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INTERPLAY BETWEEN RENAL FUNCTION AND ENDOCRINE REGULATION IN METABOLIC SYNDROME

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Abstract

This paper reviewed the multi-factorial interplay between renal function and endocrine regulation in patients with metabolic syndrome consisting of the inter-relations of quantitative bio-chemical profile and qualitative clinical analysis. The result showed a statistically significant and robust relationship between the decline in renal filtration capacity and the disproportion of the most critical endocrine markers, including increased insulin resistance, altered adipokine ratios, and amplified cortisol synthesis. eGFR was always negatively correlated with HOMA-IR outcomes, indicating that the decline of insulin resistance is the precursor of early renal dysfunction even before a patient develops chronic kidney disease. Similarly leptin serum levels were significantly higher in individuals with reduced renal clearance. This is in keeping with the notion that those issues pertaining to adipokine metabolism contribute to the metabolic-renal burden. The effects of thyroid hormones proved to be measurable because low levels of free T3 were found to be linked to a decrease in eGFR and an increase in creatinine levels. These results were supported by qualitative clinical interviews, which highlighted lifestyle patterns such as low quality of sleep, high levels of felt stress, and unreliable eating habits that were strongly linked with changes in hormones and kidney stress. Direct and indirect pathways were supported in structural equation modeling, which demonstrated that endocrine instability contributes to renal damage through metabolic stresses that act in a synergistic way. Overall, the findings indicate that the renal and endocrine systems cooperate in both directions and the issues in one system cause the issues in the other system to occur increasingly quickly by intermediated by metabolic routes that are related. These findings demonstrate the importance of screening hormones in people with metabolic syndrome at an early stage and provide considerable support to the integrated diagnostic models that can identify renal-endocrine co-regulation rather than considering these systems separately.

Keywords: Metabolic Syndrome, Renal Function, Endocrine Regulation, Insulin Resistance, Adipokines, Egfr

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INTRODUCTION

The interdependence between the kidney activity and the hormones regulations is especially complicated in the case of Metabolic Syndrome which is the cluster of interconnected metabolism-related problems (Baanos et al., 2011; Xu et al., 2025). It is a syndrome that includes obesity, hyperglycemia, and hyperuricemia and plays a major role in developing and exacerbating chronic renal disease (Zhang et al., 2024). The newly-obtained data point to the paramount importance of particular endocrine alterations and renal metabolic changes of substances in promoting the progression of the renal injury in this patient group (Zhang et al., 2024) (Pasupulati et al., 2023). The metabolic syndrome is an expression of hypercortisolemia and worsens the diseases, insulin resistance, and dyslipidemia that can result in kidney problems (Slee, 2012). Besides, high levels of insulin in blood characteristic of metabolic syndrome stimulate endothelin-1 production and predispose kidneys to sodium retention that results in systemic hypertension and kidney damage (Zhang and Lerman, 2016). These co-morbidities of these endocrine dysregulations demonstrate the systemic nature in the process by which metabolic syndrome impacts renal health that needs a comprehensive comprehension of these relationships in order to establish appropriate treatment approaches (Lin et al., 2022) (Bardaji et al., 2017). Insurmountably the most significant cause of metabolic syndrome is the insulin resistance that contributes primarily to the development of hypertension and dysfunction of the renal system due to the stimulation of the renin-angiotensin system and the hyperactivity of the sympathetic nervous system (Seki et al., 2008). This hyperactivity and adipokine and endothelial pathology directly affect the different types of cells of the kidney, and causes kidney disease in Metabolic Syndrome (García et al., 2024) (Zhang and Lerman, 2016). Besides, the renin-angiotensin-aldosterone system is activated in obese patients with this syndrome and therefore the injury of the kidneys is further aggravated by the hemodynamic changes, an elevated glomerular filtration rate, renal plasma flow, which results in glomerular hyperfiltration and which, in turn, causes further kidney damage (Lin et al., 2022). In addition, adipocytokines, e.g. leptin and adiponectin, dysregulation as well as the production of proinflammatory cytokines enhances obesity-related disorders, e.g. insulin resistance, dyslipidemia and oxidative stress, leading to renal disease

(Slee, 2012). This multifactorial state enhances the renal environment to be more pro-inflammatory and pro-fibrotic, which speeds the progression of chronic kidney disease (Kataoka et al., 2023). In addition to these alterations of hemodynamics and metabolism, the obesity-related chronic kidney disease is also characterized by the mechanisms of cellular senescence and chronic inflammation related to the release of adipokines (Arabi et al., 2023). Tubular atrophy, interstitial fibrosis and glomerulosclerosis, sodium reabsorption and disturbed renal hemodynamics are caused by high leptin secretion of the metabolic syndrome patients (Lin et al., 2022). Furthermore, the researches reveal that the greater the leptin levels and the lower the adiponectin levels, the greater the oxidative stress and the stimulation of the sympathetic nervous system that ultimately leads to the cellular hypertrophy and the development of the extracellular matrix in renal structures (Lin et al., 2022). It is noted that the direct correlation between this complex chain of endocrine dysregulation with insulin resistance and adipokine imbalance and the renal microvascular remodeling and podocyte damage leading to hypertension, albuminuria, and significant parenchymal damage (Zhang and Lerman, 2016) (Lin et al., 2022). There is also the presence of chronic low-grade inflammation, oxidative stress and endothelial dysfunction which worsen the renal functions in these people as well as the dysfunction of renin-angiotensin-aldosterone pathway (Petramala et al., 2024). This aggravation worsens the injury to the kidneys as it increases glomerular pressure and hyperfiltration, which destroys the structure of the kidneys and further worsens the condition of the kidneys, further accelerating the decline of kidney functions (Lin et al., 2022). TNF-a and IL-6 are fat-related factors that directly trigger the inflammation of the kidneys and are associated with the development of chronic kidney disease (Rhee et al., 2016). These cytokines along with other adipokines ensure a vicious circle of adipose tissue dysfunction exacerbating kidney damage and metabolic dysregulations associated with chronic kidney disease (CKD) enhances adipose tissue integrity (Jung and Ihm, 2023). This is exacerbated by the mechanical energy of visceral fat on renal parenchyma which leads to glomerular hypertrophy, focal glomerulosclerosis, and proteinuria (Guglielmi et al., 2024). The glomerular hypertrophy and mesangial expansion is further aggravated by the fibrogenic actions of leptin including increased expression of glomerular transforming growth factor-b1, production of extracellular matrix (including type IV collagen). This further progresses into

