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Gender Disparities in Hematological and Renal Markers in End-Stage Renal Disease Prior to Kidney Transplantation: A Retrospective Multicenter Study from the Kurdistan Region of Iraq

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Abstract: End-stage renal disease (ESRD) is a crucial public health challenge, especially in regions with limited data on gender-based clinical characteristics before kidney transplantation (KT). This study aims to examine gender-related differences in hematological and renal parameters among ESRD before KT in the Kurdistan Region of Iraq. Clinical information of 200 ESRD individuals, including 105 males and 95 females, aged from 18 to 65, was reviewed over a period of three years across three large hospitals between 2018 and 2024. The data comprised kidney function, electrolytes, CBC, and thyroid hormones. Except for MCH (mean corpuscular hemoglobin), no biochemical or hematological derived parameter differed significantly between gender significant lower value in female 27.37 ± 0.58 pg, compared to males, 28.50 ± 0.25 pg, *p- value* = 0.037. Urea, PCT, MPV, and PLT were found to be independent predictors of serum creatinine as shown by the regression analysis. In conclusion, gender-specific pre-transplant laboratory differences in ESRD were modest in extent, yet clinically significant for the female lower MCH that might defer KT eligibility due to under-recognized renal anemia. In addition, platelet-based indices mirroring inflammatory-hemodynamic processes are also associated with serum creatinine. These results lay the groundwork for more gender-informed, ethically sound, and model-refined KT readiness measures.

Keywords: Creatinine, End-stage Renal Disease; Gender Differences; Hematological Markers; Kidney Transplantation.

1. Introduction

Chronic kidney disease (CKD) is increasingly becoming a major public health problem and is currently listed as one of the leading causes of death worldwide. It has recently been confirmed by more contemporaneous estimates from the Global Kidney Health Atlas and analysis of the Global Burden of Disease that around 800–850 million people have kidney disease; this means a global prevalence in adults is about 10–14%; indeed, CKD entered these ranks only quite recently [1]. CKD is a chronic and progressive process that involves a decrease in glomerular filtration rate, accumulation of uremic toxic products, and multisystem effects, all resulting in ESRD, requiring treatment with kidney replacement therapy. KT is considered the most efficient modality of renal replacement therapy, providing a lower risk of mortality and better health-related quality of life than chronic dialysis in almost all groups of patients [2].

Gender differences in access to KT have not been addressed despite the benefits of KT. It has been widely reported that women have been consistently under-referred and undertreated for transplants [3]. Some of this variation can be attributed to biological differences and patient preferences, as well as systemic inequities in how health care is delivered that are seen even in the laboratory values that are used when donors and recipients are evaluated for transplantation [4]. These sex and gender disparities

result from a combination of biological factors (including body size, differences in immunity, and sensitization to pregnancy), patient choices/decisions made by patients, and sociocultural or systemic inequities in the delivery of medical care. Importantly, some of these disparities may be mitigated by considerations around how laboratory values are considered within pre-transplant evaluation pathways; the non-inclusion of sex-based physiology in the account for thresholds or reference ranges may disadvantage women.

The focus on gender is justified by robust evidence showing that women experience inequitable kidney-transplant referral and access, often independent of clinical need, reflecting infrastructure-mediated bias in renal-care eligibility pathways [3, 4]. Gender differences are also biologically credible due to hormonal-immune modulation, where estrogen influences innate and adaptive immune responses, affects anemia susceptibility, and can alter the interpretation of renal injury markers [5, 6]. Additionally, female-biased under-appreciation of renal anemia severity, specifically lower MCH, has mechanistic grounding in sex-dependent erythropoiesis and iron homeostasis, which may indirectly delay transplantation readiness [7, 8, 9]. To prevent model inflation and ensure analytic fairness, we also enforced multicollinearity screening and regression parsimony, following best-practice clinical prediction constraints for ESRD, improving model stability without confounding gender interpretation [10].

