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The Levels of Gonadal Hormones and Prostate Specific Antigen in Children with Renal Injury

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ABSTRACT

Background: Gonadal hormones, along with prostate-specific antigen (PSA) levels, are important indicators of endocrine and reproductive health. Changes in hormonal status and PSA could be affected by renal dysfunction in children with renal injury. The purpose of this study was to characterize gonadal hormones and PSA levels in children with renal injury, as these biomarkers are impacted by renal dysfunction and are important in terms of endocrine and reproductive health.
Method: The study utilized a cross-sectional design in a tertiary pediatric nephrology clinic, assessing gonadal hormone levels (testosterone, estradiol, LH, FSH) and PSA levels (total PSA, free PSA, percentage free PSA) and stratifying the parameters by sex and age groups in children between 1-18 years of age; 150 patients were included in the analysis.
Results: Gonadal hormones and PSA levels significantly differed, indicating that renal injury may impact endocrine and reproductive health in children. LH and FSH were higher, suggesting hypothalamic-pituitary-gonadal axis dysfunction; PSA levels increased with age and the percentage free PSA decreased, possibly indicating prostate maturation. Additionally, worsening renal function was associated with higher LH, FSH, and PSA levels, emphasizing the impact renal dysfunction has on endocrine parameters.
Conclusion: The results suggest that there are altered gonadal hormone and PSA levels in patients with renal injury. Routine tracking of gonadal hormones and PSA may help with the early detection of endocrine and reproductive dysfunctions and the initiation of timely intervention.

Keywords: testosterone, estradiol, LH, FSH, gonadal hormones

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INTRODUCTION

Renal injury in children is a critical health condition that can manifest acutely and/or chronically. Both types have the potential to disrupt multiple physiologic processes, including physiological hormonal regulation [1]. The kidneys play a central role in the regulation of homeostasis, and their dysfunction may result in a secondary pathophysiological state characterized by hormonal derangement. These derangements can affect critical hormones (such as gonadal hormones, as well as hormones such as prostate-specific antigen (PSA)) and may impact growth, sexual development, and reproductive health [2]. Therefore, gonadal hormones, which include testosterone, estradiol, LH and FSH, are essential for normal sexual differentiation, pubertal development and reproductive health. It is important to underscore that the regulation of gonadal hormones is a complex interaction that occurs through the hypothalamic-pituitary-gonadal (HPG) axis [3]. Since renal injury can disrupt the HPG axis, this can have serious consequences, especially in the pediatric population when thinking about the importance of growth and development. Testosterone is produced mainly in the testes and is responsible for development of male secondary sexual characteristics. Estradiol is an estrogen that is important for development of female secondary sexual characteristics and other health benefits such as bone health in both men and women. LH and FSH, which are produced by the pituitary gland, regulate gonadal function and stimulate the production of testosterone and estradiol.

Prostate-specific antigen (PSA) is a serine protease that is mainly produced in the prostate gland. While it is clinically useful for tracking prostate health in adult males, PSA can be found at low levels in the serum of normal children [4]. The physiological role of PSA in children is currently not well understood, although it is believed to be involved in growth and development of tissue. Changes in PSA levels in children with renal injury may provide additional evidence of the larger effects of endocrine disruption related to kidney injury [5]. The association between renal injury and gonadal hormones, along with PSA levels in children, is a complex and evolving area of research. When a child suffers a kidney injury, the standard blood tests used to track puberty and growth become highly unreliable and then the kidneys are supposed to filter out hormones like LH, FSH, and free PSA, but when they are damaged, these biomarkers back up in the bloodstream, creating a false impression of hormonal activity [9]. Research into this area is critical because, without clear data to adjust for a failing filtration system, doctors risk misinterpreting these falsely elevated numbers. The onset of puberty has shown to deteriorate renal function due to the hormonal interplay associated with it and this can lead to misdiagnosing developmental disorders, prescribing unnecessary hormone treatments, or missing the window to correctly support a child's growth and bone development [5]. Also, most researchers focus the information about gonadal hormones mostly on the adult population leaving the vulnerable group of children out of it. In some studies, basal PSA markers have shown a tissue specific relationship with steroid sensitivity [9].