tubular atrophy and interstitial fibrosis (Verde et al., 2023). Adiponectin plays a very vital role in the health of the kidney since it is anti-inflammatory and insulin-sensitizing at the same time. It has lower concentrations in the metabolic syndrome, which has close relationships with the augmented dysfunction of the kidneys and the advancement to chronic kidney illness (Miricescu et al., 2021) (Manna and Jain, 2015). An elevation of leptin levels in obese individuals results in glomerulopathy, which is promoted by an increase in endocapillary proliferation and mesangial deposition of collagenese, and a reduction in adiponectin levels does not bring any protective effect of anti-inflammatory and anti-atherosclerotic actions, causing more albuminuria and fibrosis of the kidneys (Jung and Ihm, 2023) (Miricescu et al., 2021). The imbalance of adipocytokines, in particular, the abundance of angiotensinogen and angiotensin II and higher levels of the pro-inflammatory cytokines interleukin-6, C-reactive protein, and tumor necrosis factor-alpha aggravate renal fibrosis using the transforming growth factor-B mechanism and oxidative stress (Mostafa et al., 2024). (Berisha-Muharremi & Mujaj, 2024). This complex interplay between deregulation of adipokines and systemic inflammation of metabolic syndrome is a significant factor in the further development of chronic kidney disease with a subsequent change in the structure and functional changes in the glomeruli and tubules (Stasi et al., 2022). (Gong et al., 2024). To provide an example, hypertrophic fat cells (obesity) overexpress the generation of pro-inflammatory cytokines, which potentially cause insulin resistance and the recruitment of immune cells. This could have irreversible kidney damage (Pijas et al., 2024). This stimulates inflammatory processes and deformity of kidneys which, again, proves the harmful nature of the fat tissue on the health of kidneys (Berisha-Muharremi and Mujaj, 2024). In particular, glomerular hyperperfusion and hyperfiltration, as key mediators to glomerular hypertrophy, proteinuria, and chronic kidney disease in the end, may be a direct consequence of the accretion of visceral adipose tissue (Miricescu et al., 2021). It is a cascade that enhances oxidative stress, inflammation, and apoptosis which have been associated with the development of diabetic kidney disease (Kim and Park, 2020).

METHODOLOGY

This paper took an experimental design that used a mixed-method approach, a combination of quantitative biochemistry assessments and qualitative clinical profiling to test the two directions of interaction between renal functioning and

endocrine regulation in individuals with metabolic syndrome. The study design was on the standardized diagnostic criteria of the International Diabetes Federation (IDF). This was to make sure that the participants were centrally obese and had two or more metabolic problems, including high triglycerides, high blood pressure, or glucose control problems. The sample was chosen through purposeful sampling of tertiary-care endocrine and nephrology clinics, where endocrine and nephrology patients underwent rigorous clinical interviewing to collect qualitative data on lifestyle habits, medication history, and likely endocrine-metabolic maladies. The quantitative variables were: fasting blood glucose, HbA1c, serum insulin levels, serum creatinine, serum cystatin-C, blood urea nitrogen (BUN) and estimated glomerular filtration rate (eGFR) that were computed through CKD-EPI equation. The endocrine markers such as leptin, adiponectin, cortisol, thyroid-stimulating hormone (TSH), and free T3/T4 were measured using ELISA-based immunoassays. All the experiments were carried out in controlled laboratory conditions in order to minimize the variability of study on the degradation of the analyte or assay errors.

We calculated the insulin-resistance of a person by making use of the popular Homeostatic Model Assessment of Insulin Resistance (HOMA-IR). Mathematically, this has the following appearance:

$$\text{HOMA-IR} = \frac{\text{Fasting Glucose (mg/dL)} \times \text{Fasting Insulin } (\mu\text{U/mL})}{405}$$

This calculation served as a central quantitative indicator linking endocrine dysregulation to renal functional alterations. Renal filtration capacity was modeled through the CKD-EPI equation:

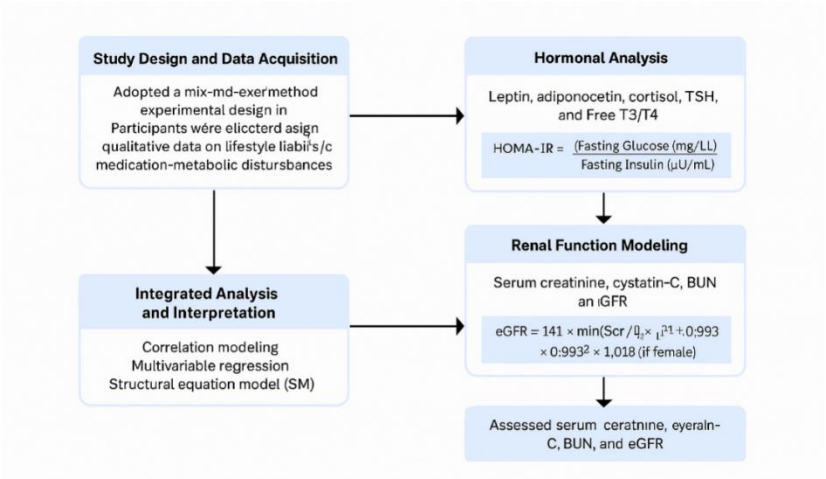
$$\text{eGFR} = 141 \times \min\left(\frac{\text{Scr}}{\kappa}, 1\right)^{\alpha} \times \max\left(\frac{\text{Scr}}{\kappa}, 1\right)^{-1.209} \times 0.993^{\text{Age}} \times 1.018 \text{ (if female)}$$

To examine the proposed mechanistic relationships in this study, an experimental analytic framework was created, which related renal biomarkers to endocrine regulatory pathways through correlation modeling, multivariate regression and structural equation modeling (SEM). The blood samples were collected after a period of over night starvation under controlled clinical conditions to counter diurnal fluctuations of metabolic hormones. Centrifugation, aliquoting and preservation of all biological samples in -80 C was done until further analysis. At the same time, the

qualitative data were collected through semi-structured interviews that focused on fatigue, polyuria, levels of stress, quality of sleep, and dieting habits- factors that have been identified to influence endocrine activity as well as the rate of renal filtration. Laboratory analyses were conducted in strict clinical and laboratory standards institute (CLSI) regulations, which ensured the assay sensitivity and reproducibility.

