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Original article

Serum Indoxyl Sulfate, p-Cresol and β2-Microglobulin in Iraqi Patients on Maintenance Hemodialysis: Circulating Concentrations, Group Separation and the Accompanying Mineral–Bone and Iron Profile

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Abstract

Background. Individuals undergoing intermittent hemodialysis, instead of being unburdened from waste products in the body, continue to be in contact with accumulated toxins that vary in size, bind to proteins found in the body, and are also not very soluble in dialysate. **Methods.** A cross-sectional case-control study was performed for a period ranging from November 2025 to February 2026 at Al-Yarmouk Teaching Hospital in Baghdad, involving 60 stable adult patients undergoing regular hemodialysis and 60 healthy adults. **Results.** Similarities were observed in terms of age ($p = 0.335$) and sex ($p = 0.461$). The body mass index was significantly lower in patients compared to healthy individuals (22.60 ± 4.79 kg/m² vs. 24.91 ± 6.48 kg/m²; $p < 0.001$). The prevalence of hypertension and diabetes was found to be 76.7 % and 51.7 % in patients tested, respectively. The levels of urea and creatinine were significantly high, while those of the aminotransferases were within normal limits. Mineral bone profile revealed low levels of calcium with high values of phosphorus, alkaline phosphatase, and parathyroid hormone (all $p < 0.001$). The amount of ferritin was elevated, while transferrin saturation was less than 20 % (both $p < 0.001$). Indoxyl sulfate (301.77 ± 271.85 ng/mL) has also been identified in patients just as p-cresol (428.34 ± 152.96 pg/mL) and β2-microglobulin (31.51 ± 17.62 mg/L). The values of the area under the curve were quite high for indoxyl sulfate (0.977) and β2-microglobulin (0.961), while being moderately low for p-cresol (0.826).

Keywords: β2-Microglobulin, Indoxyl sulfate, Urea, Creatinine, Ferritin.

1. Introduction

Chronic kidney disease (CKD) is among the most common non-communicable diseases in the world and is increasing rapidly worldwide. According to the Global Burden of Diseases, CKD prevalence rose to about 788 million adults compared to the 1990 number, which is more than twofold. Furthermore, in terms of age-standardized prevalence, North Africa and the Middle East have relatively high prevalence rates of about 18% (1). Therefore, it can be stated that Iraq lies in a more affected region around the globe and thus, the number of patients with kidney failure will also increase accordingly. When chronic kidney disease (CKD) is diagnosed at stage 5, the function of the kidneys fails to maintain the homeostasis of fluid, electrolytes, metabolism, and hormones, and it is required to start kidney replacement therapy (2).