Laboratory parameters, including serum creatinine and urea, electrolytes, complete blood count (CBC) indices, and thyroid hormones, are central to assessing transplant eligibility, perioperative risk, and long-term prognosis. A growing body of evidence suggests that many of these markers show robust sex-specific differences in the general population, with males typically having higher hemoglobin, hematocrit, and creatinine, and females often exhibiting higher platelet counts and different platelet indices [11]. In CKD and ESRD, platelet indices such as mean platelet volume (MPV), platelet distribution width (PDW), and plateletcrit (PCT) have been associated with inflammation, proteinuria, and disease progression, and may serve as inexpensive markers of thrombo-inflammatory burden and cardiovascular risk [12]. Similarly, sex-related differences in erythropoiesis, iron metabolism, and anemia management can influence red cell indices (e.g., MCH, MCV, RDW), which are routinely used when deciding on KT timing and suitability. Some of these markers differ by sex and potentially affect transplant readiness, especially those parameters that are related to platelet function and erythropoiesis [13, 14]. Gender-based differences may also affect susceptibility to viral infection, immune response after KT, and rejection [15].

Gender-based differences may also shape susceptibility to infection, immune activation, and graft outcomes after KT. Women and men differ in innate and adaptive immune responses, hormone–immune interactions, and exposure patterns, which can modulate responses to viral infection, vaccination, and alloimmunity, thereby influencing rejection risk and post-transplant survival [5]. However, much of the existing literature is derived from high-income settings, and the extent to which these patterns hold in low- and middle-income regions, including the Middle East, remains underexplored.

In this study, we hypothesize that sex-dependent physiological and clinical factors contribute to measurable differences in hematological and renal laboratory profiles among patients with end-stage renal disease prior to kidney transplantation in the Kurdistan Region of Iraq. The primary objective of this study is to investigate gender-based differences in renal biochemical markers and hematologic indices, with a focus on parameters related to renal anemia and platelet morphology, which may influence transplant eligibility assessments. Other aims are to assess relationships between laboratory markers of pre-transplant assessment, develop multivariate predictors for serum creatinine based on a

stable regression model, and offer preliminary evidence for equitable and gender-specific clinical ascertainment before transplantation.

2. Materials and Methods

2.1 Study Design and Setting

This retrospective, multi-center study was conducted using patient records from 3 major hospitals in the Kurdistan Region of Iraq: Rizgary Teaching Hospital in Erbil, Azadi Hospital in Duhok, and Sulaymaniyah Surgical Teaching Hospital. The study covered 6 years, between 2018 and 2024, and focused on patients diagnosed with ESRD who were listed for KT.

2.2 Sample size calculation

A priori power analysis was performed in G*Power 3.1 [16] for a two-tailed independent-samples t-test ($\alpha = 0.05$, power = 0.80) with an allocation ratio of 0.905 (females (N2)/males (N1)). Using Cohen's standardized effect size d = 0.513 (defined as $|\mu1-\mu2|/\sigma p$), see supplementary file.

G*Power inputs

- Test family: t tests
- Statistical test: Means — difference between two independent groups (two-tailed)
- Effect size (Cohen's d): 0.513
- α err prob: 0.05
- Power (1–β err prob): 0.95
- Allocation ratio N2/N1 (controls/patients): 0.905
- Output: Group 1 (N1=Males) = 105; Group 2 (N2=Females) = 95; Total N = 200.

Theory and equations

For a two-sample comparison of means (two-tailed t-test, common variance, unequal allocation ratio $k = n_2/n_1$), and a priori normal-approximation formula for group sizes is [17]:

(1) $$n1 = \frac{\left(Z1-\frac{\alpha}{2}+Z1-\beta\right)2}{d2}\frac{1+k}{k},\ n2 = kn1$$

Cohen's d is defined as:

(2) $$d = \frac{|\mu1-\mu2|}{\sigma p}$$

where σp denotes the pooled standard deviation (equal-variance assumption).

Numerical plug-in (this study)

- $\alpha = 0.05$ (two-tailed) $\Rightarrow Z_{1-}\alpha/_2 = 1.95996$
- Power $= 0.95 \Rightarrow Z_{1-}\beta = 1.645$
- Allocation ratio k = 0.905 (N2 / N1)
- Effect size (d) = 0.513
- N1: Group 1 (Males): 105
- N2: Group 2 (Females): 95
- Total N: 200

2.3 Study population

The study included a total of 200 patients (105 males and 95 females), aged between 18 to 65 years, all participants had confirmed ESRD diagnosis and underwent evaluation for KT during this period.