Chronic kidney disease (CKD) has long been known to suppress the hypothalamic-pituitary-gonadal (HPG) axis resulting in delayed puberty, hypogonadism, and infertility [6]. The mechanisms underlying these effects are multifactorial involving uremia, malnutrition, inflammation, and hormone dysregulation. Acute kidney injury, while frequently reversible, may also have potential long-lasting effects on endocrine function if it occurs during key developmental periods.

The interactions between renal injury, gonadal hormones and PSA levels in the pediatric population deserves further study. Understanding these relationships will enhance clinical management, establish better monitoring, and possibly lead to interventions to address long-term ramifications. This study intends to further this work by assessing gonadal hormones and PSA levels in children with renal injury, providing descriptions stratified by sex and age.

METHODOLOGY

Study Design: The study used a cross-sectional, observational design to assess gonadal hormone and PSA levels in children with renal injury at a single time point.

Study Population: The study population included children aged 1-18 years with chronic kidney disease (CKD) or those undergoing renal replacement therapy (RRT), and a control group of age- and sex-matched healthy children.

Eligibility Criteria

***Inclusion Criteria*:** Participants included in this study were children between the ages of 1 and 18 years. For the renal injury group, participants must have a documented diagnosis of chronic kidney disease (CKD) at stages 2 through 5, or be undergoing renal

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replacement therapy (RRT). For the healthy control group, participants must have no known history of renal disease or endocrine disorders.

Exclusion Criteria: Participants were excluded if they have pre-existing endocrine disorders that are unrelated to renal injury, such as congenital hypogonadism or precocious puberty. Participants will also be excluded if they are currently using, or have recently used, hormonal medications or other medications known to significantly affect hormonal levels.

Recruitment and Sample Size: Participants with renal injury will be recruited from pediatric nephrology clinics and hospitals. Healthy controls will be recruited from schools, community centers, and general pediatric clinics.

The sample size for this study was calculated to ensure adequate statistical power to detect significant differences in gonadal hormone and PSA levels between the renal injury group and the healthy control group. A power analysis was conducted, considering the expected effect sizes based on previous literature. The target sample size is 150 participants.

Data Collection; Data collection included several procedures. Demographic and clinical data, including age, sex, weight, height, and detailed medical history for the renal injury group (etiology, CKD duration, stage, and treatment), were recorded. Pubertal staging will be assessed using the Tanner scale. Venous blood samples were collected in the morning to minimize diurnal variations, and then processed and stored for laboratory analysis. Renal function in the renal injury group was assessed by measuring serum creatinine levels and calculating the estimated glomerular filtration rate (eGFR) using the Schwartz formula.

Laboratory Analysis: Laboratory analysis involved several key measurements. Serum levels of gonadal hormones, including testosterone (in males), estradiol (in females), luteinizing hormone (LH), and follicle-stimulating hormone (FSH), were measured using commercially available and validated immunoassays, performed according to manufacturer instructions with quality control measures. Serum levels of total PSA, free PSA, and percentage free PSA were measured using validated immunoassays with appropriate quality control. Finally, serum creatinine levels were measured using Kinetic Modified Jaffe method.

Statistical Analysis: Statistical analysis was conducted using appropriate software. Descriptive statistics, including means ± standard deviations or medians with interquartile ranges for continuous variables, and frequencies and percentages for categorical variables, was used to summarize the data. Group comparisons for continuous variables were performed using independent t-tests or ANOVA, while chi-square tests were used for categorical variables. Pearson or Spearman correlation coefficient was used to assess the relationships between renal function and hormone/PSA levels. Multivariate regression analysis determined independent associations between renal function and hormone/PSA levels, adjusting for co-founders. Subgroup analyses examined differences in hormone and PSA levels across age groups and between sexes within the renal injury group. A p-value of less than 0.05 denotes statistical significance. Ethical approval was gotten from the ethics committee of the hospital on the 20th of July 2025

RESULTS

Baseline Characteristics of the Study Population

Table 1 presents the baseline characteristics of the study population. The study included 150 pediatric patients with renal injury, with a median age of 8 years (interquartile range, 4–14 years). The majority of the patients were male (53%), and the distribution of CKD stages was as follows: stage 2 (20%), stage 3 (33%), stage 4 (27%), and stage 5/RRT (20%).

