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Comprehensive Haematological Alterations in Chronic Kidney Disease: Pathophysiological Mechanisms and Clinical Implications in Patients Attending Private Hospitals in Baghdad

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ABSTRACT: Chronic Kidney Disease (CKD) is a worldwide health concern related to the gradual deterioration of kidney function with various complex systemic complications. Among these complications, haematological changes, including anaemia, are widespread and warrant analysis. This cross-sectional study aimed to assess haematological parameters, including red blood cell indices, white blood cell count, and platelet count, in the management of CKD. 300 patients suffering from CKD (stages 3-5) were observed in this study. Data on demographic, clinical, and laboratory parameters were obtained, such as complete hemograms, reticulocyte counts, iron status, inflammation markers, and coagulation evaluations. The results showed that a high percentage of normocytic, normochromic anaemia was correlated with CKD stages. Elevated ferritin and low transferrin levels accompanied functional iron deficiency. At the same time, the WBC count showed pronounced lymphopenia and a high neutrophil-to-lymphocyte ratio, indicating a chronic inflammatory condition. Platelet counts were generally normal, but mean platelet volume increased with the disease process, indicating mild platelet activation. Overall, the findings prove that haematological disorders have a multiple nature and are due to the lack of erythropoietin production, toxicity of uremia, and chronic

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inflammation. When it comes to private healthcare services in Baghdad, where people suffer from different conditions, socioeconomic features, and types of care, it can seem that patients do not receive proper treatment for observed haematological alterations.

Keywords: *Chronic Kidney Disease, Haematological Alterations, Anaemia, Neutrophil-to-Lymphocyte Ratio, Uremic Toxins, Baghdad.*

Introduction

Chronic kidney disease (CKD) is a serious and increasingly critical global health problem characterised by kidney abnormalities that last for over three months, resulting in a gradual decline in glomerular filtration rate (GFR) [1]. The pathophysiological process of CKD goes far beyond the kidney's problems, as it can be described as a system-wide syndrome affecting almost every system [2]. Of all the complications of CKD beyond the kidneys, haematological complications have the broadest reach and greatest impact on patients [3]. Haematological abnormalities can include abnormal red blood cell production, an imbalance in white blood cell counts, and alterations in platelet counts and function [4]. In the past two decades, the epidemiology of CKD in Iraq, especially in Baghdad, has been alarming due to a growing occurrence of diabetes, hypertension, and chronic glomerulonephritis [5].

While previous epidemiological and clinical studies in Iraq were conducted within the public health system, a growing segment of the population seeks medical care in the private sector [6].Individuals who visit private clinics in Baghdad come from a myriad of socioeconomic backgrounds, various levels of health literacy, and disparate ways of seeking healthcare, all of which can greatly affect the timing of diagnosis, the direction of the disease, and the management of related issues such as blood-related disorders [7]. However, there remains a significant lack of local evidence on the nature and extent of blood changes among patients with CKD receiving treatment in the private sector in Baghdad. Among all blood-related complications of CKD, the most common and studied condition is anaemia, which typically appears early in the decline of kidney function and continues to worsen as patients progress to ESRD [8]. Anaemia in CKD is a complex condition with multiple causes, although it was once thought to be solely due to erythropoietin (EPO) deficiency [9].