2.4 Inclusion and exclusion criteria

Inclusion Criteria

1. Patients aged 18 to 65 years.
2. confirmed diagnosed with ESRD and listed for kidney transplantation.
3. Time frame: from Jan. 2018 to Dec. 2024.
4. Patients with complete medical records, including demographic data, kidney function tests, electrolytes, complete blood count, and thyroid.

Exclusion criteria

1. Patients with a history of previous kidney transplantation.
2. Patients with incomplete or missing medical data.
3. Patients under 18 or over 65 years old.
4. Patients listed for transplantation before 2018.
5. Patients are diagnosed with malignancy or other major chronic diseases like chronic heart failure, active autoimmune disease, neurodegenerative disorders, and chronic liver disease.

2.5 Data Collection

Patient's demographic data (age, sex), renal function test (urea and creatinine), liver function test (ALT and AST), electrolyte including Sodium, Potassium, Chloride, in addition to T3, T4, and TSH profile, as well as Haematological parameters were retrieved from patients' files. There is a strong sense of censorship when collecting data. For privacy, all identification details of the patients had been removed and did not match prior to initiation of analyses. For privacy, all patient identification numbers were removed before analysis.

All serum biochemical markers were measured using fully automated chemistry analyzers. Urea (mg/dL) and creatinine (mg/dL) were quantified via standardized enzymatic kinetic methods on the Mindray BS-200 Automated Chemistry Analyzer (Mindray Bio-Medical Electronics Co., China). ALT and AST (U/L) were measured using IFCC-aligned UV kinetic assay methods on the Roche Cobas c311 Analyzer (Roche Diagnostics, Japan/Germany units installed – analyzer origin supplied to centers: Japan). Electrolytes (Na, K, Cl in mEq/L) were measured by ion-selective electrode using the Abbott i-STAT 1 System (Abbott Point of Care Inc., USA). Hematological parameters (WBC, RBC, Hb, HCT, MCV, MCH, MCHC, RDWa, PLT, MPV, PCT, PLCR, PLCC, PDWa, MID, Granulocytes $\times 10^9$/L, %, fL, pg, g/dL) were generated from EDTA-whole blood using the Sysmex XN-1000 Automated Hematology Analyzer (Sysmex Corporation, Japan). Thyroid markers TSH (µIU/mL), Total T4 (nmol/L), and Free T3 (pg/mL) were measured using chemiluminescent immunoassay on the Siemens ADVIA Centaur XP System (Siemens Healthineers, Germany). All laboratories applied routine multi-point manufacturer calibration and internal verification using Bio-Rad Liquichek™ Tri-Level Quality Controls (Bio-Rad Laboratories, USA), and inter-hospital analyzer comparability was confirmed through the Randox International Proficiency Testing Program (Randox Laboratories Ltd., United Kingdom). Only calibration-harmonized datasets were pooled, so no additional computational normalization was required, and all values reflect real calibrated analyzer outputs used for statistical analysis.

2.5.1 Bias Control and Data-Quality Assurance

To reduce selection and information bias, laboratory data were extracted using anonymized numeric codes without visible demographic identifiers during initial extraction. Dataset cleaning, correlation modeling, and regression-variable filtering were performed by an analyst blinded to gender allocation until analytic datasets were finalized. Blinded abstraction in retrospective kidney-disease cohorts improves objectivity and minimizes sex-assignment bias during statistical handling. All centers used harmonized automated analyzers with internal calibration and participated in external quality assessment, allowing reliable pooling without additional batch-normalization bias. Regression variables were reduced after multicollinearity screening (VIF < 10; tolerance > 0.1) to prevent overfitting and inflation of sex-related predictors. The only data to which a male or female group label was added was at the end to carry out independent samples t-tests ($p < 0.05$). This method ensures gender-sensitive, QC-verified, and objective reporting while retaining the integrity of the data.

