

Association between the Life's Essential 8 Health Behaviors and Prognosis in Patients with Advanced Cardiovascular-Kidney-Metabolic Syndrome

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ABSTRACT

Background: Cardiovascular-Kidney-Metabolic (CKM) syndrome is a recently recognized multisystem condition that encompasses the coexistence of cardiovascular disease, chronic kidney disease, and metabolic dysfunction. Patients with advanced CKM syndrome experience poor prognosis, yet the impact of lifestyle and behavioral health factors on outcomes remains underexplored. The American Heart Association's Life's Essential 8 (LE8) offers a standardized framework to assess cardiovascular health behaviors and biological risk factors.

Objectives: To evaluate the association between LE8 health behaviors and prognosis in patients with advanced CKM syndrome, and to identify the individual components most predictive of adverse outcomes.

Methods: This prospective observational study was conducted at Evercare Hospital, Lahore, and Liaquat National Hospital, Karachi, between June 2022 and June 2023. A total of 120 patients with advanced CKM syndrome were enrolled. LE8 scores were calculated for each participant, and patients were categorized into low (0–49), intermediate (50–79), and high (80–100) cardiovascular health groups. The primary outcome was all-cause mortality at 12 months, while secondary outcomes included major adverse cardiovascular events (MACE), renal function decline ($\geq 30\%$ reduction in eGFR), and CKM-related hospitalizations.

Results: Of the 120 patients, 40 were categorized as low CVH, 48 as intermediate CVH, and 32 as high CVH. During the 12-month follow-up, mortality rates were significantly higher in the low CVH group (32.5%) compared to intermediate (14.6%) and high CVH groups (6.3%, $p=0.01$). The incidence of MACE (45.0% vs. 27.1% vs. 15.6%, $p=0.02$) and renal decline (40.0% vs. 27.1% vs. 15.6%, $p=0.04$) also followed this trend. Cox regression analysis identified poor blood pressure control, nicotine exposure, and poor sleep health as independent predictors of mortality.

Conclusion: Higher LE8 scores were strongly associated with improved survival, reduced cardiovascular events, slower renal decline, and fewer hospitalizations in patients with advanced CKM syndrome. Lifestyle modification and adherence to LE8 health behaviors, particularly blood pressure control, smoking cessation, and healthy sleep, should be prioritized alongside pharmacological management. LE8 scoring may serve as a practical clinical tool for risk stratification and patient counseling in CKM care.

Keywords: Life's Essential 8, cardiovascular-kidney-metabolic syndrome, prognosis, cardiovascular health, renal outcomes, lifestyle modification.

INTRODUCTION

Cardiovascular-Kidney-Metabolic (CKM) syndrome is an emerging construct that recognizes the complex and interconnected pathophysiology of cardiovascular disease (CVD), chronic kidney disease (CKD), and metabolic disorders, particularly type 2 diabetes mellitus and obesity¹. Individually, each of these conditions imposes a significant burden on global health; however, when they co-exist, they synergistically amplify morbidity, accelerate disease progression, and increase the risk of premature mortality. Patients with advanced CKM syndrome often present with recurrent hospitalizations, progressive renal impairment, major adverse cardiovascular events (MACE), and reduced quality of life, underscoring the urgent need for comprehensive strategies to improve prognosis^{2,3}.

Traditional management of CKM syndrome has largely emphasized pharmacological interventions and organ-specific treatments. While essential, this approach frequently overlooks modifiable lifestyle-related factors that contribute significantly to disease trajectory⁴. Accumulating evidence highlights the importance of behavioral and biological health determinants such as diet, physical activity, smoking, obesity, and blood pressure in shaping long-term outcomes among high-risk patients. To provide a standardized assessment of these domains, the American Heart Association (AHA) introduced the concept of Life's Essential 8 (LE8) in 2022⁵.

Life's Essential 8 is an expansion of the earlier —Life's Simple 7, II with the addition of sleep health as a new domain, reflecting the growing evidence linking poor sleep patterns to cardiovascular and metabolic dysfunction⁶. LE8 encompasses eight key components: diet quality, physical activity, nicotine exposure, sleep health, body mass index (BMI), blood lipids, blood glucose, and blood pressure. Each component is scored and combined into an overall cardiovascular health (CVH) score, ranging from poor to ideal. Higher LE8 scores have been consistently associated with lower incidence of CVD, reduced risk of CKD progression, improved metabolic control, and lower all-cause mortality in general populations^{7,8}.

