



# Intermittent fasting in Ramadan in patients on maintenance hemodialysis: Relation to malnutrition, inflammation, body composition and quality of life

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**Objective:** Many previous studies suggest that intermittent fasting has beneficial effects on health. Fasting during the month of Ramadan can be considered as a model of intermittent fasting among Muslims. The present study aimed to assess the effect of Ramadan fasting on quality of life (QOL) and body composition in hemodialysis (HD) patients.

**Material & methods:** Sixty-eight patients on maintenance HD for more than six months in Mansoura Nephrology and Dialysis Unit (MNDU) were included in this prospective observational study. Patients' nutritional status was assessed by malnutrition inflammation score (MIS). Anthropometric measurements including body weight, height, mid arm circumference (MAC), and triceps skin fold thickness (TSF) were measured. Body composition was assessed by bioelectrical impedance. Quality of life was assessed by using the Kidney Disease Quality of Life-36 (KDQOL-36™). Assessment of all patients was carried out before the start of Ramadan and repeated 3 weeks after Ramadan in patients who fasted more than 14 days.

**Results:** Forty-five patients (66%) fasted more than 14 days during the month of Ramadan. Insignificant weight gain was observed in patients who fasted after Ramadan. Interestingly, visceral fat was significantly reduced after Ramadan ( $p < 0.0001$ ). MIS score improved with lower score estimated after Ramadan; however, the difference was insignificant ( $p = 0.059$ ). Also, mental health component of QOL improved after Ramadan.

**Conclusion:** Fasting in Ramadan in HD patients was associated improvement of the metabolic profile evident by decrease in visceral fat. Ramadan fasting had a positive effect on mental wellbeing. The effect of intermittent fasting on inflammation and nutritional parameters in patients on maintenance hemodialysis needs further investigations.

**Keywords:** Ramadan fasting, nutrition, inflammation, quality of life, hemodialysis, chronic kidney disease.

## Introduction

Intermittent fasting can be considered as an alternative to daily caloric restriction for individuals who are interested in improving body composition and overall health in addition to reduce body weight and body fat. [1]

Ramadan is the 9th month of the Islamic lunar calendar during which all healthy adult Muslims are required to abstain from eating any food and drinks from dawn to sunset, with exclusions of severely ill peo-

ple, menstruating females, pre-pubertal children, and travelers. The fasting hours can vary from 12 to 17 hours, relying on the seasonal and regional features. [2] Fasting during the month of Ramadan can be considered as a model of intermittent fasting among Muslims.

In the randomized crossover trial of intermittent fasting aiming to examine the effect of changing eating frequency without caloric restriction subjects were allowed to eat only for 4 hours in the evening. Stote

and colleagues reported that body weight and fat mass were reduced with non-significant increase in fat-free mass. The authors concluded that intermittent fasting protocol could lead to a concomitant decrease in fat mass and increase in fat-free mass, it would be a beneficial and appealing dietary strategy to many individuals. [3] The impact of Ramadan fasting on physiological and biomedical markers among healthy people has been broadly studied. Research evidence suggests that Ramadan fasting is tolerable and safe for healthy adults. [4-7]

Although Islam allows ill people and those with significant health problems not to fast, [8] many patients still desire to fast during Ramadan. Several studies have examined the effect of Ramadan fasting on several markers in patients with kidney diseases. Ramadan fasting was not associated with significant adverse effects in kidney transplant patients after one year of kidney transplantation, [9] or patients with recurrent urinary stone formation. [10] However, research findings on the safety of Ramadan fasting by patients with chronic kidney disease (CKD) on maintenance hemodialysis (HD) are mixed and controversial. [11, 12] Some studies have reported that Ramadan fasting was associated with significant changes in clinical and biomedical markers, such as fluid overload and hyperkalemia, but with no significant complications requiring hospitalization. [13, 14] Other studies found no clinically important variations in medical parameters in HD patients during Ramadan fasting. [15, 16]

End stage renal disease (ESRD) is a chronic disease that exerts a great negative impact on patients' health-related quality of life (QOL) mainly due to the accompanied impairment or to the imposed limitations in almost all domains of their daily lives. [17]

To the best of our knowledge, no studies had specifically examined the effect of fasting Ramadan, as a religious form of intermittent fasting, on nutritional and body composition parameters as well as QOL in HD patients. Therefore, this study was carried out to explore the effects of Ramadan fasting on these parameters in this special category of patients. It is hypothesized that fasting in Ramadan may have beneficial effects on nutritional and inflammatory parameters of HD patients.