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While the inability of failing renal peritubular fibroblasts to produce EPO in sufficient amounts is believed to be the leading cause of anaemia, it is now understood that there are many other contributing factors as well [10]. Uremic toxins that accumulate in the blood due to kidney failure to clear them exert direct myelosuppressive effects on erythroid progenitor cells in the bone marrow, thereby preventing the bone marrow from responding even to therapeutic levels of EPO [11]. Additionally, uremic toxins significantly decrease the lifespan of red blood cells through increasing their fragility and facilitating their clearance. Dysregulation of iron homeostasis is a key aspect of anaemia in chronic kidney disease, as it results in functional iron deficiency [13]. The upregulation of hepcidin, a peptide hormone released from the liver and serving to regulate iron metabolism, occurs continuously in patients suffering from CKD [14]. Hepcidin levels rise due to chronic inflammation and impaired kidney functioning. In this case, hepcidin binds to ferroportin, which is located on the surfaces of enterocytes and macrophages, thereby facilitating its internalisation and degradation [15]. As a result, the iron gets trapped in storage elements, rendering it unavailable for either erythropoiesis or absorption by the gut despite adequate and even high levels of body iron reserves [16]. In addition, the state of oxidative stress and systemic inflammation characteristic of CKD can damage red blood cells, worsening erythropoiesis [17]. The clinical consequences of any anaemia, which has not been treated or treated ineffectively in CKD patients, can lead to left ventricle hypertrophy and congestive heart failure, along with an overall rise in cardiovascular death rate, which is a key cause of mortality in such patients [18].

Apart from the well-known abnormalities in erythropoiesis, CKD can influence white blood cell dynamics, making patients extremely vulnerable to infections and entangling them in a state of chronic systemic inflammation [19]. Uremia leads to a unique type of immune dysfunction characterised by immune activation. There is persistent and low-level activation of circulating monocytes and neutrophils because of the presence of a uremic environment, leading to increased synthesis and secretion of inflammatory cytokines, such as TNF-α, IL-6, and CRP [21]. This inflammatory status not only occurs due to renal failure and but also serves as a significant reason for worsening renal impairment and development of cardiovascular diseases, as well as erythropoietin resistance [22]. In clinical practice, this inflammation manifests itself in simple blood parameters, the most common being the ratio between neutrophils and lymphocytes (NLR) [23]. The neutrophil-

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lymphocyte ratio is a great biomarker of inflammation and adverse prognosis in several renal and cardiovascular diseases, and it is relatively cheap and readily available [24]. High NLR indices in patients with CKD are usually observed and correlate with low GFR and elevated arterial stiffness as well as mortality [25]. On the other hand, CKD patients also present with marked immunosuppression, with impaired neutrophil chemotaxis, phagocytosis, and intracellular killing, along with atypical antigen presentation by dendritic cells and macrophages [26].

In addition, lymphopenia and especially a decrease in CD4+ T-helper cells is a frequent complication in patients with advanced CKD, contributing significantly to the development of cell-mediated immunity impairments in patients with CKD [27]. The effects of chronic kidney disease (CKD) on haematology extend to primary hemostasis in the form of a complicated bleeding disorder known as uremic bleeding tendency or uremic thrombocytopathy [28]. Although it has been assumed that decreased platelet count (thrombocytopenia) leads to bleeding problems in kidney failure, sufficient evidence indicates that platelet counts are generally adequate in CKD patients until the late stages of the disease, and the complications encountered are due to qualitative defects in platelets [29]. Uremic thrombocytopathy is a complex process that includes not only intrinsic platelet abnormalities but also several external factors present in the plasma of uremic patients [30]. Intrinsic abnormalities include impaired platelet adhesion to the subendothelial layer due to deficiency or dysfunction of von Willebrand factor and reduced expression of platelet glycoprotein receptors, such as GPIb and GPIIb/IIIa [31].

Additionally, the granules of uremic platelets are often depleted, leading to reduced release of adenosine diphosphate (ADP) and serotonin, two components critical for secondary aggregation [32]. External factors related to the tendency to bleed include uremic toxins in circulation, such as guanidinosuccinic acid, phenolic acids, and urea itself, which affect platelet contractile proteins and inhibit platelet aggregation in the presence of various stimulants [33]. Besides, the anaemia that is often present in CKD is also currently known to help worsen the tendency to bleed because less erythrocyte volume results in an impeded axial flow of platelets [34]. The discussed reversals come with some peculiarities, as CKD patients seem to bleed during the course of their treatment while not being thrombocytopenic [35]. As such, the complex hemostatic situation—bleeding and thrombosis concurrently—poses particular difficulties in the treatment of CKD patients.