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While dialysis is the most used method of kidney replacement therapy, in patients undergoing it, the kidneys do not provide continuous filtration, secretion, and hormonal functions (2,3). The result is that patients on dialysis are always in a uremic state. The solutes present in the aforementioned environment were traditionally classified into three categories: low-molecular weight free water-soluble compounds, compounds bound to protein, and middle molecules. The authentication process and recent classifications introduce a descriptive approach that emphasizes clearances as predictive of clinical outcome (4,5). There are notable differences in the generation, transportation, and removal of various solutes, which means that no one marker can be representative of the total retention load (6). Solutes with low molecular weight such as urea can diffuse through the dialyzer with ease, while both protein-bound solutes and middle molecules cannot. Indoxyl sulfate is a classic example of a solute associated with proteins. It is produced from bacteria in the colon converting dietary tryptophan into indole, which is then sulfate. Indoxyl sulfate is normally eliminated through tubular secretion. However, this pathway is not available when kidney function declines. The majority of indoxyl sulfate is bound to albumin, indicating that dialysis only removes the very small fraction that is not attached. One of the main characteristics of indoxyl sulfate is that it is an endotheliotropic. It activates aryl hydrocarbon receptors and activates pro-inflammatory processes in non-specific transcription, which reduces the level of nitric oxide in the blood (7). Increased levels of indoxyl sulfate correspond to an increase in mortality rates in patients undergoing hemodialysis treatment (9). The production of p-cresol is carried out in parallel with tyrosine and phenylalanine via a microbiological pathway. High levels of circulating blood p-cresol, which is present in a bound state has an association with blood vessel damage and inflammation (8). In patients undergoing dialysis, measuring the levels of free p-cresol would predict the chances of dying (10). It is, however, worthwhile stating that the levels of serum free p-cresol can be lowered by taking fiber (11). β2-microglobulin falls under the category of the intermediate-molecular weight proteins. It is continuously produced by cells with nuclei and normally cleared from blood circulation via glomerular filtration and tubular degradation, both of which pathways of removal are compromised under renal failure, while dialytic removal remains incomplete even with advanced membranes (12). Increased concentrations have been shown to be associated with mortality risk in large global studies and in studies conducted at one center only (12,13), in addition to being associated with aortic valve calcification and development of cardiovascular complications (14,15). The combination of these three solutes is usually uncommon in a cohort; the situation in Iraq and its neighboring countries with regard to dialysis is such that these countries are significantly under-researched within the literature. In addition, the few reports on this topic are based on the classical adequacy indices and clinical aspects of dialysis. The aim of the current study was a comparative assessment of serum levels of indoxyl sulfate, p-cresol and β2-microglobulin in the blood of patients undergoing maintenance dialysis in Iraq and healthy subjects, which was based on determinations of their renal, hepatic, mineral–bone and iron status as well as on assessment of the extent to which each of these solutes separated both groups.

2. Subjects, Materials and Methods

2.1 Study design and participants

A cross-sectional case-control study was performed during the period between November 2025 and February 2026. Participants were recruited from the Hemodialysis Centre of Al Yarmouk Teaching Hospital, Baghdad. The analysis was carried out at the Institute of Genetic Engineering and Biotechnology for Postgraduate Studies, University of Baghdad. The sample size was determined using G*Power software.

The sample of patients consisted of 60 Iraqi individuals aged 18 or older with chronic renal failure in stage 5 and undergoing routine hemodialysis and who were clinically stable at the time of sampling. The control group included 60 healthy adults aged 18 years or older with no history of kidney disease. The exclusion criteria for both groups included acute kidney damage, chronic damage, liver disease, smoking, any other forms of alcohol intake, malignant disease, therapy with drugs that suppress immunity or that are still being investigated, and inability to provide written informed consent.

2.2 Clinical data and sampling

Data on age, sex, height, dry weight, dialysis duration, comorbidities, and smoking status were collected using a structured questionnaire as well as from the patients' medical records. Body mass index was calculated as dry weight in kilograms divided by the square of height in meters so as to have an accurate measurement without the influence of the for fluid retention periods resulting in weight loss, thus assigning a category based on the standard cut-off points as underweight, normal weight, overweight, and obese. Blood pressure was measured prior to dialysis treatment.

Five milliliters of peripheral venous blood was collected in a sterile manner from the study subjects just before the midweek session so that the results reported are pre-dialysis values. About 3 mL was poured into a gel serum plexiglass tube, after which it was permitted to coagulate and spun for 20 minutes at a speed of 3,000 rpm; serum was then separated and stored at 20°C without being frozen and thawed more than once.

2.3 Biochemical measurements

The measurements of phosphorus, alkaline phosphatase, iron, and calcium were performed on a Roche Cobas c311 automated photometric analyzer using biochromatic absorption and turbimetry. Phosphate was detected using the phosphomolybdate method at 340 nm; alkaline phosphatase was detected using the rate of p-nitrophenol production from the substance p-nitrophenyl phosphate; calcium ions were detected using cresol phtalein at 570/800 nm with 8-hydroxyquinoline to eliminate interference from magnesium ions, and finally iron was detected calorimetrically due to the release of acid from transferrin and conversion of Fe^{3+} to Fe^{2+}.