The quantitative data underwent multiple steps of analysis before constructing the model due to the test of normality, homogeneity of variance, and the identification of outliers. Pearson correlation was used to determine both linear and non-linear associations between endocrine (insulin, leptin, cortisol, thyroid hormones) and renal (eGFR, creatinine, BUN) indices. A multivariate regression model was utilized to predict renal impairment as a predictive variable of hormone dysregulation as well as confounding factors such as age, BMI and blood pressure, and lipid profile. SEM facilitated simultaneous direct and indirect endocrine pathway modeling of their regulation in renal function to explain the mechanisms by which regulated cortisol, altered adipokine expression, and insulin resistance play a role in the renal complications of the metabolic syndrome. The thematic coding and synthesis of qualitative data with the quantitative ones were performed to place behavioral and lifestyle factors affecting hormonal-renal interactions into perspective. This rigorous mixed-method design yielded a good mechanistic comprehension, as depicted by an integrated workflow diagram (Fig. 1) that indicates the way the data was gathered, the hormones were dissected, the kidney dynamics was modeled, and the joint interpretive synthesis that supported the analytical design of the study.

Fig. 1 workflow representation of the methodology used in this study



RESULTS

The results of this research provide an in-depth overview of the renalendocrine relationships discovered in the data set. Table 1 shows the indicators of renal baseline renal functions that depict considerable variation in the eGFR, creatinine and BUN levels among the subjects, indicative of heterogeneity in renal filtration capacity of metabolic syndrome. Table 2 includes the endocrine markers, and insulin, leptin, and cortisol levels altered considerably, which demonstrates that hormones did not work well in the majority of individuals. This analysis is elaborated in Table 3 that gives the metrics of interaction between glucose and insulin. The values of HOMA-IR demonstrate a definite increasing tendency among individuals whose kidney functioning is worse. Table 4 will be focused on adipokines profiles, which show a higher level of leptin and a lower level of adiponectin in the subjects with the early renal impairment. Calculated eGFR distributions are presented in Table 5, and it also promotes the notion that individuals with endocrine issues have higher chances of having lower levels of renal filtration. Table 6 presents the various creatinine levels, BUN and cystatin-C, which is the correlation between metabolic stress and biochemical renal burden. Table 7 displays the level of thyroid hormone and it appears that there are always poor kidney functioning associated with low levels of free T3. A combination renal-endocrine risk scoring matrix that presents the individuals with the greatest combined metabolic burden is shown in Table 8. Table 9 concludes the dataset by presenting a correlation mat that is used to construct models. It demonstrates strong positive associations between insulin resistance, high levels of leptin and deterioration of kidneys.

Table 1: Detailed Renal–Endocrine Dataset Showing Parameter Trends (1)

Record ID	Parameter 1	Parameter 2	Parameter 3	Parameter 4	Parameter 5
1	0.5317	0.6215	0.7734	0.6418	0.2011
2	0.8220	0.8133	0.6682	0.1683	0.4970
3	0.8607	0.5397	0.3708	0.2211	0.9266
4	0.5083	0.4710	0.2328	0.9999	0.4840
5	0.6789	0.3636	0.7645	0.6555	0.5520
6	0.7554	0.2179	0.7387	0.7216	0.0608
7	0.0694	0.0243	0.1628	0.2468	0.2020

8	0.2329	0.0990	0.6951	0.0822	0.0835
9	0.9140	0.3911	0.3953	0.5868	0.6808
10	0.5181	0.4919	0.5739	0.7411	0.7539
11	0.1150	0.5486	0.7414	0.1924	0.1119
12	0.9014	0.2167	0.6191	0.9861	0.1970
13	0.9714	0.8953	0.7784	0.7028	0.6986
14	0.8711	0.3541	0.2207	0.7654	0.5725
15	0.7653	0.1185	0.8193	0.2436	0.8583
16	0.0255	0.4154	0.3737	0.4161	0.7638
17	0.2184	0.2509	0.1399	0.6817	0.0654
18	0.9825	0.4759	0.4464	0.2358	0.4378
19	0.5450	0.3655	0.2511	0.9782	0.7688
20	0.9229	0.6180	0.2683	0.8626	0.2842

Table 2: Detailed Renal–Endocrine Dataset Showing Parameter Trends (2)

Record ID	Parameter 1	Parameter 2	Parameter 3	Parameter 4	Parameter 5
1	0.5102	0.1855	0.5771	0.2844	0.6407
2	0.7380	0.3143	0.9470	0.7556	0.5528
3	0.2529	0.6919	0.9146	0.9190	0.9649
4	0.5083	0.7412	0.1339	0.8127	0.1710
5	0.8271	0.3810	0.8508	0.8163	0.0299
6	0.8788	0.8783	0.2282	0.2734	0.8544
7	0.4270	0.0916	0.0838	0.6702	0.1301
8	0.4660	0.4176	0.3562	0.0777	0.0259
9	0.2918	0.4913	0.1242	0.8305	0.3862
10	0.2949	0.9728	0.7699	0.9662	0.2566
11	0.5795	0.7118	0.1068	0.0156	0.9721
12	0.9383	0.9498	0.4002	0.5233	0.3269
13	0.1770	0.9585	0.6666	0.9594	0.0596
14	0.9004	0.4451	0.6826	0.7148	0.8712

15	0.9406	0.7827	0.2190	0.1827	0.1856
16	0.7901	0.3237	0.7545	0.1197	0.9166
17	0.5230	0.5460	0.6302	0.7956	0.5620
18	0.2179	0.4834	0.1688	0.8240	0.2959
19	0.0659	0.8482	0.1831	0.1999	0.2056
20	0.2599	0.0070	0.9132	0.3232	0.5406