## Material & Methods

This prospective observational study was conducted in our unit. The study was performed in Ramadan 1440 Hijri when the fasting hours ranged from 15 to 16 hours. All patients on maintenance HD for more than six months in the unit were observed for their fasting pattern without interference from the authors and without any instruction about caloric restriction. Patients who were pregnant or lactating, or had an active infection, malignancy or evidence of heart or liver disease were excluded from the study. All patients were subjected to full history taking, including hemodialysis duration, educational and occupational status. All assessments were carried out before the start of Ramadan and repeated 3 weeks after Ramadan in patients who fasted more than 14 days.

**Anthropometric measurements:** Post dialysis body weight (kg), and height (m) of all patients were measured and body mass index (BMI) was calculated. Mid upper arm circumference (MAC) was measured in centimeters (cm) twice using a flexible, inelastic measuring tape in the non-arteriovenous fistula arm, just at the mid-point of upper arm (i.e. between the acromion process of scapula and the olecranon process of ulna), in sitting position, and the average was recorded. [18] Triceps skin fold (TSF) thickness was measured in millimeters (mm) twice using skin fold caliper at the mid-point of back of upper arm, as mentioned above, by taking a fold of skin away from muscle while the patient standing upright, with arms hanging down loosely [19] then mid arm muscle circumference (MAMC) was calculated in cm by the formula:  $MAMC = MAC - ([TSF/10] \times \pi)$ . [18]

**Body composition measurement:** Bioelectrical impedance analysis (BIA) was carried out using Tanita body composition monitor BC-601FS (TANITA Corporation, Maeno-Cho, Itabashi-ku, Tokyo, Japan) after a hemodialysis session to obtain the percentage of total body water (TBW) and total body fat, as well as the fat free mass in Kg and visceral fat rating.

**Malnutrition inflammation score (MIS):** MIS is composed of ten components, categorized in four sections—medical history (change in dry weight, dietary intake, gastrointestinal symptoms, functional capacity, and comorbidity), physical examination, body mass index (BMI), and laboratory values. Each MIS component has four levels of severity from 0 (normal) to 3 (very severe). The sum of all 10 components results in an overall score ranging from 0 (normal) to 30 (severely malnourished). [20]

**Assessment of QOL:** Assessment of QOL was performed by using the Kidney Disease Quality of Life-36 (KDQOL-36™). The first version contained the Medical Outcomes Study 36 (MOS SF-36) as a generic chronic disease core, in addition to items related to patients with kidney disease. It had 36 questions; mental health composite (MHC) and physical health composite (PHC), burden of kidney disease, symptom/problem list and effect of kidney disease components of QOL were obtained from questions 1-12, 1-12, 13-16, 17-28 and 29-36 respectively. The average scores of these five components of KDQOL-36 were ranged from 0-100 with higher scores indicating better health-related QOL. [21]

**Statistical analysis:** The collected data were recorded, coded, tabulated and analyzed for statistical purposes by utilizing the Statistical Package for Social Science (SPSS) version 25 for Windows on personal computers. Qualitative variables were described as percentages and numbers, and after testing normality by the Kolmogorov-Smirnov test, normally distributed quantitative variables were described as means [ $\pm$  standard deviation (SD)], while non-parametric variables were reported as medians (interquartile range; IQR). For paired comparison, paired t test and Wilcoxon test were used for parametric and non-parametric variables respectively. P value  $\leq 0.05$  was statistically significant.

## Results

Forty-five patients (66%) of HD patients fasted more than 14 days during the month of Ramadan. Demographic and clinical data of the patients are shown in table 1. The mean age of the patients was 47.33±14.86 years with a median HD duration of 35 months. The mean fasting days was 17.84 with SD 4.36. More than three quarters (84.4%) of the patients were hypertensive. One third of patients lived in urban regions, while the other two thirds lived in rural regions. Only 8 patients were employed, and 35 patients were educated.

Patients who fasted Ramadan were overweight (BMI: 28.7±6.06 kg/m<sup>2</sup>) with a mean total fat percentage of 29.4%. The median score of MIS was 3. Non-significant increase in BMI was observed after Ramadan (p value 0.073). MAC, TSE, MAMC, FFM, and TBW percentage were not affected by Ramadan fasting. Both total fat percentage and visceral fat rating were reduced after Ramadan fasting, but this reduction was significant for latter only (p <0.0001). The MIS value was not affected by fasting (Table 2).