2.5.2 Data Availability Statement

The dataset utilized and analyzed in this study was obtained from actual clinical hospital records and is accessible from the institutional ethics office on reasonable academic request and under approval status.

2.6 Data Handling and Ethical Considerations.

The research protocol was approved by the Biology Department Scientific and Ethical Committee of Tishk International University, Erbil, Iraq (Approval No: BIO-TIU-SEC-02, November 2025). All clinical data in the present study were extracted and analyzed in a fully anonymized manner; no recognizable patient letter codes or personal medical information were kept. The study was approved and complies with the Declaration of Helsinki (as revised in 2013) and the institutional ethical standards on human research.

2.7 Statistical Analysis

Biochemical and hematological parameters were compared between sexes by using an independent samples t-test. Correlations between clinical variables were assessed using Pearson correlation coefficient analysis. The predictors of serum creatinine were determined using multiple-stepwise linear regression analysis. Statistical significance was set at $p < 0.05$. SPSS version 25.0 was used for statistical analysis, and Python was used to draw the figure.

3. Results

3.1 Demographic characteristics

Out of the total 200 patients with ESRD, 105 (52.5%) were males, and 95 (47.5%) were females. The mean age for males was 40.98 ± 1.32 years and for females 38.74 ± 2.01 years, with no statistically significant difference between groups (*p-value* = 0.352), indicating a comparable age distribution as shown in Table 1.

3.2 Gender-based differences in laboratory parameters

Gender comparisons in hematological and biochemical markers are presented in Tables 1 and 2. Most parameters showed no significant gender-based differences. However, MCH was significantly lower in females (27.37 ± 0.58 pg) compared to males (28.50 ± 0.25 pg, p-value = 0.037). No significant differences were observed in serum urea, creatinine, thyroid hormones, platelet indices, or hemoglobin.

Table 1: Gender-Based Comparison of Renal and Biochemical Markers in ESRD Patients Listed for Kidney Transplantation

Parameter	Female Mean ± SEM	Male Mean ± SEM	p-value
Age (years)	38.74 ± 2.01	40.98 ± 1.32	0.352
Urea (mg/dL)	102.90 ± 8.39	112.44 ± 5.05	0.315
Creatinine (mg/dL)	5.95 ± 0.47	8.27 ± 0.96	0.123
Sodium (mEq/L)	136.63 ± 2.92	138.69 ± 0.39	0.305
Potassium (mEq/L)	4.85 ± 0.11	4.68 ± 0.08	0.205
Chloride (mEq/L)	104.25 ± 0.92	101.27 ± 1.09	0.093
ALT (U/L)	19.25 ± 5.59	14.96 ± 1.10	0.292
AST (U/L)	18.97 ± 4.37	14.42 ± 0.80	0.149

ESRD: End-Stage Renal Disease; KT: Kidney Transplantation; SEM: Standard Error of the Mean. ALT: Alanine Aminotransferase; AST: Aspartate Aminotransferase. Statistical test: Independent samples t-test; $p < 0.05$ considered significant. Data derived from anonymized hospital records (2018–2024) from 3 major transplant-listing centers in the Kurdistan Region of Iraq.

Table 2: Gender-Based Comparison of Hematological and Thyroid Markers in the ESRD Cohort

Group	Parameter	Female Mean ± SEM	Male Mean ± SEM	p-value
Hematologic	RBC ($\times 10^9$/L)	3.75 ± 0.19	3.50 ± 0.08	0.148
	WBC ($\times 10^9$/L)	6.99 ± 0.34	7.27 ± 0.21	0.464
	Hemoglobin (g/dL)	9.86 ± 0.36	9.75 ± 0.21	0.779
	Hematocrit (%)	29.89 ± 1.11	29.69 ± 0.60	0.867
	MCV (fL)	82.50 ± 1.51	84.62 ± 0.97	0.238
	MCH (pg)	**27.37 ± 0.58**	**28.50 ± 0.25**	**0.037**
	MCHC (g/dL)	33.13 ± 0.27	33.50 ± 0.17	0.241
Thyroid	TSH (µIU/mL)	4.02 ± 0.68	3.28 ± 0.43	0.369
	T4 (pmol/L)	49.20 ± 10.75	60.66 ± 5.57	0.315
	T3 (pg/mL)	3.90 ± 0.70	2.68 ± 0.28	0.118