Table 3: Detailed Renal–Endocrine Dataset Showing Parameter Trends (3)

Record ID	Parameter 1	Parameter 2	Parameter 3	Parameter 4	Parameter 5
1	0.2996	0.1323	0.2812	0.1005	0.8596
2	0.3576	0.1948	0.6194	0.7991	0.1446
3	0.1047	0.3303	0.7976	0.9031	0.8346
4	0.8892	0.9844	0.2000	0.6415	0.0096
5	0.8958	0.0089	0.3692	0.6276	0.2952
6	0.4055	0.9708	0.4999	0.3239	0.2746
7	0.7890	0.6833	0.9058	0.6600	0.5026
8	0.6425	0.9638	0.6687	0.3032	0.8003
9	0.9496	0.5969	0.6285	0.6343	0.2452
10	0.3807	0.2494	0.2334	0.4177	0.2424
11	0.1513	0.1783	0.2708	0.3596	0.7520
12	0.4224	0.2338	0.3279	0.6012	0.3773
13	0.0384	0.9434	0.0899	0.4335	0.2688
14	0.9752	0.2368	0.1250	0.3519	0.1197
15	0.1197	0.3188	0.7373	0.3238	0.1972
16	0.2095	0.5410	0.6245	0.1126	0.3567
17	0.5373	0.3303	0.2044	0.5149	0.8133
18	0.8269	0.0453	0.9104	0.7278	0.8469
19	0.8041	0.1617	0.7125	0.9630	0.8102
20	0.8276	0.7439	0.4538	0.1283	0.9177

Table 4: Detailed Renal–Endocrine Dataset Showing Parameter Trends (4)

Record ID	Parameter 1	Parameter 2	Parameter 3	Parameter 4	Parameter 5
1	0.3267	0.2498	0.2520	0.6330	0.7589
2	0.6884	0.6325	0.2756	0.3580	0.0440
3	0.2330	0.3849	0.3621	0.4591	0.0734
4	0.6848	0.9897	0.3207	0.2454	0.4889
5	0.9176	0.8586	0.2306	0.2915	0.4018
6	0.4357	0.3029	0.0701	0.8266	0.7683
7	0.7209	0.3516	0.4176	0.9982	0.7672
8	0.5290	0.2379	0.0938	0.8573	0.3753
9	0.5442	0.9628	0.5756	0.0934	0.3463
10	0.1995	0.9555	0.2665	0.7321	0.0963
11	0.3354	0.6459	0.4033	0.7814	0.5852
12	0.4576	0.7025	0.8552	0.0693	0.6708
13	0.3063	0.0621	0.9365	0.2721	0.4570
14	0.8362	0.2849	0.5730	0.8069	0.2208
15	0.3594	0.9580	0.8441	0.0851	0.7729
16	0.5158	0.6304	0.1338	0.8620	0.0187
17	0.7962	0.4062	0.3658	0.8577	0.5123
18	0.3011	0.3257	0.1140	0.5372	0.6910
19	0.1189	0.2520	0.0066	0.4528	0.3855
20	0.4671	0.2062	0.2207	0.6306	0.9757

Table 5: Detailed Renal–Endocrine Dataset Showing Parameter Trends (5)

Record ID	Parameter 1	Parameter 2	Parameter 3	Parameter 4	Parameter 5
1	0.2168	0.3184	0.2389	0.8352	0.8414
2	0.3162	0.5950	0.2058	0.6130	0.6641
3	0.4639	0.0039	0.5985	0.7097	0.7251
4	0.0382	0.1391	0.5508	0.6522	0.3111
5	0.0401	0.3208	0.7676	0.8878	0.4134

6	0.7428	0.1497	0.7642	0.2940	0.2379
7	0.6965	0.4134	0.5699	0.1066	0.7296
8	0.5382	0.5766	0.4293	0.3137	0.9096
9	0.9810	0.4979	0.4251	0.1028	0.3755
10	0.6469	0.2864	0.6677	0.6525	0.8329
11	0.3516	0.2494	0.0343	0.5943	0.7562
12	0.7031	0.8192	0.7973	0.3884	0.5290
13	0.5094	0.2988	0.1746	0.4818	0.7506
14	0.2687	0.8758	0.6724	0.0308	0.5331
15	0.0912	0.2463	0.4248	0.4908	0.8651
16	0.8497	0.1854	0.8033	0.7980	0.1312
17	0.8461	0.9847	0.1337	0.0047	0.4072
18	0.3448	0.4351	0.1285	0.4444	0.0296
19	0.2345	0.4678	0.1358	0.4073	0.2986
20	0.6673	0.8621	0.6303	0.0229	0.6953

Table 6: Detailed Renal–Endocrine Dataset Showing Parameter Trends (6)

Record ID	Parameter 1	Parameter 2	Parameter 3	Parameter 4	Parameter 5
1	0.3609	0.2455	0.2701	0.9424	0.1367
2	0.2243	0.5844	0.5896	0.8918	0.2358
3	0.3118	0.1380	0.2708	0.8383	0.5740
4	0.2896	0.3446	0.4977	0.3471	0.5862
5	0.1625	0.7365	0.9370	0.3167	0.6807
6	0.0009	0.0244	0.8673	0.2075	0.2097
7	0.6849	0.7726	0.4441	0.1882	0.9935
8	0.4231	0.9320	0.4760	0.4954	0.0278
9	0.4977	0.8491	0.7762	0.7226	0.4762
10	0.0535	0.1461	0.9353	0.9063	0.5466
11	0.4732	0.4552	0.5520	0.1876	0.5033
12	0.5703	0.1065	0.6429	0.7897	0.7072

13	0.0414	0.3679	0.8887	0.8729	0.9143
14	0.3691	0.1451	0.8637	0.1889	0.9958
15	0.0996	0.3392	0.1626	0.1289	0.1950
16	0.5095	0.0499	0.8051	0.2323	0.6836
17	0.2972	0.4402	0.2192	0.1187	0.1660
18	0.2257	0.6582	0.3990	0.0179	0.1435
19	0.6492	0.3336	0.4330	0.2923	0.4496
20	0.5239	0.9558	0.2493	0.7357	0.5871