Using iron in excess, the assessment of unsaturated capacity was conducted. The sum of unsaturated iron-binding capacity and serum iron determines total iron-binding capacity, whereas transferrin saturation expresses serum iron as a percentage of total iron-binding capacity. Ferritin and intact parathyroid hormone were assessed through the immune assay method on Cobas e411. Routine automated methods were used to measure urea, creatinine, and aminotransferases. All tests were calibrated and subjected to quality control.

The quantities of indoxyl sulfate, p-cresol, and β2-microglobulin were determined using an enzyme-linked immunosorbent assay (ELISA). Sample wells that had the analyte-specific capture antibody pre-coated in them were incubated with the samples and controls, followed by the addition of a biotin-conjugated detection antibody and streptavidin-peroxidase conjugate, after which the wells were washed. Using tetramethylbenzidine as a substrate, the signal produced was proportional to the analyte present. The entire process involved equilibrating the reagents before use, preparing appropriate working solutions as per the required dilution factor shortly before the commencement of the assay, and maintaining the integrity of the lyophilized standards by performing twofold dilution of the solutions after reconstituting them in appropriate volumes.

2.4 Statistical analysis

Analysis of data was carried out using SPSS version 26 (IBM Corporation). Continuous variables are expressed in terms of mean ± standard deviation and

categorical variables in terms of frequencies and percentages. Shapiro–Wilk test was performed to verify normality of data. Comparison between groups was analyzed through either the independent-samples t-test (if data were normally distributed) or Mann–Whitney U test (if data were not normally distributed) for continuous variables and chi-square test for categorical variables. Receiver operating characteristic was used to determine the separation between each solute measured in terms of the area under curve with a 95% confidence interval, and the threshold was generated using the Youden index. All tests conducted were two-tailed, and the significance level was set at $p \leq 0.05$.

2.5 Ethical considerations

The research protocol received approval from both the ethical and scientific committees at the Institute of Genetic Engineering and Biotechnology for Postgraduate Studies in Baghdad University and from the relevant bodies within the Ministry of Health [to include approval number and date], and the study was carried out in line with the Declaration of Helsinki. Written informed consent from all participants was obtained, and all data were treated confidentially.

3. Results

3.1 Demographic and clinical characteristics

The demographic characteristics of the subjects under study were well-matched: the mean age of the patients was 55.70 ± 5.22 years as compared to 54.80 ± 4.96 years for the controls ($t = 0.968$; $p = 0.335$), while 60 percent of the patients were males compared to 53.3 percent of the controls ($\chi^2 = 0.543$; $p = 0.461$). BMI of the patients was significantly lower (22.60 ± 4.79 compared to 24.91 ± 6.48 kg/m²; $p < 0.001$), while the blood pressure of the patients was higher, with 46 patients (76.7 percent) having hypertension and 31 patients (51.7 percent) being found to have diabetes mellitus, neither of which was found in the controls. The duration of dialysis was found to average 52.90 ± 18.09 months, with 26 patients (43.3 percent) suffering from cardiovascular disease (Table 1).

3.2 Conventional biochemical profile

The excretory function of the kidneys was seriously impaired: urea levels were 134.06 ± 28.07 mg/dL versus 31.73 ± 8.16 mg/dL, and creatinine levels were 7.67 ± 2.71 mg/dL versus 0.99 ± 0.14 mg/dL (both $p < 0.001$). The levels of the aminotransferases were normal in both groups (aspartate aminotransferase 16.89 ± 7.01 mg/dL versus 17.77 ± 7.67 mg/dL, $p = 0.464$; alanine aminotransferase 15.98 ± 10.13 mg/dL versus 17.89 ± 10.04 mg/dL, $p = 0.232$), supporting the absence of any liver ailment.

The mineral-bone profile showed persistent abnormalities with low calcium levels, high phosphorus concentration, approximately a three-fold elevation of alkaline phosphatase, and the highest parathyroid hormone concentration, which reached seven times higher than normal. In contrast, iron parameters were dissociated, as ferritin level was approximately 6.5 times higher than in the control group, while transferrin level was less than half of the reference level. Thus, the difference in the ferritin level was significant, as indicated by the maximum value of the Mann-Whitney U-statistic (Table 2, Figure 1).