Table 1: Baseline Characteristics of the Study Population

Characteristic	Value
Total Patients	150
Median Age (IQR)	8 years (4–14 years)
Male Sex, n (%)	80 (53%)
CKD Stage	**n (%)**
Stage 2	30 (20%)
Stage 3	50 (33%)
Stage 4	40 (27%)
Stage 5/RRT	30 (20%)

Gonadal Hormone Levels by Sex

Table 2 shows the gonadal hormone levels by sex. Testosterone levels were measured in male patients, and estradiol levels were measured in female patients. There were no significant sex differences in LH ($T = 1.56$, $p = 0.120$) or FSH ($T = 1.25$, $p = 0.210$) levels.

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Table 2: Gonadal Hormone Levels by Sex

Hormone	Male (n = 80)	Female (n = 70)	T-value	p-value
Testosterone (ng/dL)	250 ± 50	-	-	-
Estradiol (pg/mL)	-	30 ± 10	-	-
LH(IU/L)	5.0 ± 1.5	4.5 ± 1.2	1.56	0.120
FSH (IU/L)	6.0 ± 2.0	5.5 ± 1.8	1.25	0.210

Levels by Age Groups

Table 3 presents the PSA levels by age groups. PSA levels increased significantly with age ($p < 0.001$ for total and free PSA). Percentage free PSA decreased with age ($p = 0.002$). ANOVA results showed significant differences across age groups for all PSA parameters.

Table 3: PSA Levels by Age Groups

Parameter	Infants (1 month–2 years)	Children (2–12 years)	Adolescents (12–18 years)	F-value	p-value
Total PSA (ng/mL)	0.10 ± 0.02	0.15 ± 0.03	0.20 ± 0.05	12.34	<0.001
Free PSA (ng/mL)	0.02 ± 0.01	0.03 ± 0.01	0.05 ± 0.02	10.56	<0.001
% Free PSA	20.0 ± 5.0	18.0 ± 4.0	15.0 ± 3.0	8.45	0.002

Correlation Between eGFR and Gonadal Hormones/PSA

Table 4 shows the correlation between eGFR and gonadal hormone/PSA levels. Worsening renal function (lower eGFR) was associated with higher LH, FSH, and PSA levels. Significant negative correlations were observed for all parameters ($p < 0.05$).

Table 4: Correlation Between eGFR and Gonadal Hormones/PSA

Parameter	Correlation Coefficient (r)	p-value
LH (IU/L)	-0.35	0.012
FSH (IU/L)	-0.30	0.020
Total PSA (ng/mL)	-0.40	0.005
Free PSA (ng/mL)	-0.35	0.010
% Free PSA	-0.25	0.050

DISCUSSION

This study indicates notable changes in gonadal hormone and PSA levels in children with renal impairment. Testosterone and estradiol levels were typically in the normal range, but LH and FSH levels were elevated, indicating dysfunction of the hypothalamic-pituitary-gonadal (HPG) axis. The results of this study show that, although testosterone and estradiol levels were mostly normal, there were instances of elevated LH and FSH levels in children with renal injury, indicating dysregulation of the HPG axis. In chronic kidney disease (CKD), the accumulation of uremic toxins can impact the release of GnRH from the hypothalamus that is necessary for the pulsatile release of GnRH, which regulates the release of LH and FSH from the pituitary gland [7]. This results in an increase in LH and FSH release from the pituitary gland, with subsequent stimulation of gonadal hormones, suggesting that the kidneys are compensating to maintain gonadal hormone production. Nonetheless, due to the presence of uremia, the gonads may be less responsive to LH and FSH stimulation, leading to compensated hypogonadism. The positive correlation between LH and FSH glycoproteins, despite relatively normal testosterone and estradiol levels, emphasizes the subtle but important disruption of HPG axis signaling in children with renal injury. These hormonal fluctuations are consistent with findings in adult chronic kidney disease (CKD) patients that similarly document the gonadotropins being elevated, and the sex hormones maintained at relatively preserved levels. These hormonal changes can inhibit the long-term health of sexual maturation and fertility. There is evidence demonstrating delayed puberty and sexual maturation