However, data remain scarce on whether adherence to LE8 domains continues to influence prognosis in advanced CKM syndrome, a stage characterized by irreversible organ damage and increased vulnerability to adverse outcomes⁹. Given the global rise in CKM-related morbidity and the associated healthcare burden, it is crucial to investigate the prognostic utility of LE8 in this specific patient group. Identifying lifestyle behaviors that retain prognostic relevance despite advanced disease may help clinicians tailor interventions, stratify risk, and design comprehensive management strategies that extend beyond pharmacotherapy¹⁰.

This study therefore aims to evaluate the association between Life's Essential 8 health behaviors and prognosis in patients with advanced CKM syndrome. By analyzing the relationship between LE8 scores and clinical outcomes including mortality, major cardiovascular events, renal function decline, and hospitalizations this work seeks to provide insights into the

Received on 09-07-2023

Accepted on 18-09-2023

potential role of lifestyle behaviors as modifiable determinants of survival and disease progression in this high-risk population¹¹.

MATERIALS AND METHODS

Study Design and Setting: This study was designed as a prospective observational analysis conducted at two major tertiary care centers in Pakistan, namely Evercare Hospital, Lahore, and Liaquat National Hospital, Karachi. Both hospitals receive a large number of patients with combined cardiovascular, renal, and metabolic conditions, making them suitable sites for this research. The study was carried out over a period of twelve months, from June 2022 to June 2023.

Study Population and Sample Size: A total of 120 patients diagnosed with advanced Cardiovascular-Kidney-Metabolic (CKM) syndrome were enrolled consecutively during the study period. Advanced CKM syndrome was defined as the coexistence of established cardiovascular disease, metabolic dysfunction, and stage 3 or above chronic kidney disease. Patients were required to be 18 years of age or older and in stable clinical condition for at least four weeks prior to recruitment. Individuals with acute infections, sepsis, malignancy, prior renal transplantation, or those undergoing dialysis were excluded. Patients unable or unwilling to provide informed consent were also not included in the study.

Data Collection Procedures: Baseline data were obtained through structured clinical interviews, physical examination, and review of medical records. Demographic variables such as age, sex, and socioeconomic background were recorded along with relevant medical history and medication use. Anthropometric measurements including weight, height, body mass index (BMI), and waist circumference were documented. Vital signs were assessed at baseline, with particular attention to systolic and diastolic blood pressure. Laboratory investigations included fasting blood glucose, glycated hemoglobin (HbA1c), lipid profile, and serum creatinine, which was used to calculate the estimated glomerular filtration rate (eGFR).

Assessment of Life's Essential 8: Each participant was evaluated using the American Heart Association's Life's Essential 8 (LE8) scoring system, which provides a standardized measure of cardiovascular health. The eight domains assessed included diet quality, physical activity, nicotine exposure, sleep health, body mass index, blood lipids, blood glucose, and blood pressure. Each domain was scored on a scale ranging from 0 to 100, and an overall composite score was derived by averaging the individual component scores. Based on these results, patients were classified into three categories of cardiovascular health: low (0–49), intermediate (50–79), and high (80–100).

Outcome Measures: All patients were followed up for a period of twelve months to assess prognostic outcomes. The primary outcome of interest was all-cause mortality during the follow-up period. Secondary outcomes included the occurrence of major adverse cardiovascular events (MACE), hospitalization related to CKM complications, and renal function decline defined as a reduction of 30% or more from the baseline eGFR.

Ethical Considerations: The study protocol was reviewed and approved by the Institutional Review Boards of Evercare Hospital, Lahore, and Liaquat National Hospital, Karachi. All participants provided written informed consent prior to enrollment. The research was conducted in full compliance with the principles of the Declaration of Helsinki (2013 revision) to ensure ethical integrity.

Statistical Analysis: All statistical analyses were performed using SPSS version 26.0 (IBM Corp., Armonk, NY, USA). Continuous variables were summarized as mean values with standard deviation or as median with interquartile range depending on distribution, while categorical variables were presented as frequencies and percentages. Comparisons across the three LE8 score categories were carried out using analysis of variance (ANOVA) for continuous variables and the chi-square test for categorical variables. Kaplan–Meier survival curves were

constructed to evaluate differences in survival between groups, and the Cox proportional hazards model was employed to identify independent predictors of prognosis after adjusting for potential confounders such as age, sex, and comorbidities. A two-tailed p-value less than 0.05 was considered statistically significant.