Regarding QOL, the MHC domain of QOL improved after Ramadan (p=0.057). However, none of the five domains of health related QOL showed significant change in the HD patients after Ramadan fasting (Table 2).

## Discussion

Intermittent fasting is a broad term that encompasses a variety of programs that manipulate the timing of eating occasions by utilizing short-term fasts in order to improve body compo-

**Table 1.** Demographic and medical history of fasted group.

Parameter	Fasting group n=45 (%)
Age of at diagnosis	47.33 ± 14.86 years
Gender	
Male	21 (46.7%)
Female	24 (53.3%)
Duration of HD (months)	35 (14.5–74.5)
Fasting days, mean ± SD	17.84 ± 4.36
Diabetes milletus	
Yes	5 (11.1%)
No	40 (88.9%)
Hypertension	
Yes	38 (84.4%)
No	7 (15.6%)
Residence	
Urban	15 (33.3%)
Rural	30 (66.7%)
Occupation	
Employed	8 (17.8%)
Unemployed	37 (82.2%)
Education	
Illiterate	10 (22.2%)
Educated	35 (77.8%)
Marital status	
Married	30 (66.7%)
Unmarried	15 (33.3%)

**Table 2.** Anthropometric measures and QOL of fasting group before and after Ramadan fasting.

Parameter	Before Ramadan	After Ramadan	P value
Body mass index (Kg/m <sup>2</sup> ), mean ± SD	28.7±6.06	29.04±6.09	0.073
Mid-arm circumference (cm), mean ± SD	30.9±5.25	30.8±5.33	0.69
Triceps skin fold thickness (mm), median (Q1-Q3)	14 (12–21.5)	14 (10–20)	0.41
Mid-arm muscle circumference (cm), mean ± SD	25.5±3.08	25.6±3.11	0.84
Total fat percentage, mean ± SD	29.4±10.96	28.2±10.64	0.36
Fat free mass (kg), mean ± SD	51.48±9.2	52.48±9.4	0.228
Total body water percentage, mean ± SD	51.8±8.74	52.7±8.65	0.45
Visceral fat rating, median (Q1-Q3)	7 (4–10)	4 (2–8.5)	<0.0001
Malnutrition inflammation score, median (Q1-Q3)	3 (2–5.5)	3 (2–5)	0.059
Symptom/problem list, median (Q1-Q3)	77.1 (70.8–89.5)	81.2 (69.7–91.6)	0.800
Effect of kidney disease, median (Q1-Q3)	75 (56.2–89.0)	81.2 (64–90.6)	0.150
Burden of kidney disease, median (Q1-Q3)	50 (28.1–75)	50 (25–75)	0.180
Physical health composite, median (Q1-Q3)	41 (30.7–45.9)	36 (29.3–48)	0.490
Mental health composite, median (Q1-Q3)	47.25 (39.5–57.5)	51.7 (43.6–60.8)	0.057

sition and overall health. [1] Time-restricted feeding protocols involve adhering to a daily routine that requires fasting for a certain number of hours and feeding for the remaining hours in a 24-hour period. [22] Many previous studies suggest that intermittent fasting has beneficial effects on health. [23-25] Ramadan fasting is one of the five pillars of Islam and is obligatory for all healthy adults. Although chronic HD patients are exempt from Ramadan fasting, many of them insist to fast. Safety of Ramadan fasting in chronic HD patients is debatable. Evidence is lacking as regard the effect of Ramadan fasting as a model of intermittent fasting on body composition and nutritional parameters HD patients. Therefore, this study aimed to assess the effect of Ramadan fasting on nutritional parameters and body composition as well as QOL in a group of HD patients in a single HD center.

Forty-five patients (66%), out of 68 patients, in our center fasted more than 14 days in Ramadan. The Frequency of fasting Ramadan in HD patients reported in previous studies is variable. Adnan et al [16] stated that 89% of patients in three HD centers in Malaysia fasted in Ramadan. In Pakistan, the frequency of fasting in Ramadan was 13.5% as reported by Imtiaz and his coworkers. [15] In another study conducted in Saudi Arabia, 64.1% out of the included 635 HD patients fasted. [26] In a recent study conducted in Egypt, 46.96% of the included 2055 Muslim HD population in 27 HD centers fasted at least few days of Ramadan. [27] This difference may be due to different demographic characteristics of the investigated HD patients. Furthermore, Megahed et al, stated that the absence of specific guidelines advocating or prohibiting fasting in this special situation makes fasting in HD population an individual decision that mirrors patients' own motivation and capability. [27]