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Therefore, an assessment of haematological parameters in CKD should not be limited to haemoglobin but should include a detailed investigation of erythrocyte parameters, information about leukocyte composition, inflammatory indices, and data on platelets. In this regard, this study was conducted to explore various aspects of haematological changes in CKD patients at private hospitals in Baghdad and to examine the underlying pathophysiological mechanisms and features characteristic of the healthcare setting.

Methodology

The observational and cross-sectional research took 12 months, between January 2023 and December 2023, in three major private hospitals in different regions of Baghdad, namely Al-Karkh, Al-Rusafa, and Al-Mansour. The selection of these private healthcare institutions was deliberately designed to provide a representative sample from the middle to upper socio-economic classes of the Baghdad population seeking renal treatment, away from the crowded public healthcare facilities.

The study protocol was thoroughly described and received formal permission from the respective Institutional Ethical Review Boards of the three involved private hospitals, hence maintaining adherence with the ethical principles described in the Declaration of Helsinki. During recruitment, the objectives and nature of the study were thoroughly explained to all prospective participants, who were asked to provide written informed consent to enrollment before the actual recruitment. The target population comprised adult patients aged 18 years and older who had most recently been diagnosed with chronic kidney disease, based on the Kidney Disease: Improving Global Outcomes (KDIGO) Clinical Practice Guidelines [1]. The diagnosis was verified by identifying the presence of structural and functional abnormalities that lasted for over three months; hence, the study relied on the results of albuminuria, abnormal findings in urine sediment, as well as histological results combined with a lowered estimated glomerular filtration rate (eGFR) of less than 60 mL/min/1.73 m^2. The patients' eGFR was estimated using the CKD-EPI (Chronic Kidney Disease Epidemiology Collaboration) 2021 creatinine equation, which includes age, sex, and standardised serum creatinine levels. Patients were divided into three groups based on eGFR. The three groups formed were Stage 3 CKD (eGFR 30-59mL/min/1.73m^2), Stage 4 CKD (eGFR 15-29mL/min/1.73m^2), and Stage 5 CKD (eGFR

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<15mL/min/1.73m²), where the participants included both dialysis-dependent patients and those who are not dependent on dialysis.

To ensure the homogeneity of the subjects and exclude findings attributable solely to CKD from the analysis, strict exclusion criteria must be met. Thus, patients with pre-existing medical conditions, such as aplastic anaemia, myelodysplastic syndromes, leukaemia, lymphoma, or other hereditary hemolytic anaemias, were excluded. Individuals who had received a blood transfusion within 90 days were excluded to avoid any influence of external RBCs on the studied parameters. Additionally, it can be noted that individuals with infectious diseases, malignancy, chronic liver diseases (Child-Pugh class B and C), and overt gastrointestinal bleeding at the time of enrollment were also excluded from the analysis. Pregnant women, breastfeeding women, and those receiving immunosuppressive therapy for post-renal transplantation and autoimmune diseases in general were excluded from the analysis. Thus, the total number of subjects included in the study is 300 patients, as determined beforehand using an equivalent sample size calculation formula. The percentage of the sufferings from the disease was set at about 75%. The margin of error was assumed to be 5% at a 95% confidence level.

After enrollment in the study, all the needed demographic data were collected. Demographic information such as the age of each participant, gender and location of their residence in Baghdad was noted. Case history was noted, where the main cause leading to the occurrence of chronic kidney disease and its duration and existing comorbidities like hypertension, diabetes mellitus, and cardiovascular diseases were recorded. Likewise, an assessment of the drugs used was conducted, particularly for erythropoietin drugs, oral or intravenous iron supplements, angiotensin-converting enzyme inhibitors (ACE), angiotensin-II receptor blockers, and antiplatelet and anticoagulant drugs. Anthropometric parameters, such as height and weight, were measured to calculate BMI for each participant. Blood pressure was measured after at least 5 minutes of rest while sitting.

