studies being experience reports, with four retrospective and three prospective cohorts, in addition to two clinical trials.

The studies consisted of samples containing from 13 to 322 patients. They were carried out in single or multicenter centers, contemplating data from countries on the European, Asian and American continents. The follow-up period ranged from 6 months to 17 years, time defined according to each study design.

During the analysis, a predominance of males was identified in all studies, with percentages ranging from 56.7 to 100% of the participants. Most studies did not describe the patients' race and only three studies reported this data. In all of them there was a prevalence of white race with more than 70% [20 – 24].

Note That 2 New References Have Been Introduced Here

Regard to etiology, only one study did not describe the causes of CKD in its participants [23]. In other studies, CAKUT were the main causes of loss of renal function. In the study by Hillesheim et al the incidence reached 82.4% of the sample [25]. Participants in selected studies had to be under 18 years of age, as described in the applied methods. Among the selected studies, the one by Gil et al presented a sample with the highest mean age of 15.52 ± 1.8 and control with 14.36 ± 1.13 years [3].

Pre-transplant RRT modalities were cited in five studies. Tönshoff et al used a sample in which almost 40% of transplant recipients had not undergone any dialysis therapy [26] while Hillesheim et al had less than 15% of participants without RRT pre-KRT [25].

Three studies did not discriminate the type of donor. Among the studies that reported this data, the deceased donor was the most described, except in the analysis by Kumar et al which presented a sample with 80% of living donors [27].

The maintenance ISS regimens showed variations regarding the use of corticosteroids, but in general, they were similar in all the studies that cited them. Only Tönshoff et al evaluated a group using sirolimus (SRL) instead of mycophenolate mofetil (MMF) [26].

Table 1: General sample data of selected articles

Source	Sample size	follow-up time	Male	Caucasians	Age	CKD etiology	Type of TRS pre Tx
Lopez-Gonzalez et al, 2020	95 patients	2008 - 2018	0.615	NR	7.83 (IQR: 3.3–14.4)	CAKUT 40%	Preemptive 32.6% / HD 50.5%
Kumar et al, 2019	30 patients	2010-2018	0.567	NR	9.8 ± 3.77	CAKUT 33.3%	Preemptive 10% / HD 20%
Delucchi et al, 2019	30 patients	6 months to 1 year post TX	0.567	NR	7.8 ± 4.3	CAKUT 60%	NR
Tönshoff et al, 2019	106 patients	12 months	0.566	0.839	EVR + TAC 10.2 (4.9) MMF + TAC 10.3 (4.8)	CAKUT 47.1%	Preemptive 38.6% / HD 30.1%
Gil et al, 2018	23 patients	1999-2012	1	NR	sample 15.52 ± 1.8 X control 14.36 ± 1.13	CAKUT 76.6% X 70%	NR
Franke et al, 2013	322 patients	May 1998 - January 2015	0.602	NR	4.5 -13.2	CAKUT 45.9%	Preemptive 29.8% x 39.5%
Swolin-Eide et al, 2018	13 patients	1030 days	0.692	NR	9.3 (3.4-15.0)	CAKUT 61.5%	NR
Webb, et al. 2015	188 start / 113 (1 year) /106 (2 year)	2 years	67.3%x control 60.2%	80.6% x 91.8%	<12 years 43.8% x 46.9%	NR	NR
Hillesheim et al, 2016	17 patients	24 months	0.823	0.706	9.1 ± 4.1	CAKUT 82.4%	Preemptive: 12% / DP 70.6% / DP + HD 12% / HD 5.9%

Three studies did not use GH or did not report it in the results [21,24,28]. Regarding the assessment of the children's height, all used the Z-score to perform the analysis, however, each study evaluated growth in a different way. Some authors compared growth between the different groups that used or not GH after transplantation [1,3,23,28,29], others according to age at the time of PKTx, history of prematurity [29], use of corticosteroids [23,24,29], and ISS schedules [21,28]. The findings were very diverse in the selected studies. In general, they found a gain in the height of the participants after PKTx, as shown in Table 2.