Mean patients BMI in the current study was  $28.7 \pm 6.06$  kg/m<sup>2</sup>. This may explain the high frequency of fasting in our HD center. Although fasting in Ramadan is expected to be associated with weight loss due to decrease in meals frequency and caloric intake, the BMI was insignificantly increased after Ramadan in the studied HD patients. Al Wakeel, Imtiaz et al and Adnan et al studies also reported non-significant change in dry body weight after Ramadan fasting. [13, 15, 16]

Although BMI is considered as a key nutritional assessment tool in patients with CKD, [28] it cannot represent the real nutritional status in HD patients. [29] Skinfold thickness and percentage of body fat have been reasonably well validated against established gold standards and provide estimates of fat mass superior to BMI in CKD patients. [30] In the current study, TSF as well as total fat percentage showed non-significant change after Ramadan fasting. Interestingly, visceral fat rating decreased significantly after Ramadan fasting.

Visceral adipose tissue is found mainly in the mesentery and omentum and has been described to be more metabolically active, more sensitive to lipolysis, and more insulin-resistant compared to subcutaneous fat. Further, visceral adipose tissue is more cellular, vascular, and innervated, and it contains a larger number of inflammatory and immune cells as compared to subcutaneous fat. Also, it has a greater capacity than subcutaneous fat to generate free fatty acids and to take up glucose. [31-37] Epidemiologic and clinical studies over the past 30 years have

clearly demonstrated a strong link between visceral fat and the development of clinical syndrome characterized by atherogenic dyslipidemia, hyperinsulinemia/glucose intolerance, hypertension, atherosclerosis, and adverse cardiac remodeling/heart failure. [38] Abdominal obesity underlies a high risk of all-cause and cardiovascular mortality in patients with end stage renal disease. [39] This decrease in visceral fat rating observed after fasting in the studied HD patients denotes improvement in metabolic profile and suggest a possible protection of intermittent fasting from cardiovascular diseases in hemodialysis.

Degaldo and his coworkers in 2017 performed linear regression analyses to examine the extent to which proxies of visceral and subcutaneous fat were associated with inflammation, nutrition, and adiposity-related hormones in HD patients. They concluded that proxies of visceral and subcutaneous fat appear to have opposing associations with biomarkers of inflammation and nutrition. Subcutaneous fat may be an indicator of nutritional status, and visceral fat, an indicator of inflammation. [40] According to the results of the current study, MIS showed non-significant decrease after fasting ( $p=0.056$ ). Although it is difficult to draw a clear conclusion about the effect of short-term intermittent fasting in HD patient on inflammation, it is evident that Ramadan fasting does not adversely affect nutritional status in the studied cohort. More investigations are needed to explore the extent to which visceral fat loss after intermittent fasting affect markers of nutrition and inflammation in patients on HD.

Fasting was not associated with muscle mass loss. Anthropometric measures (MAC and MAMC) as well as fat free mass showed no significant change after Ramadan fasting. The preservation of muscle mass is very important in HD patients as it is related to lower all-cause mortality, [41] and improved muscle function. [42] In the current study, fasting was not associated with muscle mass loss. MAC and MAMC as well as fat free mass did not change significantly after Ramadan fasting; a finding that matches the results of a Malaysian multicenter, prospective observational study of 87 HD patients. However, they observed improved muscle function, assessed by hand grip strength (HGS). They explained that the improvement in HGS, despite no change in muscle mass, may be due to the increased physical activity induced by performing extended hours of praying after the sunset. [43]

Fasting the month of Ramadan is a very special type of worship associated with many spiritual benefits. Mental health composite of QOL in the studied HD patients improved after Ramadan ( $p=0.057$ ). The positive outcome of Ramadan fasting on mental wellbeing may be related to the fact that fasting discipline soul and moral behavior. During the blessed month, there is increase sense of gratitude and social relationships.

Finally, we admit that this study has some limitations; namely, the small sample size and the single-center nature of the study. Furthermore, it would be better to assess more biochemical, inflammatory, and nutritional parameters. However, detailed assessment of the effect of Ramadan fasting on the body composition in HD patients is considered one of the strengths of this study.

## Conclusion

In conclusion, fasting Ramadan in a cohort of Egyptian HD patients was not associated with detrimental effects on the studied nutritional, inflammatory and anthropometric parameters. Moreover, it may be associated with an advantageous effect on the metabolic profile. However, more studies including a larger number of HD patients from multiple center and assessing more biochemical, inflammatory, and nutritional biomarkers are needed.

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