The blood samples of each participant were analysed using haematological methods. Blood samples were collected in the early morning after a minimum of 8-10 hours of overnight fasting to minimise variation in treatment measurements. In this case, because the participant was already receiving hemodialysis, the blood sample was collected from the arterial side of the arteriovenous fistula to prevent alterations in measurement results.

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Moreover, the blood sample was collected according to aseptic principles, and for the complete blood count (CBC), approximately 3 millilitres of blood with anticoagulant potassium ethylenediaminetetraacetic acid were collected. CBC analysis was performed within 2 hours of collection on a Sysmex XN-1000, a six-part automated haematological analyser. CBC parameters analysed included haemoglobin concentration, haematocrit, red blood cell count, MCV, MCH, MCHC, RDW, WBC count, and a detailed five-part differential WBC count comprising neutrophils, basophils, monocytes, lymphocytes, and eosinophils. Moreover, the neutrophil-to-lymphocyte ratio was computed by dividing the absolute neutrophil count by the absolute lymphocyte count. Platelet parameters examined included total platelet count and volume. To assay bone marrow erythropoietic activity, reticulocytes in EDTA-anticoagulated blood were stained with new methylene blue supravital stain, and the count was performed manually by a certified haematologist under light microscopy.

For the evaluation of inflammatory markers and iron status, another 5 millilitres of blood were collected in a plain serum separator tube, left at room temperature for 30 minutes until clotting occurred, and then centrifuged for 10 minutes at 3000 RPM to separate serum. To maintain the volatility of analytes, the serum samples were frozen at -20 degrees Celsius and then cooled until batch analysis was done. Colourimetric methods were used to quantify serum iron (µg/dL) and total iron-binding capacity (TIBC; µg/dL) using an automated analyser (Roche Cobas c702). Transferrin saturation (TSAT) was computed as (serum iron/TIBC) × 100. Serum ferritin was determined by chemiluminescent microparticle immunoassay (CMIA) on an automated analyser (Abbott Architect i1000SR). High-sensitivity C-reactive protein (hs-CRP) was also measured to assess the level of inflammation affecting blood parameters. The basic coagulation tests were performed to assess secondary hemostasis. This process involved adding 2.7 mL of blood into vacuum tubes containing sodium citrate (0.109 mol/L; 3.2%) and centrifuging it at 2500 revolutions per minute. Prothrombin time (PT), international normalised ratio (INR), and activated partial thromboplastin time (aPTT) were measured using a coagulometer (Sysmex CS-5100).

The Statistical Package for the Social Sciences (SPSS) version 26.0 was used for statistical analysis (IBM Corp., Armonk, NY, USA). The Shapiro-Wilk test and visual inspection of histograms were used to assess the normality of the continuous variables. Mean ± standard

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deviation (SD) was used to report the continuous variables with normal distribution, whereas median and interquartile range (IQR) were used to present the variables with non-normal distribution. The categorical variables were summarised by frequency and percentage. Comparison of the continuous haematological parameters between the CKD stages was done using one-way analysis of variance (ANOVA), which was followed by Tukey's post-hoc tests for pairwise comparisons. The non-normally distributed variables were analysed using the Kruskal-Wallis H test and Dunn's test with a Bonferroni correction. Categorical variables were compared using the Chi-square test or Fisher's exact test when appropriate. To identify correlations between the haematological parameters (haemoglobin, NLR, and MPV) and the continuous clinical parameters (eGFR, ferritin, and hs-CRP), Pearson's correlation was performed on normally distributed data, and Spearman's correlation was used for non-normally distributed data. Multiple regression analyses were performed to identify factors associated with haemoglobin levels and the severity of anaemia.

Results

The study included 300 patients with chronic kidney disease. The demographic details and the baseline clinical features of the study participants are presented in Table 1. The average age of the complete cohort is 58.4 ± 11.2 years, while male patients tend to be slightly higher than females (56.3%, n=169). Diabetic nephropathy was the most common cause of CKD (the aetiology of all cases was 42.0%), while hypertensive nephrosclerosis was the second most common cause (31.7%). The numbers of patients in each stage were as follows: 35.0% in Stage 3 (n=105), 33.3% in Stage 4 (n=100) and 31.7% in Stage 5 (n=95). Among Stage 5 patients, 68.4% of patients (n=65) were on maintenance hemodialysis. The increase in uptake of erythropoiesis-stimulating agents (ESAs) and iron supplements was statistically significant with advancing CKD stages ($p<0.001$).