Table 2: Type of donor and drugs used after transplantation

Source	GH use	deceased donor	ISS type
Lopez-Gonzalez et al, 2020	0.442	92.6%	Basilix. / TAC + MMF + PRED
Kumar et al, 2019	0	0.2	Basilix. 43.3%/ Germany 43.3%/ Thymus 3.4%/ TAC + MMF + PRED
Delucchi et al, 2019	0	NR	basilix. 100% / TAC + MMF with/without PRED
Tönshoff et al, 2019	0	0.518	Basilix. 100% and PRED + TAC + EVR OR + TAC + MMF
Gil et al, 2018	0.564	NR	NR
Franke et al, 2013	44.7% x 32.5% (pre) and 11.7% x 7.5%	Living donor: 23.4% x control 39.5%	PRED until 2008 daily
Swolin-Eide et al, 2018	0.46	NR	PRED daily for 3 months -> alternate days for another 3 months, calcineurin inhibitors and MMF.
Webb et al, 2015	NR	68.4%x 74.5%	TAC + PRED + MMF / TAC + MMF + PRED AND DACLIZUMAB
Hillesheim et al, 2016	0.12	64.7%	CI + 100% ANTIPROLIFERATIVE + PRED WITH VARIOUS DOSE

5. Discussion

The stigma of CKD and other chronic diseases found in the pediatric age group is mainly related to short stature and the difficulty in gaining weight in these patients, as mentioned above. In most cases, this disease marker cannot be mitigated or resolved, however, in CKD we found a feasible possibility of improving these data and consequent resolution of the deleterious effects in the long term [2]. Pediatric KTx is known to be the gold standard for the treatment of CKD, however, some factors may contribute to a better outcome in the height and weight of these patients [2].

The studies evaluated in this review described factors that could contribute to better growth and weight gain in children after KTx. Lopez-Gonzalez et al found better growth results than those found in other cohorts [1]. According to the authors, such factors could be associated with a high rate of preemptive KTx and the use of GH in the pre and post KTx period. The duration of the use of corticosteroid in this study demonstrated its negative impact on the patient's linear growth during the first year after KTx ($p \leq 0.05$), but no significant impact on the patient's height at final follow-up [1].

Gil et al found results similar to those of Lopez-Gonzalez et al with regard to the use of GH [1,3]. In this study, the authors studied the use of GH in a group of patients and compared it with a control group that did not have the medication [3]. A significantly higher mean height was found in children using GH than in control (-1.8 ± 0.8 vs. -2.9 ± 1 SD; $p = 0.018$). One data analyzed in this study was the difference between creatinine clearance (ClCr) at baseline and at the end of the study in each group, where the follow-up period was from six months to one year after transplantation [3]. The study concluded that there were no significant differences for either group (GHGr $p = 0.28$; CGr $p = 0.064$) [3].

Likewise, the study by Franke et al also found a positive correlation between the height gain of the patients analyzed with regard to the use of GH and preemptive Tx, with $p<0.05$ for small-for-age children gestational age (SGA) [30]. Unlike what was seen by Gil et al, the CrCl had an impact at the end of the height assessment of SGA patients. Those who had higher CrCl were those who had greater growth at the end of the study ($p<0.01$) [1,31-33]. Franke et al also identified that lower exposure to steroids was associated with better longitudinal growth, but also with a lower degree of body disproportion in premature patients ($p<0.05$), a fact that was not identified by Lopez-Gonzalez et al [30,1].