Table 1. Demographic and clinical characteristics of the study groups.

Variable	Patients (n = 60)	Controls (n = 60)	Test statistic	p value
Age (years)	55.70 ± 5.22	54.80 ± 4.96	t = 0.968	0.335 NS
Sex, male, n (%)	36 (60.0)	32 (53.3)	$\chi^2 = 0.543$	0.461 NS
Sex, female, n (%)	24 (40.0)	28 (46.7)	—	—
Body mass index (kg/m²)	22.60 ± 4.79	24.91 ± 6.48	U = 980	< 0.001
Systolic/diastolic blood pressure (mmHg)	160.50 / 84.90 ± 8.68	119.00 / 77.63 ± 7.69	U = 3124	< 0.001
Hypertension, n (%)	46 (76.7)	0 (0.0)	$\chi^2 = 71.30$	< 0.001
Diabetes mellitus, n (%)	31 (51.7)	0 (0.0)	$\chi^2 = 39.62$	< 0.001
Duration of dialysis (months)	52.90 ± 18.09	—	—	—
Cardiovascular disease, n (%)	26 (43.3)	—	—	—

Values are mean ± standard deviation or n (%). NS, not significant.

Table 2. Renal, hepatic, mineral–bone and iron status markers in the study groups.

Variable	Patients (n = 60)	Controls (n = 60)	Test statistic	p value
Urea (mg/dL)	134.06 ± 28.07	31.73 ± 8.16	U = 3600	< 0.001
Creatinine (mg/dL)	7.67 ± 2.71	0.99 ± 0.14	U = 3480	< 0.001
Aspartate aminotransferase (U/L)	16.89 ± 7.01	17.77 ± 7.67	U = 1660	0.464 NS
Alanine aminotransferase (U/L)	15.98 ± 10.13	17.89 ± 10.04	U = 1572	0.232 NS
Calcium (mg/dL)	7.04 ± 0.89	9.12 ± 0.26	U = 6.0	< 0.001
Phosphorus (mg/dL)	6.25 ± 1.34	3.81 ± 0.47	U = 3484	< 0.001
Alkaline phosphatase (U/L)	331.73 ± 199.60	111.22 ± 30.02	U = 3346	< 0.001
Parathyroid hormone (pg/mL)	364.43 ± 263.61	51.83 ± 15.09	U = 3572	< 0.001
Ferritin (ng/mL)	629.22 ± 236.41	97.13 ± 59.71	U = 3600	< 0.001
Transferrin saturation (%)	13.93 ± 4.34	28.40 ± 8.81	U = 238	< 0.001

Values are mean ± standard deviation. NS, not significant.