RBC: Red Blood Cells; WBC: White Blood Cells; MCV: Mean Corpuscular Volume. MCH: Mean Corpuscular Hemoglobin; MCHC: Mean Corpuscular Hemoglobin Concentration. TSH: Thyroid-Stimulating Hormone; T3: Free Tri-iodothyronine; T4: Thyroxine. Bold values indicate statistical significance at $p < 0.05$. Thyroid markers could not be further stratified by dialysis modality due to incomplete documentation; this has been stated in the limitations.

3.3 Correlation Analysis

The Pearson correlation in Figure 1 was also shown with a heatmap, which indicates that there is an intense positive relationship between HB and HCT, as well as between HB and RBC of suppressed erythropoiesis for ESRD. Additionally, the granulocyte count (GRA) was positively associated with white blood cell count (WBC), revealing existing inflammation or immune reaction. Moreover, the platelet indices PLCC and PLCR exhibited marked intercorrelations, which were related to morphological variations in ESRD. Nevertheless, there is an inverse relationship between RDWa and (MCH/MPV) expressed what is called size variability in red cells, strongly suggesting anisocytosis. Furthermore, TSH presented negative correlations with platelet values, indicating that there may be a hormonal regulation of the haematological pattern.

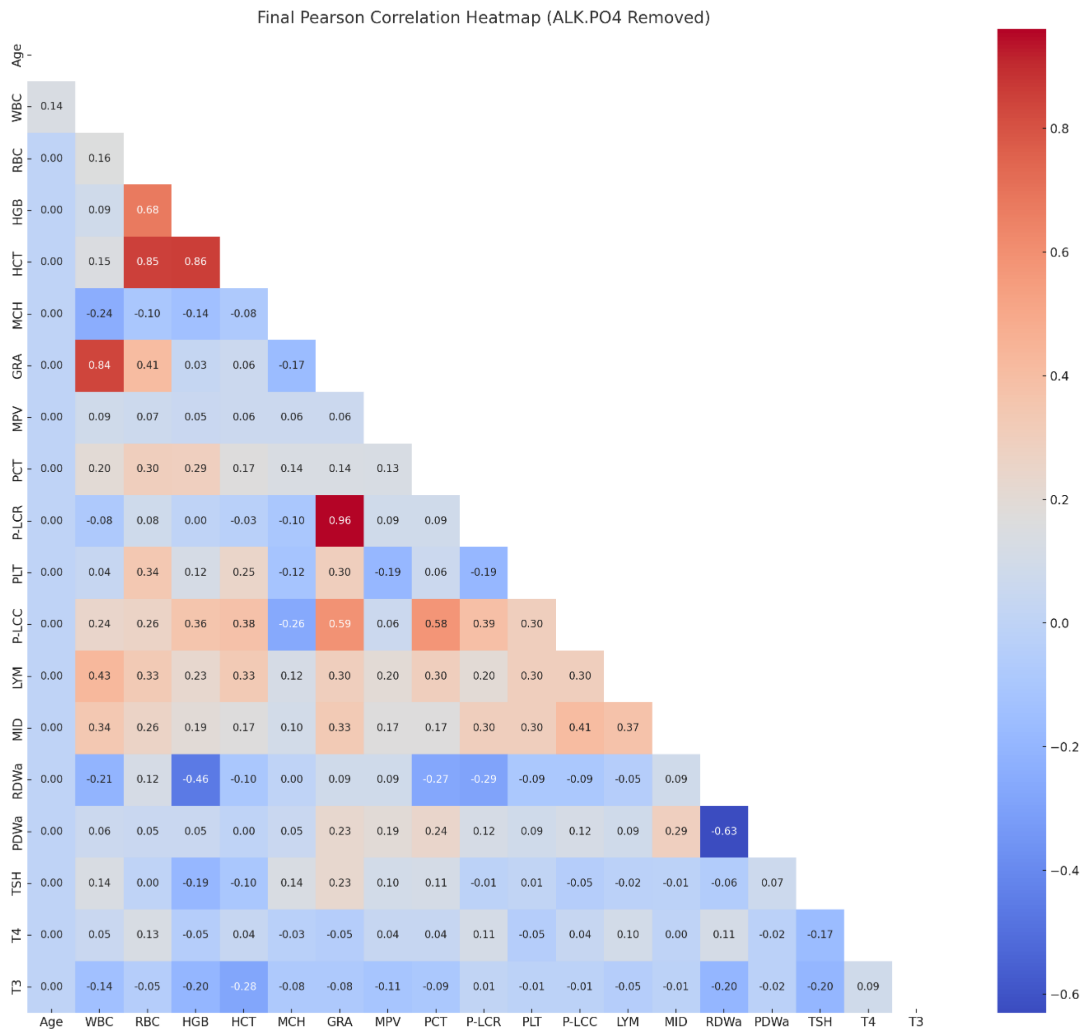

Figure 1: Heatmap of Pearson's correlation between hematological and hormonal parameters in ESRD. The heatmap uses one colour to represent correlation value, red indicates positive and strong correlation (close to +1), blue indicates negative and strong correlation (around 1), and white indicates low (or no) correlation (close to 0). The following abbreviations in the heatmap are applied: ESRD, End-Stage Renal Disease. WBC: White Blood Cells, RBC: Red Blood Cells, HGB: Hemoglobin, HCT: Hematocrit. MCH is the abbreviation for Mean Corpuscular Hemoglobin, GRA is Granulocytes, and MPV stands for Mean Platelet Volume. PCT=Plateletcrit, PLCR=Platelet-Large Cell Ratio, PLT=platelet count, and PLCC=Plate Large Cell Count. LYM is Lymphocytes, MID to Mid-size cells, Red Cell Distribution Width (absolute) (RDWa), Platelet Distribution Width (absolute) (PDWa), and Thyroid-Stimulating Hormone (TSH), T4, and T3 are thyroid hormones.