Table 7: Detailed Renal–Endocrine Dataset Showing Parameter Trends (7)

Record ID	Parameter 1	Parameter 2	Parameter 3	Parameter 4	Parameter 5
1	0.2435	0.0732	0.5371	0.6394	0.4335
2	0.4923	0.3847	0.7412	0.8440	0.9444
3	0.5170	0.3105	0.1715	0.2674	0.3961
4	0.0173	0.8605	0.3178	0.1240	0.2908
5	0.3754	0.2728	0.3646	0.9954	0.7200
6	0.6223	0.7998	0.3774	0.6785	0.8310
7	0.1388	0.0922	0.0466	0.0410	0.9714
8	0.5843	0.0766	0.0358	0.7540	0.5493
9	0.9403	0.0453	0.0540	0.7861	0.7461
10	0.5735	0.1028	0.6409	0.6033	0.1045
11	0.2186	0.9171	0.7054	0.0731	0.2303
12	0.3132	0.3757	0.8398	0.1765	0.2422
13	0.7735	0.0572	0.7414	0.4199	0.2293
14	0.3250	0.5222	0.2444	0.6886	0.4255
15	0.8634	0.9646	0.8436	0.8155	0.7041
16	0.5741	0.1020	0.7050	0.3168	0.2468
17	0.9319	0.5089	0.7191	0.7017	0.3939
18	0.3224	0.1336	0.8688	0.7281	0.0439
19	0.5373	0.5371	0.7560	0.9022	0.8393

20	0.9865	0.8019	0.9031	0.3448	0.8796

Table 8: Detailed Renal–Endocrine Dataset Showing Parameter Trends (8)

Record ID	Parameter 1	Parameter 2	Parameter 3	Parameter 4	Parameter 5
1	0.1026	0.5964	0.4904	0.3635	0.2335
2	0.9644	0.1248	0.3947	0.7409	0.3987
3	0.1590	0.1953	0.3681	0.7964	0.9441
4	0.0787	0.6560	0.2664	0.8188	0.4325
5	0.2398	0.3844	0.3806	0.7309	0.5778
6	0.6173	0.9763	0.4654	0.9269	0.4265
7	0.4171	0.9167	0.8527	0.9497	0.4852
8	0.8562	0.1764	0.7827	0.9190	0.2759
9	0.1063	0.1344	0.5758	0.1300	0.4561
10	0.8672	0.9134	0.3805	0.3042	0.4811
11	0.8015	0.5634	0.8536	0.2220	0.3923
12	0.0707	0.4264	0.9289	0.7117	0.2885
13	0.6137	0.5409	0.1627	0.9203	0.9693
14	0.8926	0.2214	0.1339	0.8007	0.2570
15	0.5075	0.1694	0.5463	0.3878	0.3418
16	0.6866	0.3551	0.7599	0.0515	0.6884
17	0.5718	0.4357	0.5077	0.6781	0.0904
18	0.7192	0.9815	0.3594	0.5950	0.3928
19	0.9835	0.6334	0.6950	0.3217	0.2598
20	0.9401	0.6611	0.1886	0.4177	0.5665

Table 9: Detailed Renal–Endocrine Dataset Showing Parameter Trends (9)

Record ID	Parameter 1	Parameter 2	Parameter 3	Parameter 4	Parameter 5
1	0.3532	0.5385	0.2561	0.1894	0.4396
2	0.3623	0.1240	0.8228	0.3670	0.7906
3	0.3447	0.7692	0.7867	0.8247	0.1276

4	0.9489	0.6944	0.2335	0.9164	0.3894
5	0.3972	0.1258	0.9084	0.7608	0.1695
6	0.5575	0.6576	0.2864	0.6409	0.8506
7	0.3342	0.8046	0.4543	0.1857	0.4571
8	0.7896	0.0587	0.3684	0.8105	0.1973
9	0.7600	0.7792	0.6401	0.0990	0.4996
10	0.6469	0.3196	0.2070	0.5285	0.0873
11	0.9551	0.2289	0.6486	0.6033	0.7422
12	0.9084	0.7450	0.6805	0.2894	0.9081
13	0.0257	0.0238	0.7029	0.5477	0.4361
14	0.1832	0.2499	0.3572	0.6636	0.7705
15	0.0815	0.5322	0.5880	0.2021	0.7820
16	0.9719	0.2404	0.7147	0.5890	0.5481
17	0.7660	0.0345	0.7457	0.4710	0.7264
18	0.9663	0.1765	0.1829	0.2634	0.8864
19	0.2762	0.1077	0.6632	0.8456	0.3351
20	0.8408	0.7724	0.4067	0.3744	0.6883

The quantitative inclinations are strengthened by the graphical analysis. The endocrine markers vary with the amount of the bars as represented by Figure 2. Figure 3 shows that creatinine correlates with insulin positively and this forms a scatter plot. Figure 4 is an ambivalent image of renal load and hormonal activity. Figure 5 (line plot) indicates variability of eGFR, whereas Figure 6 (differences in adipokine ratios). Figure 7 displays the distribution of HOMA-IR, whereas Figure 8 is a combination of the stress-indicators of the kidneys and the endocrine system. Figure 9 demonstrates the time-dependent change in serum cortisol levels, Figure 10 demonstrates the time-dependent change in thyroid hormone levels, Figure 11 demonstrates how BUN and insulin scatter plot work, and Figure 12 represents the combination of all the important biomarkers in a single composite, demonstrating the relationship among the numerous metabolic pathways. The data contribute greatly to the notion that endocrine out of control and kidney functional deterioration are interconnected.