Table 1: Demographic and Clinical Characteristics of CKD Patients Stratified by Disease Stage (N=300)

Variable	Total (N=300)	Stage 3 (n=105)	Stage 4 (n=100)	Stage 5 (n=95)	P-Value
Age (years), Mean ± SD	58.4 ± 11.2	55.1 ± 10.5	58.9 ± 11.1	61.5 ± 11.3	0.001
Male Gender, n (%)	169 (56.3)	58 (55.2)	57 (57.0)	54 (56.8)	0.965
BMI (kg/m²), Mean ± SD	27.8 ± 4.2	28.5 ± 3.9	27.9 ± 4.1	26.8 ± 4.5	0.015
Aetiology, n (%)					0.022
- Diabetic Nephropathy	126 (42.0)	32 (30.5)	44 (44.0)	50 (52.6)	

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- Hypertensive Nephrosclerosis	95 (31.7)	38 (36.2)	32 (32.0)	25 (26.3)	
- Chronic Glomerulonephritis	47 (15.7)	22 (21.0)	15 (15.0)	10 (10.5)	
- Other/Unknown	32 (10.6)	13 (12.3)	9 (9.0)	10 (10.6)	
Systolic BP (mmHg), Mean ± SD	142.5 ± 16.8	138.2 ± 14.5	143.1 ± 16.2	147.1 ± 18.5	0.002
ESA Use, n (%)	112 (37.3)	8 (7.6)	34 (34.0)	70 (73.7)	<0.001
Iron Supplement Use, n (%)	95 (31.7)	5 (4.8)	28 (28.0)	62 (65.3)	<0.001

The extensive details regarding haematological parameters and iron status in patients are shown in Table 2. The total prevalence of anaemia, defined as haemoglobin values of 13.0 g/dL or below in men and 12.0 g/dL or below in women according to the KDIGO guidelines, was 82.0% (n=246). There were statistically significant decreases in mean haemoglobin levels from Stage 3 to Stage 5 ($p<0.001$). Most anaemic patients at all stages showed normocytic, normochromic blood, as characterised by normal MCV and MCH values. There is a statistically significant increase in RDW in the later stages, thus indicating increased anisocytosis. The reticulocyte counts were low, below expected levels for the degree of anaemia. When it comes to iron studies, they have shown a typical pattern of functional iron deficiency - serum iron and TSAT were significantly lower depending on CKD stage, but serum ferritin levels were considerably higher, showing 2 markers of iron excess in storage and inflammation in the acute phase.

Table 2: Haematological Parameters and Iron Status across CKD Stages

Variable	Total (N=300)	Stage 3 (n=105)	Stage 4 (n=100)	Stage 5 (n=95)	p-value
Hemoglobin (g/dL), Mean ± SD	10.2 ± 2.1	12.1 ± 1.2	10.0 ± 1.3	8.1 ± 1.5	<0.001
Hematocrit (%), Mean ± SD	31.5 ± 5.8	36.8 ± 3.5	30.9 ± 4.1	26.1 ± 4.8	<0.001
MCV (fL), Mean ± SD	86.5 ± 6.2	85.8 ± 5.1	86.9 ± 6.5	87.0 ± 7.0	0.450
MCH (pg), Mean ± SD	28.4 ± 3.1	28.1 ± 2.5	28.5 ± 3.3	28.6 ± 3.5	0.610
RDW (%), Mean ± SD	14.8 ± 1.9	13.9 ± 1.2	14.8 ± 1.8	15.9 ± 2.1	<0.001
Reticulocyte Count (%), Median [IQR]	1.2 [0.8-1.6]	1.5 [1.1-2.0]	1.1 [0.8-1.5]	0.9 [0.6-1.2]	<0.001
Serum Iron (µg/dL), Mean ± SD	58.4 ± 22.5	72.5 ± 20.1	58.2 ± 18.5	42.1 ± 18.2	<0.001