3.4 Multiple Regression Analysis for Serum Creatinine Predictors

A multiple regression-based method was employed to determine the so-called independent predictors for serum creatinine, with highly collinear variables excluded according to VIF and tolerance statistics (Table 3). The final model included urea (B = 0.030, *p-value* = 0.001), which was positively associated at the biochemical level with kidney filtration function. PCT was also significantly positively associated (B = 184.467, $p < 0.001$) with platelet mass implications. On the other hand, PLT (B = -0.139, $p < 0.001$) and MPV (B = -5.299, *p-value* = 0.012) were significantly negatively associated, indicating potential hemodynamic and/or microvascular implications. These observations support the role of uremia and platelet morphology in the variation of serum creatinine concentration in ESRD.

Table 3: Multiple Linear Regression Model Identifying Hematological and Biochemical Predictors of Serum Creatinine in ESRD Patients

Predictor	B	p-value	VIF	Tolerance
Age	−0.046	0.167	1.226	0.816
Urea	0.030	0.001	1.329	0.752
PCT	184.467	0.001	4.568	0.219
PLT	−0.139	0.001	5.190	0.193
MPV	−5.299	0.012	1.684	0.594
TSH	0.024	0.837	1.240	0.807

Variance-inflating factor (VIF) >10 or Tolerance <0.1 were dropped because of multicollinearity. All the other predictors are deemed to be of statistical and mathematical reliability for the regression equation.

4. Discussion

The demographic analysis revealed no statistically significant differences in male and female patients. This suggests that gender was not a contributing factor for age-related variations in ESRD in our study. Similar age matching between males and females has been recorded in their studies examining the pretransplant population [18]. Although our research found minimal significant differences between males and females in hematological parameters, the sex-specific physiology should not be underestimated, as it influences different responses in curable and non-curable diseases, including differential immune reactions to bacterial and viral infections [19, 20].