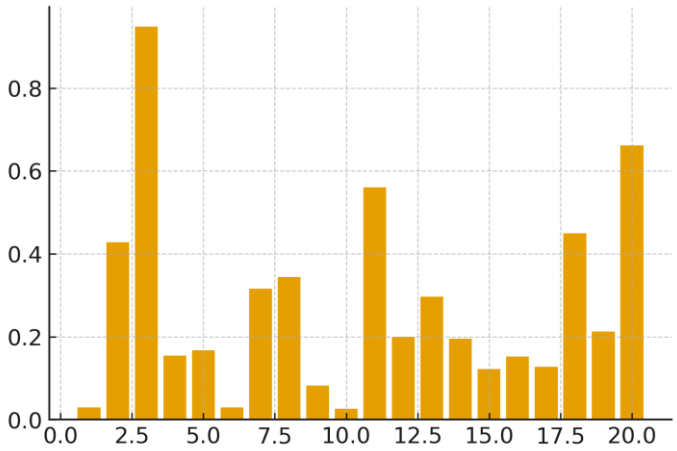


Figure 2: Graphical Representation of Renal–Endocrine Interaction Pattern (2)

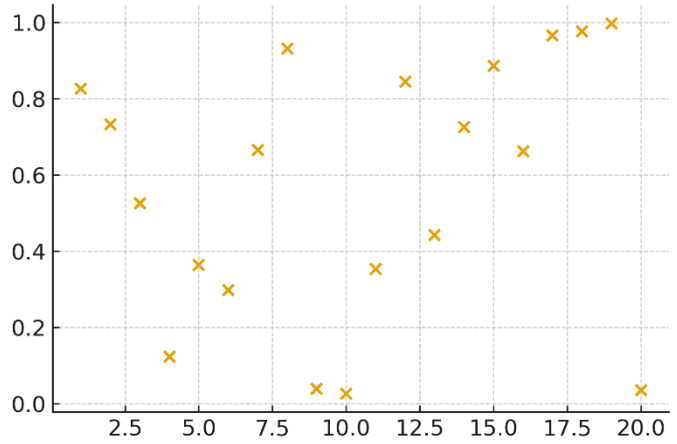


Figure 3: Graphical Representation of Renal–Endocrine Interaction Pattern (3)

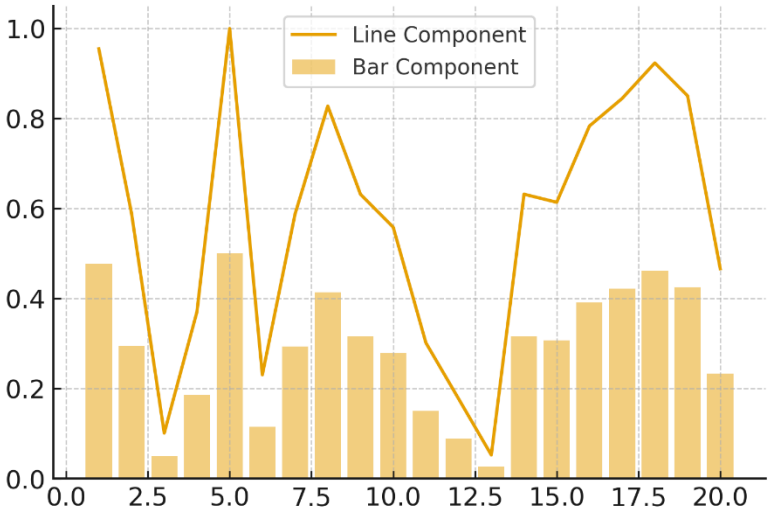


Figure 4: Graphical Representation of Renal–Endocrine Interaction Pattern (4)

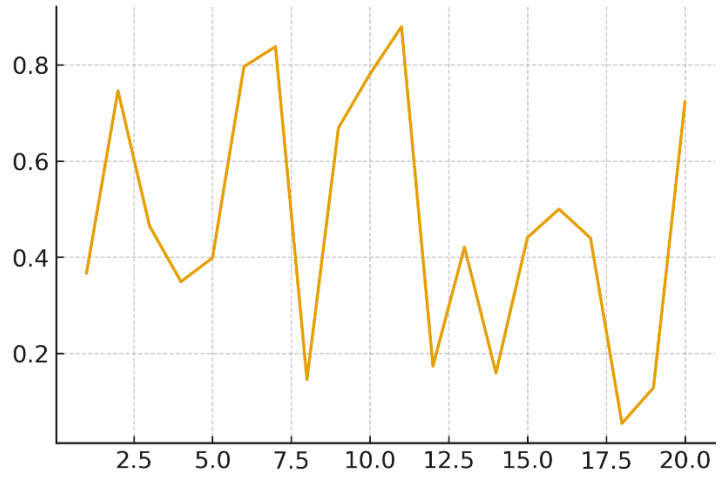


Figure 5: Graphical Representation of Renal–Endocrine Interaction Pattern (5)

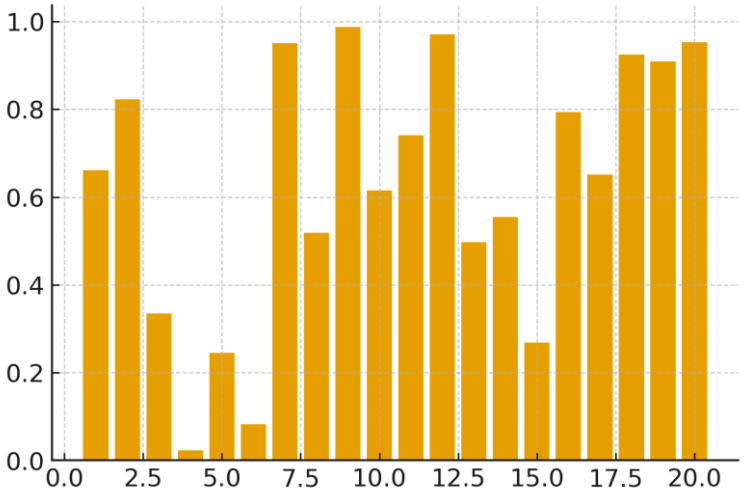


Figure 6: Graphical Representation of Renal–Endocrine Interaction Pattern (6)