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TIBC (µg/dL), Mean ± SD	245.5 ± 38.2	265.2 ± 32.1	245.8 ± 35.4	223.1 ± 36.5	<0.001
TSAT (%), Mean ± SD	23.8 ± 9.1	27.4 ± 7.5	23.7 ± 8.2	19.0 ± 9.8	<0.001
Serum Ferritin (ng/mL), Median [IQR]	312 [185-498]	185 [120-280]	315 [210-465]	520 [350-780]	<0.001
hs-CRP (mg/L), Median [IQR]	5.8 [2.9-11.5]	2.8 [1.5-4.5]	5.9 [3.5-9.8]	12.1 [7.5-18.2]	<0.001

The findings on the dynamics of white blood cells, the profile of platelets, and the parameters of coagulation are illustrated in Table 3. The total white blood cell count did not change significantly at early stages but increased slightly and significantly at Stage 5 chronic kidney disease (CKD). However, critically, the differential count showed that absolute lymphocyte counts decreased, resulting in a very significant, gradual increase in the neutrophil-lymphocyte ratio (NLR) from Stage 3 to Stage 5 ($p<0.001$). Platelet counts remained mostly within the normal range, and no significant differences were observed across the stages. On the contrary, mean platelet volume (MPV) indicated a significant progressive increase at advanced CKD stages, which implied that the platelets transformedfrom smaller to larger and more reactive forms. Coagulation testing showed that while PT and INR did not vary significantly across the stages, aPTT was significantly higher in the stage 5 group compared to earlier stages.

Table 3: Leukocyte, Platelet, and Coagulation Parameters across CKD Stages

Variable	Total (N=300)	Stage 3 (n=105)	Stage 4 (n=100)	Stage 5 (n=95)	p-value
WBC (x10³/µL), Mean ± SD	7.5 ± 2.2	7.1 ± 1.8	7.5 ± 2.1	8.0 ± 2.6	0.018
Neutrophils (x10³/µL), Mean ± SD	4.9 ± 1.8	4.2 ± 1.2	5.0 ± 1.7	5.6 ± 2.1	<0.001
Lymphocytes (x10³/µL), Mean ± SD	1.8 ± 0.7	2.2 ± 0.6	1.7 ± 0.6	1.4 ± 0.6	<0.001
NLR, Median [IQR]	2.7 [1.9-3.8]	1.9 [1.5-2.5]	2.8 [2.2-3.6]	3.9 [2.9-5.2]	<0.001
Platelet Count (x10³/µL), Mean ± SD	238.5 ± 65.2	245.1 ± 60.5	238.2 ± 68.1	231.2 ± 66.5	0.410
MPV (fL), Mean ± SD	9.2 ± 1.1	8.8 ± 0.9	9.2 ± 1.0	9.7 ± 1.2	<0.001
PT (seconds), Mean ± SD	12.5 ± 1.2	12.3 ± 1.0	12.5 ± 1.2	12.8 ± 1.4	0.055
INR, Mean ± SD	1.05 ± 0.12	1.03 ± 0.09	1.05 ± 0.12	1.08 ± 0.14	0.060
aPTT (seconds), Mean ± SD	31.2 ± 4.5	29.8 ± 3.2	31.0 ± 4.1	33.1 ± 5.5	<0.001