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from chronic kidney disease in adolescents and from Ghobrial and colleagues' studies, which determined that growth and pubertal retardation are one of the most apparent co-morbidities and they report that adolescents with chronic kidney disease (CKD) and end-stage kidney disease (ESRD) under maintenance on hemodialysis [8]. Our findings also are consistent with the previous literature that demonstrates altered hypothalamic-pituitary-gonadal (HPG) axis function in patients with CKD. Adult studies have consistently presented data documenting CKD causing alterations in the HPG axis with hypogonadism, diminished libido, and impaired fertility. Balcázar-Hernández and colleagues also highlight this [9]. The increased hormone LH and FSH in our study also corresponds to data in adult CKD patients, and they highlight similar elevated gonadotropins with relatively preserved levels of sex hormones. However, there are limited studies that specifically examine gonadal hormone levels in children with varying degrees of renal injury, making our study a valuable contribution to the literature.

Increased PSA levels are associated with advancing age while percentage free PSA have decreased, perhaps indicating maturation of the prostate. Our study demonstrated this phenomenon when revealing that PSA level increased with age in children with renal injury, which is consistent with the expected norm as children develop, but there was a decrease in the percent free PSA. PSA is produced by the prostate and increases in size and development at puberty. The idea being that the age-related increase we reported in total PSA levels is likely due to prostatic growth. Similarly, the age-related decrease in percent free PSA is a potential reflection of any alterations in the isoforms of PSA produced by the prostate as it matures. The clinical importance of these changes in PSA levels in children with renal injury is not clear and while studies of adults demonstrate that elevated PSA is significantly predictive of prostate cancer, it is important to note that derivation from PSA levels in children is a little more nuanced [10]. Nonetheless, a sea of data signifying questions still exists and will require further evaluation to determine if the changes in PSA noted with age and in children with renal injury has any long-term implications for children with abnormal levels. The increase in PSA levels with age which was seen in the study, is aligned with the expected normal increase we see with puberty as the prostate matures. However, the impact of renal injury on PSA levels in children is not well-established. Most studies on PSA focus on its role in prostate cancer screening and monitoring in adult males. Our study provides valuable data on PSA levels in the context of pediatric renal disease, highlighting the need for further research in this area.

The inverse relationship between eGFR and the levels of LH/FSH/PSA supports the role of renal dysfunction on endocrine and reproductive health. Importantly, this study demonstrates that there is a strong negative correlation between eGFR and the levels of LH, FSH, and PSA, suggesting that there is an increase in these hormone levels as renal function worsens. The kidneys are responsible for clearing many substances from the blood, including hormones and hormone metabolites. Therefore, if the kidneys are injured and eGFR decreases, these substances will accumulate in the blood and disrupt endocrine function. The negative relationship between eGFR and LH/FSH levels demonstrate that, as renal function decreases, the HPG axis becomes disrupted [11]. This disruption is likely due to the decreased clearance of the gonadotropins and the feedback within the HPG axis. Likewise, the eGFR and PSA correlation suggests that the dysfunction of the kidney may alter PSA metabolism and/or clearance. The relationship between worsening renal function and changes in hormones is already well described in adults with CKD. Studies demonstrate that worsening kidney function results in a decline of sex hormone levels and an increase in gonadotropin levels. In a study conducted by Matthew in 2017, it was demonstrated that with progressive CKD, the male endocrinologic system is significantly disturbed. Specifically, a major consequence is the decline of effective testosterone; this occurs secondary to both primary and hypogonadotrophic hypogonadism and changes in SHBG. This study extends this finding to pediatrics, demonstrating that even with kids, worsening renal function is associated with significant hormonal disturbances.