The review by Delucchi et al also found an association between prednisone therapy and reduced longitudinal growth, as did Franke et al [30,34]. A new finding in this study was that corticosteroid use was the association with a decrease in bone mineral density and an increase in body fat. In addition, there was an increase in levels of fibroblast growth factor 23 (FGF23) when compared to longer withdrawal. The study also showed that there was no worsening of renal function in that group in which the steroid was withdrawn, an important fact since it can be inferred that there was no increase in the number of rejections. [34]

The study by Webb et al as well as the study of Delucchi et al demonstrated that early initiation of corticosteroid withdrawal (six months after PKTx) improves growth up to two years after KRT, with this recovery being more prominent in the prepubertal population [34,35]. The prepubertal and pubertal subgroups showed better growth at one-year follow-up than at two years, overall. Another relevant finding was the identification that prepubertal individuals using corticosteroids had a higher body mass index (BMI) at one year when compared to the group that did not use corticosteroids (0.64 - 95% CI; 0.19, 1.09; $p = 0.006$) [34,35].

Tönshoff et al [26] assessed children's growth according to the type of maintenance ISS (everolimus or mycophenolate). Data analysis did not identify differences in growth or renal function between the groups [26]. Swolin-Eide et al evaluated a sample containing 13 participants and, throughout the study, an increase in the average height, as well as in the BMI and weight of the evaluated patients was identified [36]. During the study period, the evaluation of bone resorption markers telopeptide of carboxy-terminal cross-linking of collagen type I (CTX) and TRACP5b, pro-collagen type I intact amino-terminal propeptide (PINP), alkaline phosphatase (FA), osteocalcin, PTH, and vitamin D. A reduction in their values was identified initially with subsequent maintenance of the levels. On the other hand, bone formation markers (PTH, vitamin D, alkaline phosphatase) increased successively throughout the analysis [36].

In the study by Hillesheim et al, who followed up a pediatric population for two years after KTx, it was identified that after 24 months of KTx, growth was insufficient for the recovery of stunting and weight gain was excessive [25]. It was found that the greatest growth occurred in younger patients and with greater stunting at the time of KTx [25]. Webb et al [35] and Delucchi et al [34], found no relationship of corticosteroids and short stature.

However, the use of prednisone on alternate days has resulted in better growth in relation to daily use.

Early withdrawal of corticosteroids (six months after KTx) as well as the use of GH had a positive impact on the final height of patients undergoing these interventions in the studies evaluated. More research evaluating these approaches would be important for a better understanding of the growth of these patients.

Among the limitations described by the studies, the most recurrent was the small number of participants, which is considered a limiting factor for the application of some results in some cases. Another limitation, which is common to retrospective studies, was the lack of data in the medical records collected, a fact that harmed some analysis. In prospective studies, the lack of some variables that would bring more robust information and conclusions to the studies were omitted or not reported. Some studies presented inadequate control groups, which compromised the analysis of the outcomes found.

6. Conclusion

Weight and height gain after pediatric KTx is an important outcome to be evaluated, mainly to determine the factors that could contribute to this gain and the changes that could be implemented in the services to achieve the desired results. The early use of GH after KTx in children and the earlier withdrawal of corticosteroids can be used as tools to improve this gain, although further studies are important to define the moment to start and withdraw these drugs.

According to what has already been mentioned, in underdeveloped or developing countries such as Brazil, where in addition to the chronic disease we find the nutritional and economic precariousness that the families of these patients are subjected to, it is very important to know the factors that greatly contribute to the impairment. height and weight gain of these patients.

Controlled and randomized studies that find answers for the height and weight control of pediatric patients after KTx and that can be applied in our environment are desired.