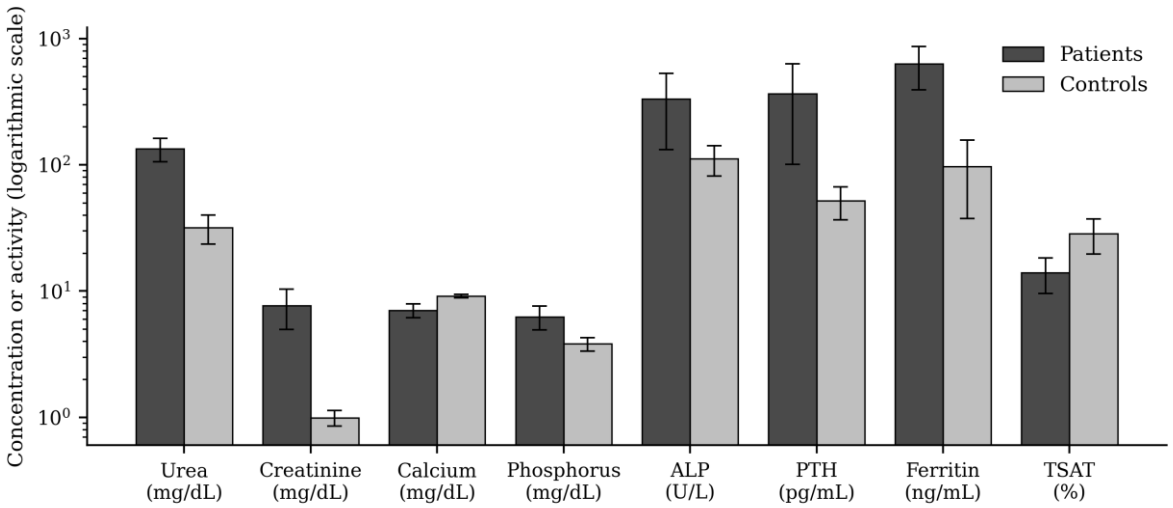


Figure 1. Renal, mineral–bone and iron status markers in hemodialysis patients and healthy controls. Bars are means and error bars are one standard deviation; a logarithmic ordinate is used because the markers differ by three orders of magnitude.

3.3 Serum uremic retention solutes

The concentrations of all three solutes were considerably elevated in the patient group; however, there were some discrepancies in the extent and consistency of these elevations. Indoxyl sulfate increased by around 4.7 times from 64.70 ± 6.00 to 301.77 ± 271.85 ng/mL, characterized by a standard deviation unusually high relative to the mean, thereby causing considerable variation among the patients. The change for p-Cresol is also significant but not to this extent, as it only increased by about 1.8 times, moving from 238.26 ± 126.55 to 428.34 ± 152.96 pg/mL, with resultant distributions overlapping extensively. β2-Microglobulin revealed the highest relative increase of around 11.4 from 2.76 ± 1.72 to 31.51 ± 17.62 mg/L. The findings for all the three substances were statistically significant at $p < 0.001$ (Table 3, Figure 2).

3.4 Separation of the study groups by each solute

The performance of indoxyl sulfate was excellent, with an area under the curve of 0.977 (95% confidence interval 0.944-1.000), and with a threshold of 78.52 ng/mL, it achieved a sensitivity of 93.3% and specificity of 100.0%. β2-microglobulin obtained comparable performance among the other solutes, with an area of 0.961 (0.931-0.985) and, at a concentration of 5.98 mg/L, achieving sensitivity of 83.3% and specificity of 100.0%. p-Cresol performed much less efficiently, with an area of 0.826 (0.747-0.901), yet achieving sensitivity of 83.3% at a threshold of 350.58 pg/mL and specificity of 80.0%. All models were significant ($p \leq 0.001$), and the confidence interval of p-cresol did not overlap those of the aforementioned solutes (Table 4, Figure 3).

Table 3. Serum concentrations of uremic retention solutes in the study groups.

Solute	Patients (n = 60)	Controls (n = 60)	Test statistic	p value
Indoxyl sulfate (ng/mL)	301.77 ± 271.85	64.70 ± 6.00	U = 3518	< 0.001
p-Cresol (pg/mL)	428.34 ± 152.96	238.26 ± 126.55	U = 2976	< 0.001
β2-Microglobulin (mg/L)	31.51 ± 17.62	2.76 ± 1.72	U = 3462	< 0.001

Values are mean ± standard deviation.