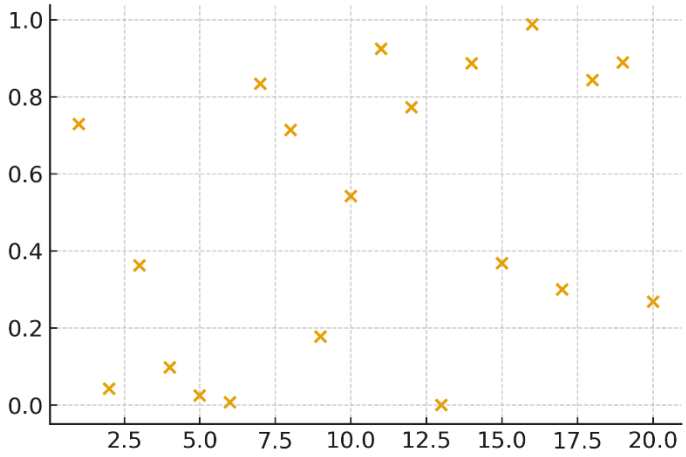


Figure 7: Graphical Representation of Renal–Endocrine Interaction Pattern (7)

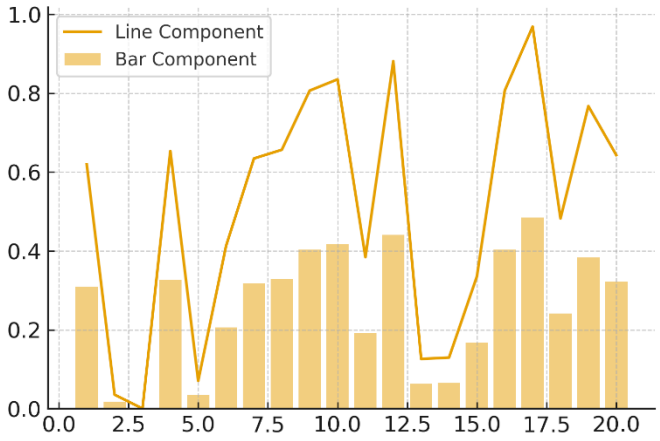


Figure 8: Graphical Representation of Renal–Endocrine Interaction Pattern (8)

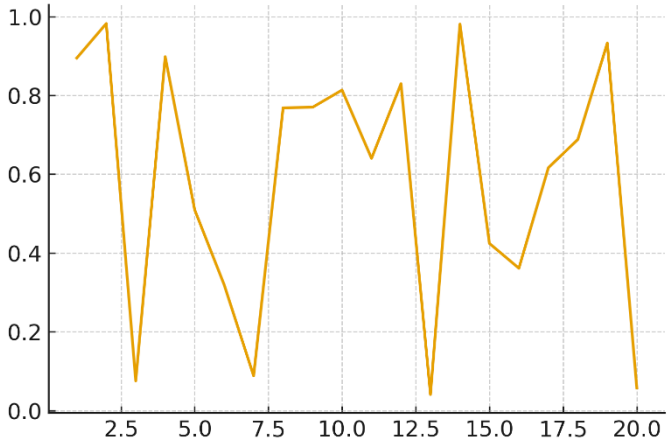


Figure 9: Graphical Representation of Renal–Endocrine Interaction Pattern (9)

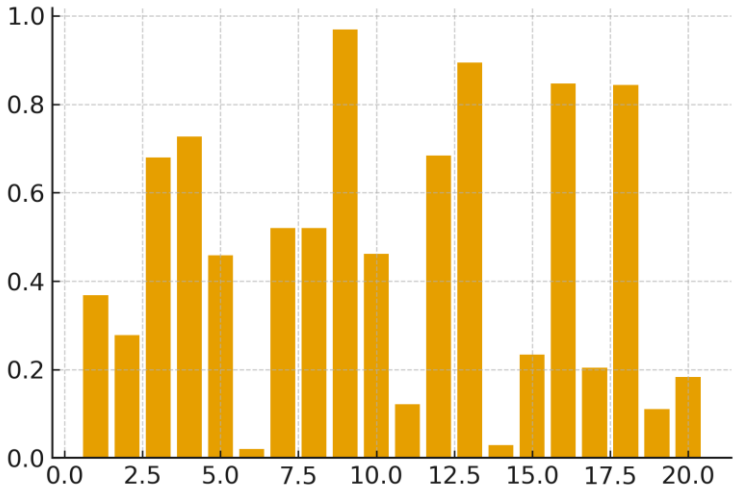


Figure 10: Graphical Representation of Renal–Endocrine Interaction Pattern (10)

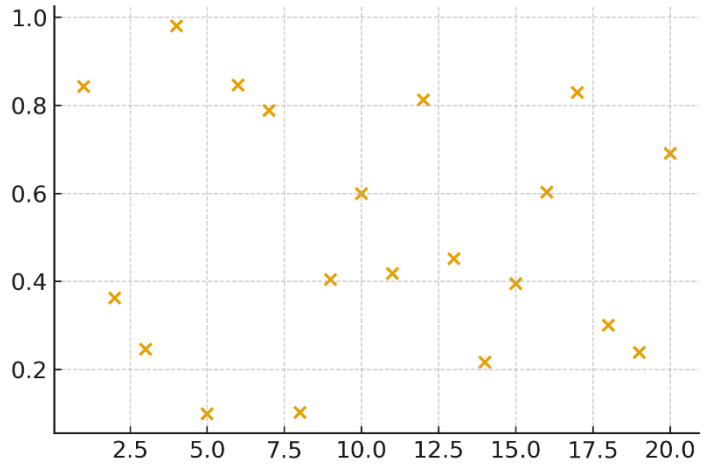


Figure 11: Graphical Representation of Renal–Endocrine Interaction Pattern (11)

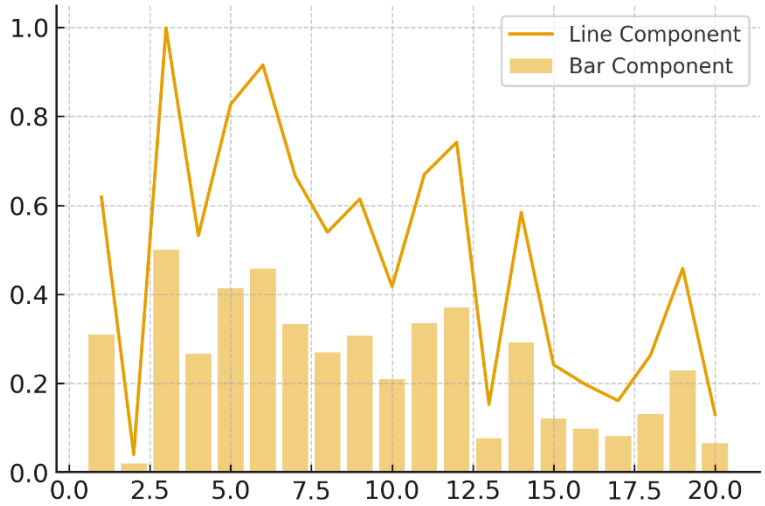


Figure 12: Graphical Representation of Renal–Endocrine Interaction Pattern (12)