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Discussion

The results of this cross-sectional study provide a comprehensive analysis of haematological alterations observed in patients with chronic renal failure receiving care in private hospitals in Baghdad, confirming that the systemic effects of renal failure significantly affect the haematological system. The most striking finding was the very high incidence of anaemia at 82.0%. Although this figure is similar to the corresponding data from other studies, it poses a considerable challenge, given that patients are expected to receive specialised medical care within a healthcare system that provides access to modern treatment options [8]. This study clearly shows that a fall in haemoglobin and hematocrit, matching the stage of CKD, marks a reduction in renal mass and an inability of the kidneys to respond to the body's erythropoietic needs [9]. Besides, anatomical studies of red blood cells demonstrate that the majority of patients with anaemia had normal red blood cell size, with corresponding mean red blood cell sizes indicating that the development of the morphological features of anaemia was occurring regardless of haemoglobin levels in patients with all stages of CKD. These findings suggest that this morphological feature is typical of anaemia of chronic disease or anaemia resulting from CKD, indicating erythropoietin deficiency and suppression of the bone marrow, rather than deficiencies of nutrients such as vitamin B12 and folate, which typically indicate macrocytic anaemia [17].

At the same time, the investigation of iron studies and red blood cell width revealed serious complications related to blood formation in patients from Baghdad.Although serum iron levels and transferrin saturation declined with disease progression, serum ferritin levels increased notably at the severe stages. This peculiar biochemical state is representative of functional iron deficiency, a condition increasingly recognised as impeding CKD-related anaemia therapy. High ferritin levels in patients do not indicate sufficient iron stores in the body. In the present study, patients showed a significant increase in high-sensitivity CRP, suggesting that elevated ferritin values should be attributed to inflammation. CKD contributes to chronic inflammation, which triggers oxidative stress and leads to infection, accumulation of uremic toxins, and stimulation of hepatocytes and macrophages to secrete hepcidin in large amounts.The current excerpt has important implications for CKD patients' management in private hospitals in Iraq, as it suggests that iron supplementation

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based only on raised ferritin levels can be harmful and aggravate oxidative stress. Thus, there is a significant need to apply more advanced measures, such as reticulocyte haemoglobin content or the hypochromic red blood cell percentage, to diagnose and treat functional iron deficiency in patients with CKD [38]. Moreover, the drastic rise of red blood cell distribution width in the later stages of the study cohort confirms the presence of an aberrant and stressed erythropoietic environment due to the presence of immature red blood cells of various sizes. This process is independent and associated with a higher risk of cardiovascular disease among patients with renal disease [39].

In addition to the erythroid lineage, we focused on leukocyte alterations in CKD, particularly given the utility of the neutrophil-to-lymphocyte ratio. While the total white blood cell count was within the normal range in our patients and masked immune dysfunction, the differential analysis indicated the development of significant lymphopenia alongside relative neutrophilia at later CKD stages, resulting in a stepwise increase in NLR levels from Stage 3 to Stage 5. The elevated NLR levels at CKD can be understood because of the chronic low-grade systemic inflammation observed in patients with renalUremic toxins, especially those that are protein-bound such as indoxyl sulfate and p-cresyl sulfate and which occur due to poor renal functioning, stimulate the release and production of pro-inflammatory cytokines, e.g., tumor necrosis factor-alpha and interleukin-6, from monocytes and endothelium, thus creating a pathological inflammatory environment that leads to relative neutrophilia and apoptosis of the circulating lymphocytes (such as CD4+T-cells) and resulting in increased lymphopenia [11][27]. In this respect, our findings indicate a strong association between NLR and hs-CRP, with a reliable negative correlation between NLR and eGFR, making NLR an effective, simple, and inexpensive tool for measuring systemic inflammation and immune dysfunction. An elevated NLR in patients with CKD is not a random laboratory finding, but a powerful predictor of poor cardiovascular outcomes, death from any possible causes, and renal dysfunction progression [24]. The high NLR among patients at Stage 5 indicates that the population is at increased risk of cardiovascular events, which should prompt private health care officers in Baghdad to implement this simple blood test in risk assessment protocols to provide appropriate treatment [25].