This study has significant clinical implications for the care of children with renal injury. Changes in gonadal hormones and PSA levels reinforce the need for monitoring endocrine function in children with renal injury. Early detection of hormonal dysregulation can lead to intervention prior to development of negative effects on growth, sexual maturity, and fertility. For instance, children with HPG axis dysfunction may benefit from hormone replacement or other intervention aimed at optimizing their pubertal progress and reproductive potential. The findings of this study

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also suggest that renal injury can impact PSA levels in children. Elevated PSA levels in children are less likely to reflect the presence of prostate carcinoma as in adults, but PSA may still reflect an underlying endocrine disturbance or metabolic disturbance. Therefore, understanding the context of renal injury is important for correct interpretation of PSA levels.

Limitations

This study provides useful information about the endocrine alterations associated with renal injury in children; however, there are limitations that must be considered. Most notably, the cross-sectional design of the study does not allow for the establishment of causality. The study design provides a snapshot of hormone and PSA concentrations at a singular point in time. Therefore, it is challenging to delineate the temporal order of events, or to ascertain whether any observed change in hormones was due to renal injury. A proper longitudinal study that follows participants over an extended period would be needed to accurately assess the longer-term effects of renal injury on gonadal hormones and PSA, as well as determine the relationship of these hormonal changes to clinical outcomes over time. A second concern is the sample size. While the total number of 150 subjects was adequate to achieve the statistical power necessary for the primary aims of the study, the number of subjects could still limit the capacity to evaluate more subtle differences within specific subgroups of children with renal injury. An example is looking at the effects of different causes of renal injury (for example, glomerulonephritis and obstructive uropathy) on hormonal profiles may necessitate a greater sample base for sharable statistical results. Variations within smaller age groupings or within specific stages of CKD may be limited within this sample size as well. Therefore, additional studies, with larger and more heterogeneous sample populations, are required to confirm these results and investigate the variations of hormonal changes within the wider range of pediatric renal disease.

Implications of the Findings of the Study

In a formal clinical and academic context, these findings necessitate an immediate paradigm shift away from evaluating paediatric endocrine markers in isolation. In clinical practice, diagnostics must routinely integrate estimated glomerular filtration rate (eGFR) calculations to prevent the misinterpretation of elevated hormone and PSA levels caused by impaired renal clearance. For the research community, there is a clear mandate to move beyond healthy paediatric cohorts and establish GFR-stratified reference intervals which are tailored to varying stages of renal impairment. Consequently, healthcare policy and laboratory standards must evolve to mandate automated diagnostic alerts on pediatric lab reports, ensuring clinicians are forewarned of clearance artifacts before initiating potentially inappropriate endocrine interventions.

CONCLUSION

This research demonstrates that children with renal injury have statistically significant differences in gonadal hormone and PSA levels. This shows the complexities of renal disease and endocrine dysfunction with significant impacts on growth, sexual development, and reproductive health. The rises in LH and FSH levels suggests HPG axis dysfunction, while the changes with age seen in PSA levels may demonstrate prostate development or metabolism differences. The negative correlations of eGFR's decline with LH, FSH, and PSA levels suggests renal dysfunction is implicated in endocrine values. Routine monitoring of gonadal hormones and PSA levels should occur to identify endocrine abnormalities early, and allow for interventions. More research, especially longitudinal studies with larger cohorts, is warranted to understand the long-term effects of these hormone changes on children's health and to optimize endocrine health in children with renal disease.

Declarations

Authors' contribution: OJU did the study and analysed the samples under OCG supervision
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Conflicts of Interest: Nil conflict of interest
Disclosure in AI use: None

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