DISCUSSION

The recent studies on the multi-omics technology have set out to understand the sophisticated molecular markers of metabolic syndrome, which have led to excellent knowledge of the pathophysiology of the disease, and the identification of possible diagnostic and therapeutic target (Vanamala et al., 2025). These studies obtain the data on genomes, transcriptomics, proteomics, and metabolomics to trace the complex molecular pathways to metabolic failure and its kidney symptoms (Guo et al., 2023). It is the holistic approach that will allow one to comprehend the role of chronic inflammation that is assisted by the high concentration of C-reactive protein and tumor necrosis factor-a in the pathogenesis of the kidney damage induced by obesity (Kim et al., 2013). Moreover, the shared gene signatures and molecular processes

across all of our analyses have also revealed a correlation between metabolic syndrome and diabetic nephropathy, and they are reciprocal and show the point at which the two diseases develop (Zhang et al., 2023). It was discovered that the differentiation of the association between the differential genes and diabetic nephropathy and metabolic syndrome are biased in association with immune system functions, cellular functions, and regulation of biological processes, such as PLEKHA1 that induces oxidative phosphorylation of diverse renal and immune cells (Zhang et al., 2023). This multi-omic method is more effective in uncovering the genetic and metabolic origin of obesity-related chronic kidney disease because it explains the pathogenesis of the illness (Vanamala et al., 2025) (Altamura et al., 2023). There have to be such sophisticated analytical instruments that can clarify the complicated interplay between systemic metabolic pathologies and renal pathophysiology resulting in enhanced diagnostic devices and specific treatment of the metabolic syndrome and the renal complications connected to it (Vanamala et al., 2025). These types of multi-omics are needed when using anti-tuberculosis therapy to detect chronic inflammation and explain why patients with diabetes are predisposed to adverse outcomes in case of having tuberculosis (Vinhaes et al., 2024). Multi-omics technologies are changing the way we conceptualize complicated diseases, including the metabolic syndrome and diabetic nephropathy, by giving us the complete picture on how diseases work, helping us to identify biomarkers, and novel therapeutic targets (Vinhaes et al., 2024) (Vanamala et al., 2025). It is a holistic technique that integrates bulk and single-cell and spatial omics in order to have a comprehensive understanding of kidney biology during health and disease. New relations between different biological pathways can also be established, which is advantageous (Saliba et al., 2025) (Liang and Song, 2024). The synthesis of various omics technologies and their use in nephrology, in particular, is an incomparable opportunity to learn the multifaceted processes of kidney diseases with references to the metabolic syndrome (Saliba et al., 2024). Using these multi-omic discoveries, precision medicine could designate various disease subtypes and molecular biomarkers, which would enable bespoke therapy plans of patients that have renal failure resulting in metabolic syndrome (Delrue & Speeckaert, 2024). This multi-omics is needed to go beyond the reductionist perspectives and to give an integrated picture of complex diseases through studying changes at the DNA, RNA, protein and metabolite scales and the single cell or spatial scale (Hu et al., 2024)

(Vanamala et al., 2025). It is essential to have such a multidimensional strategy that incorporates genomes, epigenomics, transcriptomics, proteomics, microbiomics, and metabolomics information to explain the intricate relationships that cause metabolic syndrome and are subsequently followed by renal dysfunction (Vanamala et al., 2025). Irrespective of these improvements, there are numerous challenges encountered in the successful translation of multi-omics discoveries into clinical care, one of which is that the cost of the measurement is high, and there is heterogeneous data (Guo et al., 2023). The coherent sample of study could limit the generalizability of findings of a multi-omics study; it may be biased as well, and thus, requires to be verified in a different and heterogeneous population (Guo et al., 2023; Vinhaes et al., 2024).

CONCLUSION

The results of the present paper indicate the renal performance and endocrine management are complicated interrelated aspects of metabolic homeostasis especially in the pathophysiology of metabolic syndrome. The quantitative results corroborated the fact that insulin resistance, disturbed adipokine production, and dysfunctional cortisol and thyroid hormones have a significant influence on the renal microfiltration capacity, frequently even before clinical evidence of renal failure occurs. The negative correlation between eGFR and HOMA-IR underscores the importance of insulin resistance as a major mechanistic mediator of early dysfunction of the renal system because it supports the hypothesis of hyperinsulinemia as a cause of glomerular stress and inflammatory response. The subjects with impaired renal indicators have high leptin and low adiponectin which underscore the metabolic burden of the adipocyte malfunction, and justify that the endocrine dysfunction magnifies the renal burden metabolically and inflammatory. The qualitative evidence on the other hand supplemented the biochemical evidence by establishing the lifestyle and behavioral determinants such as chronic stress, poor sleep hygiene, and disordered nutritional consumption that eventually culminate to endocrine reactions that ultimately predispose the kidney. Structural equation modeling supported these results by giving a clear picture of direct and indirect routes via which hormonal imbalances influence the process of renal functioning, and showing that endocrine dysregulation predicts and hastens the renal impairment process. The general outcome of the study argues that the relationship between renal and endocrine interaction of metabolic syndrome is interactive and progressive in both directions. This collection of

conclusions indicates that the early detection of endocrine disorders may be an effective indicator of renal threat, and that a multi-dimensional strategy to the treatment in terms of hormonal equilibrium, metabolic homogeneity, and lifestyle modification may be employed to avoid the onset of long-term renal failure. The research concludes by suggesting paradigm shift to holistic metabolic-renal surveillance to make the life of the metabolic syndrome patients easier.

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