RESULTS

Baseline Characteristics: A total of 120 patients with advanced CKM syndrome were enrolled in the study. The mean age of the cohort was 59.3 ± 10.7 years, with a predominance of males (68 patients, 56.7%) compared to females (52 patients, 43.3%). Patients were stratified into three groups based on Life's Essential 8 (LE8) cardiovascular health scores: low CVH ($n = 40$, 33.3%), intermediate CVH ($n = 48$, 40.0%), and high CVH ($n = 32$, 26.7%). Baseline clinical and laboratory variables are presented in Table 1.

Patients in the high LE8 score group tended to be younger, had lower body mass index, better blood pressure control, and more favorable lipid and glucose profiles compared to those in the low CVH category. Smoking exposure and poor sleep health were more frequently observed in the low CVH group.

Table 1. Baseline demographic and clinical characteristics according to LE8 score categories

Variable	Low CVH (n=40)	Intermediate CVH (n=48)	High CVH (n=32)	p-value
Age, years (mean \pm SD)	62.4 \pm 9.1	59.8 \pm 10.5	55.6 \pm 11.0	0.04
Male sex, n (%)	25 (62.5)	26 (54.2)	17 (53.1)	0.61
BMI, kg/m ² (mean \pm SD)	30.1 \pm 4.8	28.6 \pm 4.2	26.9 \pm 3.9	0.02
Systolic BP, mmHg (mean \pm SD)	148 \pm 18	139 \pm 16	128 \pm 14	<0.01
HbA1c, % (mean \pm SD)	8.5 \pm 1.1	7.9 \pm 1.0	7.1 \pm 0.9	<0.01
eGFR, mL/min/1.73m ² (mean \pm SD)	41.5 \pm 8.9	44.3 \pm 9.2	46.9 \pm 7.6	0.05
Nicotine exposure, n (%)	18 (45.0)	14 (29.2)	6 (18.8)	0.03
Poor sleep (<6 hrs), n (%)	22 (55.0)	19 (39.6)	9 (28.1)	0.04

Prognostic Outcomes: During the 12-month follow-up, a total of 22 deaths (18.3%) occurred across the study cohort. Mortality was highest in the low CVH group (13 deaths, 32.5%) compared with the intermediate (7 deaths, 14.6%) and high CVH groups (2 deaths, 6.3%, $p=0.01$). Major adverse cardiovascular events (MACE) were also more frequent among patients with lower LE8 scores, occurring in 45.0% of the low CVH group, 27.1% of the intermediate group, and only 15.6% of the high CVH group ($p=0.02$).

Renal outcomes demonstrated a similar trend. A $\geq 30\%$ decline in eGFR occurred in 40.0% of low CVH patients, 27.1% of intermediate CVH patients, and 15.6% of high CVH patients ($p=0.04$). Hospitalization rates followed the same pattern, with the low CVH group requiring the most frequent admissions for CKM-related complications as shown in table 2.

Table 2. Prognostic outcomes across LE8 score categories

Outcome	Low CVH (n=40)	Intermediate CVH (n=48)	High CVH (n=32)	p-value
All-cause mortality, n (%)	13 (32.5)	7 (14.6)	2 (6.3)	0.01
MACE, n (%)	18 (45.0)	13 (27.1)	5 (15.6)	0.02
$\geq 30\%$ decline in eGFR, n (%)	16 (40.0)	13 (27.1)	5 (15.6)	0.04
≥ 1 hospitalization, n (%)	24 (60.0)	20 (41.7)	9 (28.1)	0.03

Survival Analysis and Predictors: Kaplan–Meier survival analysis demonstrated significantly better survival in patients with

higher LE8 scores (log-rank test, $p=0.008$). Cox regression analysis further confirmed that low LE8 scores were independently associated with higher mortality risk (HR: 2.8; 95% CI: 1.3–5.7, $p=0.01$). Among the individual LE8 domains, blood pressure control, smoking abstinence, and adequate sleep health were the strongest predictors of improved survival as shown in table 3.

Table 3. Cox proportional hazards regression analysis for predictors of mortality

Variable	Hazard Ratio (HR)	95% CI	p-value
Low vs High LE8 score	2.8	1.3–5.7	0.01
Age ≥ 65 years	1.6	0.9–3.0	0.08
Poor blood pressure control	2.4	1.2–4.6	0.01
Nicotine exposure	2.1	1.1–4.0	0.02
Poor sleep health	1.9	1.0–3.7	0.04

Overall, the results of this study demonstrate a clear relationship between Life's Essential 8 scores and prognosis in advanced CKM syndrome. Patients with higher LE8 scores experienced fewer adverse outcomes, including lower mortality, reduced incidence of MACE, slower decline in renal function, and fewer hospitalizations. Importantly, behavioral domains such as nicotine abstinence and sleep quality emerged as equally important as biological risk factors in determining patient prognosis.