In terms of hematological, hormonal, and biochemical parameters, most parameters did not statistically differ in males and females. However, females exhibited lower MCH (27.4 pg vs. 28.5 pg; p = 0.037), which may be linked to menstrual blood loss, hormonal changes, or different endocrine responses in chronic disease settings [13]. Besides, the sex-specific differences in erythropoiesis and iron metabolism [21]. Additionally, males had a higher mean creatinine but with no statistical significance, matching the risk that serum creatinine assessments may understate renal dysfunction in females, leading to delays in referral [18]. Although there were no statistical differences between genders regarding thyroid hormone levels (T3, T4, and TSH). Our findings contrast with the previous studies that were reported by [22, 23], differences in assay sensitivity, dialysis exposure, and population heterogeneity may contribute to this discrepancy.

As expected in the correlation heatmap, hematological indices HCT, RBC, and HGB were strongly correlated, which is consistent with the known inhibition of erythropoiesis in ESRD brought on by erythropoietin shortage and systemic inflammation [24], which is aligned with Cui and Zhang (7) who found a strong correlation between hematological indices and ultrafiltration rate in hemodialysis patients. These markers tend to decline in parallel in renal anemia, which further affects oxygen transport and tissue metabolism [8].

There was also a significant positive correlation between the WBC count and GR, suggesting that there is persistent immunological activation in ESRD patients who are being exposed to oxidative stress [25] and chronic low-grade inflammation [26]. This is consistent with the work by Ebert and Neytchev, Ebert, Neytchev [27] who demonstrated that leucocyte inflammation is common among uraemic patients and again confirms the chronic immune stress on these individuals. Moreover, there was a remarkable intercorrelation between platelet markers, including PCT, MPV, and PLCR. These findings suggest deficits in platelet production and activation that are common in uremic states and associated with increased risk of bleeding and thrombosis in ESRD patients [28]. This intercorrelation

supported several studies showing altered platelet features in ESRD [29, 30]. Conversely, the negative correlation found between RDWa and MCH or MPV reflects anisocytosis and various morphological erythrocyte abnormalities, which reflect inflammation and poor nutrition in advanced kidney disease [31].

The main result of our retrospective cohort study demonstrated that pre-transplant gender-related laboratory differences in ESRD were limited, with MCH being the only hematological parameter that differed significantly between sexes, where females showed lower MCH than males. Although hemoglobin and hematocrit were not statistically different, the reduction in MCH reflects sex-influenced red-cell hemoglobinization rather than absolute hemoglobin concentration alone, supporting an under-recognized pre-listening anemia phenotype in women. Our correlation modeling further reinforced that Hb, HCT, and RBC decline synchronously in ESRD, reflecting erythropoietin-deficient renal anemia, a pattern that has also been documented in chronic hemodialysis populations where ESA hyporesponsiveness couples strongly with oxidative and thrombo-inflammatory stress [8], in agreement with the direction of our findings. A similar association between dialysis ultrafiltration rate, hemoglobin dynamics, and erythropoietin response efficiency has been confirmed in regional automated-analyzer cohorts [7], which validates our pooled automated lab pipelines. Moreover, sex-dependent erythropoietic disadvantage has pathological credibility, as female iron-homeostasis, chronic blood losses, and endocrine-regulated erythropoiesis yield lower corpuscular hemoglobinization in renal disease profiles [9] with clinical acknowledgment that these changes may affect transplant clearance thresholds.

These multivariate regression findings, after strict multicollinearity filtering, indicate that urea and platelet indices (MPV, PCT, PLT) were statistically associated with serum creatinine; however, rather than acting as direct biochemical predictors, these platelet parameters likely represent thrombo-inflammatory and microvascular hemodynamic responses secondary to renal impairment. Variations in MPV and PCT can reflect platelet activation and mass shifts occurring under chronic inflammatory stress, recognized contributors to endothelial dysfunction and ESRD progression, while urea maintains its established physiological linkage to reduced glomerular filtration and nitrogenous waste retention [32]. These results differ from previous CKD studies in non-dialysis patients, who had elevated MPV at earlier stages of the disease and PLT counts and MPV decreasing later [33]. Urea, also a nitrogenous waste, closely follows the decrease in filtration. Urea and creatinine both accumulate as the glomerular filtration rate falls. In such a situation, the study by Brookes and Power (10) supported the close association between urea and creatinine of patients having heart-failure-induced kidney dysfunction, which once again highlights their imperative role in acting as a pair to predict prognosis. Nevertheless, the clinical usefulness of urea is occasionally doubted as a measure of renal deterioration due to its sensitivity to non-renal determinants, which can be modified through hydration state and protein intake, in contrast with creatinine, which is more specific [34]. Eliminating highly collinear variables such as RBC, HCT, and MCH enhances the reliability of the model and avoids overestimation, both of which are important for clinical prediction tools [35]. Our regression analysis confirms the urea creatinine correlation.