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The study of platelets and blood clotting presented important information on the contradictory hemostatic characteristics of advanced CKD patients, who were initially treated as representatives of uremic thrombocytopenia.In addition, we found that overall platelet levels did not change significantly and remained consistently normal across all stages of chronic kidney disease progression, indicating that the hemostatic abnormalities observed in these patients are primarily qualitative rather than quantitative [29]. At the same time, the abnormal initial growth in average platelet size across Stages 3 to 5 provides significant insight into platelet mechanisms of function. The increase in the average platelet size is regarded as a typical sign of platelet activation enhancement, as large-sized platelets are responsible for the presence of large granules inside, high amounts of surface glycoprotein receptors and high ability to exert procoagulant activity compared to small platelets [40]. The increase in the size of platelets in patients with severe chronic kidney disease indicates the increases in the number of platelets produced by bone marrow in response to peripheral destruction or activation, which is caused by the interaction of platelets and uremic endothelium. This fact, regarding platelet size growth in patients, together with the prolongation of activated partial thromboplastin time in the Stage 5 group, indicates the paradox of uremic hemostasis. Indeed, the prolongation of activated partial thromboplastin time is likely due to qualitative defects in the intrinsic pathway and to the activity of uremic circulating inhibitors that prevent thrombin production and fibrin formation, resulting in a bleeding tendency [30]. However, the presence of increased average platelet size indicates their previous activation and formation of thrombogenic activity, and the increased levels of platelets are also accompanied by increased levels of fibrinogen and factor VIII, which produce the effect of acute phase reactants, which in their turn bring about the increased frequency of the development of venous thrombosis and thromboembolic disorders among patients suffering from chronic kidney disease [35].In the management of these patients in Baghdad, clinicians are confronted with the problems of hemostatic equilibrium; bleeding diathesis correction techniques like desmopressin or cryoprecipitate administration must be balanced against the chances of catastrophic thrombotic complications occurring in patients with known cardiovascular problems or ongoing dialysis procedures.

In the current study, conducted exclusively in private hospitals in Baghdad, socioeconomic and health service access issues are integrated into the pathophysiological processes under

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consideration. Patients in private healthcare in Iraq are generally from the better-paid population subgroups and have better access to treatment products such as medications compared to patients in the public healthcare system. However, the severity of the haematological disorders, particularly anaemia and iron deficiency, is too severe to be only explained by the availability of medications. This means that long delays in visiting nephrology specialists continue to be an important issue in the private healthcare systemMoreover, the environmental aspects particular to the region of Baghdad, such as the exposure to high levels of airborne particles, the long-term state of mental distress regarding urban unrest, and the eating habits of the residents, may contribute to the increase in the level of general systemic inflammation, which in its turn determines the dysregulation of iron metabolism through the action of hepcidin and changes the value of NLR significantly in excess of the parameters of other regions [5]. Despite being detailed and accurate, the research is also limited by several factors. The aforementioned research structure does not allow for the establishment of foolproof cause-and-effect relationships between eGFR reduction and the changes observed in haematology. Thus, although objective biochemical markers such as hs-CRP and ferritin were used to determine inflammation, the absence of laboratory testing of hepcidin and other more advanced techniques for measuring erythropoietic activity, such as reticulocyte haemoglobin content, decreases the accuracy of the pathophysiological conclusions. Another limitation of the research is that the investigation of platelet activity was not too elaborate, and therefore the outcomes were taken for granted.

In conclusion, the research thoroughly analyses the nature of changes in haematological parameters among patients with chronic kidney disease receiving treatment in private hospitals in Baghdad. The information on the matter indicates that CKD leads to a serious type of anaemia that presents as normocytic-normochromic, primarily due to functional iron deficiency and ongoing inflammatory processes rather than simply iron deficiency. However, the white blood cells show considerable signs of functional disturbance, as measured by the neutrophil-to-lymphocyte ratio, which increases alongside declining kidney function and rising inflammation. The hemostatic equilibrium is also disturbed, with the average platelet volume remaining high while platelet count is normal, which is incompatible with the increased thrombotic activity. The existing findings indicate that the treatment of haematological problems amongst CKD patients cannot be limited to the mere

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use of agents that stimulate red blood cell production but requires a thorough and individualised approach to addressing these issues.

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