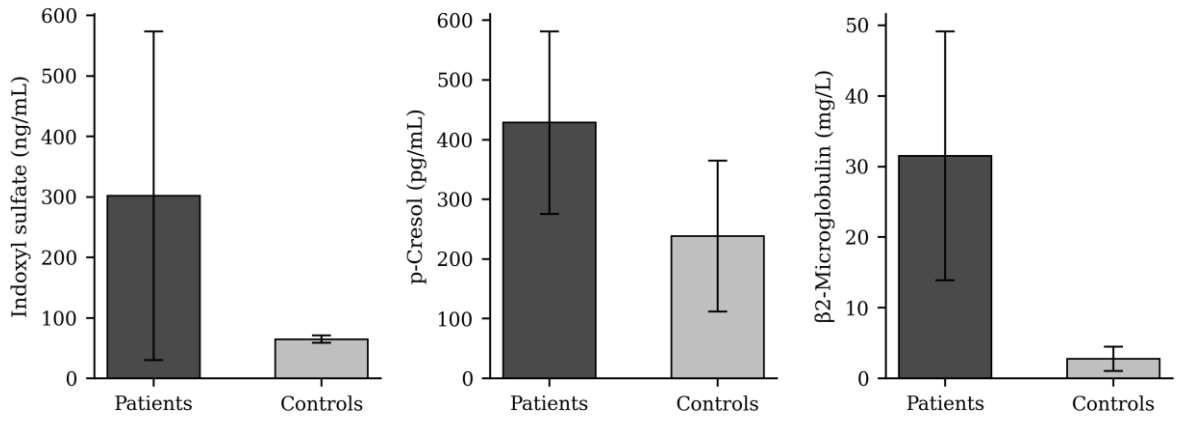


Figure 2. Serum indoxyl sulfate, p-cresol and β2-microglobulin in haemodialysis patients and healthy controls. Bars are means and error bars are one standard deviation; each solute is plotted on its own scale.

Table 4. Receiver operating characteristic analysis of the three uremic retention solutes.

Solute	AUC	95 % CI	Threshold	Sensitivity (%)	Specificity (%)	p value
Indoxyl sulfate	0.977	0.944–1.000	78.52 ng/mL	93.3	100.0	< 0.001
p-Cresol	0.826	0.747–0.901	350.58 pg/mL	83.3	80.0	< 0.001
β2-Microglobulin	0.961	0.931–0.985	5.98 mg/L	83.3	100.0	< 0.001

AUC, area under the curve; CI, confidence interval. Thresholds were derived from the Youden index.

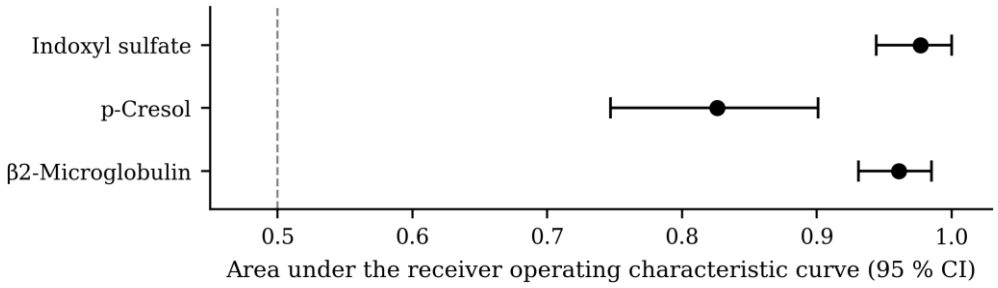


Figure 3. Areas under the receiver operating characteristic curve with 95 % confidence intervals for the three uremic retention solutes. The dashed line marks the value expected from chance alone.

4. Discussion

In this study, three uremic retention substances were identified and coded in various physicochemical categories from a single hemodialysis patient group in Iraq. While it was anticipated that all three of these substances would show increased levels, it was the extent of the increase and consistency of increase of these substances that differed significantly from each other.

4.1 Cohort profile

The lack of age and gender differences signifies that the biochemical differences reported in this study are probably not due to demographic differences in the population involved. The clinical characteristics of the study sample were typical of a common dialysis population, with time on dialysis greater than four years and most people identified as having hypertension and diabetes, in line with worldwide statistics that show that high fasting blood glucose, high body mass index, and high blood pressure are the major risk factors for CKD (1) and with data from other studies in patients undergoing dialysis from Iraq (16). The low body mass index of patients can be explained by a combination of low food intake, constant inflammation, loss of nutrients during dialysis, and the catabolic effect of uremia, in which case protein-energy deficit is regarded as a systemic reflection of retention of solutes (6). Normal aminotransferases prove that liver disease was excluded, which is significant because both protein-bound solutes undergo liver transformation before releasing into the bloodstream.