7. References

1. Lopez-Gonzalez M, Munoz M, Perez-Beltran V, Cruz A, Gander R, Ariceta G. Linear Growth in Pediatric Kidney Transplant Population. Front Pediatr. (2020); 8:569616.
2. Harambat J, Bonthuis M, van Stralen KJ, Ariceta G, Battelino N, Bjerre A, et al. Adult height in patients with advanced CKD requiring renal replacement therapy during childhood. Clin J Am Soc Nephrol. (2014); 9:92–99.
3. Gil S, Aziz M, Adragna M, Monteverde M, Belgorosky A. Nearadult height in male kidney transplant recipients started on growth hormone treatment in late puberty. Pediatr Nephrol. (2018); 33:175–180.
4. Fine RN, Martz K, Stablein D. What have 20 years of data from the North American Pediatric Renal Transplant Cooperative Study taught us about growth following renal transplantation in infants, children, and adolescents with end-stage renal disease? Pediatr Nephrol. (2010); 25:739–746.
5. Cantarovich D. Corticosteroid minimization after renal transplantation*. Transpl Int. 2012 Mar;25(3):272-3. Epub 2011 Dec 27. PMID: 22212179.
6. Franke D, Winkel S, Gellermann J, Querfeld U, Pape L, Ehrich JH, et al. Growth and maturation improvement in children on renal replacement therapy over the past 20 years. Pediatr Nephrol. (2013); 28:2043–2051.
7. Andre JL, Bourquard R, Guillemin F, Krier MJ, Briancon S. Final height in children with chronic renal failure who have not received growth hormone. Pediatr Nephrol. (2003); 18:685–691.
8. Englund MS, Tyden G, Wikstad I, Berg UB. Growth impairment at renal transplantation–a determinant of growth and final height. Pediatr Transplant. (2003); 7:192–199.
9. Haffner D, Schaefer F, Nissel R,Wuhl E, Tonshoff B,Mehls O. Effect of growth hormone treatment on the adult height of children with chronic renal failure. German Study Group for growth hormone treatment in chronic renal failure. N Engl J Med. (2000); 343:923–390.
10. Al-Uzri A, Matheson M, Gipson DS, Mendley SR, Hooper SR, Yadin O, et al. The impact of short stature on health-related quality of life in children with chronic kidney disease. J Pediatr. (2013); 163:73641.e1.
11. Wong CS, Gipson DS, Gillen DL, Emerson S, Koepsell T, Sherrard DJ, et al. Anthropometric measures and risk of death in children with end-stage renal disease. Am J Kidney Dis. (2000); 36:811–819.
12. Fine RN, Martz K, Stablein D. What have 20 years of data from the North American Pediatric Renal Transplant Cooperative Study taught us about growth following renal transplantation in infants, children, and adolescents with end-stage renal disease? Pediatr Nephrol. (2010); 25:739–746.
13. Klare B, Montoya CR, Fischer DC, Stangl MJ, Haffner D. Normal adult height after steroid-withdrawal within 6 months of pediatric kidney transplantation: a 20 years single center experience. Transpl Int. (2012); 25:276–282.
14. Hartung EA, Furth SL. Growth in children on renal replacement therapy: a shrinking problem? Pediatr Nephrol. (2013); Oct;28(10):1905-1908. Epub 2013 Jun 23. PMID: 23793884; PMCID: PMC3755089.
15. Englund MS, Tyden G, Wikstad I, Berg UB. Growth impairment at renal transplantation–a determinant of growth and final height. Pediatr Transplant. (2003); 7:192–199.
16. Furth SL, Stablein D, Fine RN, Powe NR, Fivush BA. Adverse clinical outcomes associated with short stature at dialysis initiation: a report of the North American Pediatric Renal Transplant Cooperative Study. Pediatrics. (2002); 109:909–913.
17. Ku E, Fine RN, Hsu CY, McCulloch C, Glidden DV, Grimes B, et al. Height at First RRT and mortality in children. Clin J Am Soc Nephrol. (2016); 11:832–839.
18. Critical Appraisal Skills Programmer (CASP https://casp-uk.net. Accessed on 09/09/2022
19. Guyatt GH, Oxman AD, Vist GE, Kunz R, Falck-Ytter Y, Alonso-Coello P, et al. GRADE: an emerging consensus on rating quality of evidence and strength of recommendations. BMJ (Clinical research ed). (2008); 336(7650):924-926.
20. Martz K, Stablein DM. North American Pediatric Renal Trials and Cooperative Studies (NAPRTCS) 2008 annual report. Emmes,
21. Rodig NM, McDermott KC, Schneider MF, Hotchkiss HM, Yadin O, Seikaly MG, Furth SL, Warady BA. Growth in children with chronic kidney disease: a report from the Chronic Kidney Disease in Children Study. Pediatr Nephrol (2014); 29:1987–1995
22. North American Pediatric Renal Trials and Cooperative Studies (NAPRTCS) 2011 annual dialysis report. Emmes,
23. North American Pediatric Renal Trials and Cooperative Studies (NAPRTCS) 2014 annual transplant report Emmes,
24. Karlberg J, Schaefer F, Hennicke M, Wingen AM, Rigden S, Mehls O. Early age-dependent growth impairment in chronic renal failure. Pediatr Nephrol (1996); 10:283–287
25. Hillesheim E, Ambrósio VL, Facincani I. Development of Height and Body Mass Index After Pediatric Kidney Transplantation: Experience of the Nephrology Pediatric Service at HCFMRP-USP, 2005-2014. J Bras Nefrol. (2016); Jul-Sep;38(3):327-333. English, Portuguese.