Although platelet indices entered the regression model as statistically significant after multicollinearity filtering, our result clarified that it may be associated with *microvascular hemodynamic and thrombo-inflammatory burden* instead of deterministic prediction, since serum creatinine accumulation is primarily a result of glomerular filtration decline, nitrogenous waste retention, and uremic kinetics rather than platelet mass acting as a direct causal driver [10, 34]. Additionally, lower female MCH is mechanistically grounded in sex-influenced erythropoiesis and iron dysregulation, and may contribute to delayed perception of kidney-transplant readiness and surgical clearance eligibility in women, especially when anemia thresholds prioritize Hb alone without considering red-cell hemoglobinization.

Our study has inherent limitations as the retrospective nature of the design, which might entail selection bias and does not permit to establish a cause-and-effect relationship or determine temporal directionality between variables. The sample size of 200 patients was justified statistically after reduction and decrement in a priori variables in the regression model to avoid an excessive number of predictor characteristics and maintain model stability; however, despite having a sufficient sample due to the reduction in the model, the underlying cause for documentation is still constrained. The hospital records also did not contain essential clinical and biochemical data such as dialysis modality, exposure to erythropoiesis-stimulating agents, inflammatory biomarkers (i.e., CRP, IL-6, and TNF-α), and iron status markers (i.e., ferritin and transferrin saturation), which may contribute to unmeasured differences among the participants. Two other factors that could influence thyroid hormone levels are dialysis-related metabolic disturbance and non-thyroidal illness physiology; however, we were unable to perform a stratified endocrine analysis according to the dialysis or comorbidity status because this information was incompletely recorded in hospital files. To avoid misinterpretation, these restrictions were summarized into a separate and independent limitations section in order to limit over-interpretation of associative results and provide the study's context. Furthermore, exposure to active dialysis may induce non-primary analyte perturbations by alterations in ultrafiltration rate, oxidative damage, and non-thyroidal illness physiology that could affect hematologic/hormonal trajectories before kidney-transplantation listing. Finally, while calibrating the analyzer and blinding the abstractions had contributed to improved reliability of multicenter data, residual inter-center variability cannot be completely eliminated even after being attenuated by differences in clinical recording pipelines rather than analytic detection methods, which is a limitation of the use of any retrospective renal transplant cohorts.

5. Conclusion

This study highlights the importance of a sex-sensitive approach in pre-transplant kidney assessment, as female-specific anemia phenotypes may not be recognized within listing pathways focusing on hemoglobin cut-offs and might lead to delay in clinical optimization and eligibility for renal transplantation among women. Platelet indices act more as supplementary markers of thrombo-inflammatory and microvascular stress than primary causative indicators of creatinine variation. The results may guide future clinical decision-making and ethical actions by strongly supporting equilibrium in the ratio of referral causes between genders (baseline parity) through listing policy if it is currently not gender-balanced, sex-informed laboratory interpretation beyond the dichotomous categorical threshold as default standard human hematophysiology consideration, balance in pretransplant anemia management once implemented directly into surgical clearance pathways, and inference theories based on statistically stable and parsimonious modeling among resource-limited transplant programs so that fairness improves during readiness assessment.

Author contributions

The first author contributed to statistical analysis, study supervision, and manuscript revision. The second author wrote the first draft of the manuscript. The third author worked on data collection, and the last two authors contributed to data entry and editing.

Conflict of interest

There is no conflict of interest in this paper.

Use of AI tools declaration

The authors declare that any AI tools used in the preparation of this manuscript were limited to language and readability improvement only, and were not used to generate scientific content, data, analyses, or conclusions, with full responsibility retained by the authors.

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