4.2 Indoxyl sulfate

The near fivefold increase in indoxyl sulfate is biologically reasonable since its production from dietary tryptophan is not hindered by kidney failure and the renal excretion route is lost, while albumin binding limits its clearance through dialysis to the small free portion (4,7). The most significant aspect of these findings is variability instead of mean values. Patients on comparable dialysis regimens exhibited vastly different indole burdens, which is in accordance with published findings that in-pre-dialysis protein-binding solute variance might be

greater than 60% of the inter-patient heterogeneity even in clinically stable patients (17).

The intake of dietary proteins, the composition of microbes at the level of the colon, the time the process of digestion takes, the work of the kidneys, and the binding of albumin are all important factors that ought to be taken into consideration here. The takeaway here is that one pre-dialysis measurement would be sufficient for assessing this population, but only partially for every individual patient.

The significance in clinical terms does not only extend to retention. Indoxyl sulphate engages endothelial aryl hydrocarbon receptors and downstream pro-inflammatory transcription factors, brings into action the generation of reactive oxygen species, and decreases the bioavailability of nitric oxide, and plasma levels of this compound correlate with vascular calcification and markers of atherosclerosis (7,8); in a cohort of 500 patients receiving maintenance hemodialysis and followed up prospectively, higher levels of indoxyl sulphate were associated with higher rates of all-cause mortality and cardiovascular death (9). Since cardiovascular disease was detected in 43.3 % of the current cohort, the burden observed here cannot be biologically inert.

4.3 p-Cresol

The increase in p-cresol was the least, and it had the greatest incidence, as seen from the smallest area under the curve. There are two aspects to this. First, the concentration of p-cresol depends greatly on the quantity of protein being consumed and on the activity of the intestinal bacteria, both of which can be variable in different people independently of kidney function; and the fact that it has been shown that fermentation fiber has an ability to reduce the serum level of p-cresol without any influence on the concentration of indoxyl sulfate indicates that the production of the compound is an important factor in its concentration (11).

Moreover, the generation of p-cresol by a healthy person occurs continuously. Therefore, the control distribution does not get close to zero, and the maximum attainable separation would be lower. This does not imply that the solute is biologically irrelevant since the free serum level of p-cresol is related to the mortality of patients on hemodialysis (10) and p-cresol and its sulfate conjugate are consistently detected among the solutes suspected to cause oxidative stress and inflammation in the endothelium (8).

4.4 β2-Microglobulin

A significant increase in β2-Microglobulin of more than eleven times the reference value is a low molecular weight substance of approximately 11.8 kDa and is usually eliminated through the proximal tubular area, which is inactive in case of chronic kidney disease. Dialysis is insufficient in removing the substance even at high-free dialysis studies as evidenced in the Dialysis Outcomes and Practitioners Patterns Studies showing the increasing level of the substance even after the introduction of high-free dialysis process. (12)

The consistent value of the elevation indicates that it is informative, as the derived threshold shows specificity since the production value is rather stable and the elimination is largely dependent on both renal and dialytic clearance. Therefore, β2-microglobulin serves as a stable marker of middle-molecule retention, unlike the substances that are produced by the intestines which are regulated by nutritional and microbial factors. The stability of β2-microglobulin is proved by the fact that its higher levels show its associations with the rate of death (12,13), with the calcification of heart valves and with the development of cardiovascular events (14,15). The average age of the participants of more than four years enables placing them in the exposed cohort, since this particular window of time is the one in which the retention of middle molecules acquires clinical significance.

4.5 Mineral–bone and iron disturbance

The findings regarding the solutes did not come as isolated incidents. The same individuals also suffered from hypocalcemia, hyperphosphatasemia, elevated alkaline phosphatase levels, and very high levels of parathyroid hormone, indicative of chronic kidney disease-mineral and bone disorder. According to the current opinion of the experts, these abnormalities should be interpreted in conjunction with each other instead of considering them as independent findings. Parathyroid hormone by itself cannot serve as a marker of bone turnover (17). There were some extreme variations between alkaline phosphatase and parathyroid hormone in this case, which suggests that an idea relying completely on the disturbances in phosphate and parathyroid hormones cannot be considered complete in terms of assessing the risks linked to fractures and vessels (18, 19).