26. Tönshoff B, Ettenger R, Dello Strologo L, Marks SD, Pape L, Tedesco-Silva H, et al. Early conversion of pediatric kidney transplant patients to everolimus with reduced tacrolimus and steroid elimination: Results of a randomized trial. Am J Transplant (2019); 19(3), 811–822.
27. Kumar G, AlIsmaili Z, Ilyas SH, Ayyash BM, Tawfik E, AlMasri Oet al. Good outcome of the single-center pediatric kidney transplant program in Abu Dhabi. Pediatr Transplant, (2019); 23(7), 1–9.
28. Martz K, Stablein DM. North American Pediatric Renal Trials and Cooperative Studies (NAPRTCS) 2008 annual report. Emmes,
29. Bertram JF, Goldstein SL, Pape L, Schaefer F, Shroff RC, Warady BA. Kidney disease in children: latest advances and remaining challenges. Nature (2016); 12:182-191
30. Franke D, Steffens R, Thomas L, Pavičić L, Ahlenstiel T, Pape L, et al. Kidney transplantation fails to provide adequate growth in children with chronic kidney disease born small for gestational age. Pediatr Nephrol. (2017); 32(3), 511–519.
31. Mehls O, Wuhl E, Tonshoff B, Schaefer F, Nissel R, Haffner D. Growth hormone treatment in short children with chronic kidney disease. Acta Paediatr. (2008); 97:1159–1164.
32. Mehls O, Lindberg A, Haffner D, Schaefer F, Wühl E; German KIGS Board; ESCAPE Trial Group. Long-term growth hormone treatment in short children with CKD does not accelerate decline of renal function: results from the KIGS registry & ESCAPE trial. Pediatr Nephrol (2015); 30:2145–2151
33. Zhang H, Zheng Y, Liu L, Fu Q, Li J, Huang Q, et al. Steroid Avoidance or Withdrawal Regimens in Paediatric Kidney Transplantation: A Meta-Analysis of Randomised Controlled Trials. PLoS ONE (2016); 11(3): e0146523.
34. Delucchi Á, Toro L, Alzamora R, Barrientos V, González M, Andaur R, et al. Glucocorticoids Decrease Longitudinal Bone Growth in Pediatric Kidney Transplant Recipients by Stimulating the FGF23/FGFR3 Signaling Pathway. JBMR. (2019); 34(10), 1851–1861.
35. Webb NJA, Douglas SE, Rajai A, Roberts SA, Grenda R, Marks SD, et al. Corticosteroid-free kidney transplantation improves growth: 2-Year follow-up of the twist randomized controlled trial. Transplantation, (2015); 99(6), 1178–1185.
36. Swolin-Eide D, Hansson S, Magnusson P. A 3-year longitudinal study of skeletal effects and growth in children after kidney transplantation. Pediatr Transplant (2018); 22(6), 1–9.

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