DISCUSSION

The present study demonstrates a significant association between Life's Essential 8 (LE8) health behaviors and prognosis in patients with advanced Cardiovascular-Kidney-Metabolic (CKM) syndrome⁹. Patients with higher LE8 scores experienced lower mortality, reduced incidence of major adverse cardiovascular events (MACE), slower decline in renal function, and fewer hospitalizations compared with those who had low scores. These findings highlight the importance of lifestyle and behavioral determinants even in advanced stages of multisystem disease where traditional pharmacological therapy often dominates clinical management¹⁰.

Our results are consistent with prior population-based studies where higher LE8 scores have been linked to improved cardiovascular health, reduced all-cause mortality, and better metabolic outcomes¹¹. However, this study extends the evidence to a more complex patient population with overlapping cardiovascular, renal, and metabolic dysfunction. The observation that blood pressure control, nicotine abstinence, and sleep health emerged as strong independent predictors of survival underlines the multidimensional nature of CKM syndrome, where modifiable lifestyle factors play a critical role alongside medical therapy^{12,13}.

The inclusion of sleep health as a domain in LE8 proved to be particularly relevant in this study. Poor sleep quality and short duration were associated with adverse prognosis, which aligns with growing evidence that sleep disturbances contribute to sympathetic overactivity, metabolic dysregulation, and progression of CKD. Similarly, the burden of smoking and uncontrolled hypertension on cardiovascular and renal outcomes reinforces the need for aggressive risk factor modification in this high-risk group^{14,15}.

Importantly, our findings indicate that lifestyle interventions may yield measurable benefits even in advanced disease states¹⁶. While pharmacological management remains indispensable, incorporating structured lifestyle programs—such as dietary counseling, smoking cessation support, physical activity promotion, and sleep hygiene education—can potentially modify disease trajectory. This holistic approach resonates with the integrative framework of CKM syndrome proposed by recent guidelines, which advocate for early and sustained lifestyle modification as part of comprehensive care^{17,18}.

Nevertheless, this study has limitations. The sample size was modest, and recruitment was limited to two tertiary care

centers in Pakistan, which may limit generalizability. The follow-up period of 12 months, though sufficient to capture meaningful outcomes, may not reflect long-term survival trends¹⁹. In addition, lifestyle behaviors were partly assessed using self-reported questionnaires, which may be subject to recall bias. Despite these limitations, the study provides robust evidence that LE8 scores retain prognostic relevance in advanced CKM syndrome and offers practical insights for clinical application^{20,21}.

CONCLUSION

In conclusion, this study highlights that adherence to Life's Essential 8 health behaviors is strongly associated with improved prognosis in patients with advanced CKM syndrome. Higher LE8 scores were linked to lower mortality, fewer cardiovascular events, slower renal decline, and reduced hospitalization rates. Among the individual domains, blood pressure control, smoking abstinence, and adequate sleep health were particularly important predictors of favorable outcomes. These findings underscore the necessity of integrating structured lifestyle modification strategies into the routine care of patients with CKM syndrome, even at advanced stages of disease. Life's Essential 8 scoring can serve as a practical clinical tool for risk stratification and patient counseling, providing a bridge between evidence-based lifestyle medicine and conventional therapeutic approaches. Future research with larger, multi-center cohorts and longer follow-up periods is warranted to further validate these findings and to explore targeted interventions that improve LE8 scores in this high-risk population.

Conflict of Interest: The authors declare that they have no conflict of interest.

Ethical Approval: This study was approved by the Institutional Review Boards of Evercare Hospital, Lahore, and Liaquat National Hospital, Karachi. Written informed consent was obtained from all participants.

Authors' Contributions

- MAM: Conceptualization, study design, manuscript drafting.
- MSS: Data collection, literature review, critical revision.
- II: Methodology, statistical analysis, interpretation of results.
- MAK: Laboratory analysis, data interpretation, manuscript editing.
- ARH: Patient recruitment, clinical supervision, critical input in discussion.
- SNZ: Data acquisition, proofreading, formatting, final approval of manuscript.

Acknowledgements: The authors would like to thank the staff of Evercare Hospital, Lahore, and Liaquat National Hospital, Karachi, for their assistance in patient management and data collection.

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This article may be cited as: Maqsood MA, Saleem MS, Ilahi I, Khan MA, Hammad AR, Zehra SN; Association between the Life's Essential 8 Health Behaviors and Prognosis in Patients with Advanced Cardiovascular-Kidney-Metabolic Syndrome. *Pak J Med Health Sci.* 2023; 17(10): 355-358.