The level of iron in the body was reflected by the high ferritin level and the low transferrin saturation, meaning that iron availability was restricted rather than iron depletion. This distinction is important clinically since ferritin is an acute-phase reactant and hence it tends to overestimate the actual usable iron during dialysis, while transferrin saturation indicates the availability of iron for erythropoiesis; this combination is linked to the increased incidence of cerebrovascular and cardiovascular accidents and mortality in patients receiving hemodialysis. It can be concluded that it is possible for iron to coexist with a high solute burden, as inflammation can be seen as a result of matter retention and at the same time cause iron disorder (6,8).

4.6 Interpretation of the receiver operating characteristic analysis

Chronic dialysis clients were evaluated versus healthy non-clients in separate groups along the entire disease spectrum, and the diagnosis has been made long before any of the solutes are to be measured. Consequently, the established threshold values cannot be used for diagnosing the condition at hand. There are already established parameters in the serum creatinine/estimated glomerular filtration rate/albuminuria trio for the purpose in question (2,3)

The findings of the analysis are quantitative measures of biological distance between various groups for each solute per each retention class. The analysis indicates that the results are informative, as indoxyl sulfate and β2-microglobulin could clearly differentiate the separated groups, whereas p-cresol could only place one control and one patient with higher retention deviation above the limits. A study limited to conventional adequacy parameters would not have noticed this divergence, as both urea and creatinine are able to cover only one retention class.

4.7 Limitations

The cross-sectional design allows to provide information on relationships but it does not allow to make inferences concerning causation and prognosis, while recruitment from one center limits the universality of the findings although the number of people was determined beforehand. The sample of only one pre-dialysis test per participant is a disadvantage, as it is known that due to variability of protein-bound substances it is possible to characterize a group better than an individual (17).

Assays for solutes were performed using immunoassay methods instead of traditional chromatographic means with mass spectrometric detection, as reported in most of the reference literature as well as studies confirming their prognostic value (10,11). Immunoassay data are considered absolute values and are normalized using assay kit-specific values; thus, they cannot be compared with values obtained via chromatographic methods. As a result, while internal between-group comparisons are still valid, they should refrain from making cross-study comparisons. Besides that, p-cresol concentration determined during the assay is total not free concentration since free concentration is associated with occurrence of clinical events (10). Finally, Kt/V dialysis dose, residual renal function,

dialyzer flow rate, protein intake, serum albumin levels, and inflammatory marker status were not identified in the obtained results; in particular, the last factor was crucial for better interpretation of ferritin and β2-microglobulin levels.

5. Conclusions

The burdens of uremic retention in Iraqi adults undergoing maintenance hemodialysis were substantial but varied for different solutes. The greatest level of retention was seen in β2-microglobulin, followed by indoxyl sulfate and p-cresol. Other problems were the altered pattern of the minerals and some biochemical signs indicating the limitation of iron.

The different behavior shown by the three solutes signifies that they show differences among each other and therefore belong to different classes of retention, rather than being considered as equivalent measurements of the uremic condition. This means that the conventional small solutes that are measured to assess the adequacy of dialysis only represent a partial contribution to the overall burden of solutes retained in uremia. Further prospective studies are needed to investigate possible prognostic implications of these differences in relation to the relationship between dialysis dose, remaining kidney function, inflammatory process, and outcome of treatment when applying chromatography for measuring free and total fractions of solutes.

Ethical approval. Approved by the scientific and ethical committee of the Institute of Genetic Engineering and Biotechnology for Postgraduate Studies, University of Baghdad, ETH/503/26. Written informed consent was obtained from every participant.

Conflict of interest. The authors declare no conflict of interest.

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Data availability. The datasets are available from the corresponding author on reasonable request.

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