

REVIEW ARTICLE

# Body Mass Index Paradox in Hemodialysis Patients: A Review

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## ABSTRACT

Among population, the higher the body mass index (BMI), it would increase the risk of chronic illness and as a result, the risk of mortality. But this does not happen in the population of hemodialysis patients, so the risk of mortality decreases with increasing BMI. This paradox is attributed to a variety of factors including blood pressure, inflammation, and muscular mass; that is, in moderate hemodialysis patients, the blood pressure would be higher and therefore, its control would be less. In addition, the higher the BMI, the greater would be the muscular mass in these patients which is likely to increase the survival of them. Patients with a higher BMI would also experience more nutritional reserves and therefore their tolerance for inflammation would be higher. Although an increase in BMI reduces the risk of mortality in these patients, an increase in muscular mass would be better than an increase in body fat mass.

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## Introduction

End Stage Renal Disease (ESRD) occurs when the kidneys lose their ability to dispose and discharge waste materials, balance the water and electrolytes, and produce some hormones. ESRD can be caused for a variety of reasons. Usually 90% of patients who reach the ESRD stage have chronic diabetes mellitus, and chronic hypertension or glomerulonephritis. When kidney failure progresses, the levels of the waste material that moves in the body and the blood circulation would increase resulting into symptoms like uremia. When the patient reaches from chronic kidney disease stage 4 (CKD4) to CKD5 stage, choices for treatment include dialysis, kidney transplantation, and drug treatment (1).

## ESRD Outbreak

The number of patients with ESRD who start treatment annually was shown to have an increasing trend up to 130% from 2000 to 2006. Between 1997 and 2006, the number of new cases of diabetes-related ESRD has been doubled and it has risen from 16% in 1997 to 31% in 2006. It also affected men more than women (2). In a study in Iran in 2004, it was estimated that about 700,000 people suffered from CKD and 61,000 were predicted to be as new CKD cases (3). In December 2005 in Tehran, in a study of 2,630 patients, the prevalence and incidence of hemodialysis patients was 194.8 and 77.3, respectively, and the main causes of ESRD in these patients were diabetes and hypertension (4).

In a study in the United States in 2006, about

30 million people were diagnosed with CKD, and it was estimated that by 2010 more than 600,000 people needed kidney transplantation. Also, in India, the population has exceeded a billion people, and it is a reservoir of chronic diseases, including diabetes and hypertension that leads to CKD. As a result, it is estimated that approximately 25-40% of these patients would suffer from CKD. So, the ESRD burden is increasing and requires a health care program (5). Many factors affect the death of hemodialysis patients, including cardiovascular diseases, malnutrition, and inflammation (6, 7). In hemodialysis subjects, weight and BMI were mentioned as important factors. Basically, a low BMI and its associated parameters represent malnutrition and is an important prognosis for mortality in hemodialysis patients.

#### *The Relationship between BMI and Mortality in Normal Population*

In the normal population, high BMI is associated with an increased risk of chronic illnesses, such as cardiovascular diseases and renal failure, and ultimately increase mortality (8, 9).

#### *The Relationship between BMI and Mortality in Hemodialysis Patients*

Although obesity is a risk factor for CKD, many epidemiological studies have observed that there is an inverse relationship between obesity and other risk factors for CKD and mortality in patients with CKD (10, 11). In this regard, Fleischmann *et al.* for the first time observed that mortality rate among obese and overweight patients, (BMI>27.5) were significantly lower than those who had normal weight (BMI between 20 and 27.5) or thin patients (BMI less than 20). The data also indicated that for each unit the BMI is added, the risk factor (relative risk) for death is reduced by 10%. In connection with the reduction of mortality, overweight people had significantly higher levels of nutritional markers and, at the same time, had the lowest hospitalization rates. Additionally, underweight patients were hospitalized for longer periods of time (12).

Some studies indicated that there was an inverse relationship between the prevalence of hypertension and its poor control and the BMI. That is, the higher the BMI, the lower the prevalence of hypertension would be and its poor control. In contrast to the normal population, hemodialysis patients who are obese tend to have a lower blood pressure (13). The higher prevalence of hypertension and its poor control in thinner hemodialysis patients may be due to different reasons. For example, obese patients can emit large volumes of extracellular fluid better, so

they will not get hypertension. In addition, increased muscle mass can be associated with increased expression of the reninase enzymes (Because the higher the BMI, the more it can be an indicator of the muscle mass) (14).

Reninase is a metabolizing enzyme of catecholamines that is expressed in skeletal muscle and can reduce the level of catecholamines in the blood. Therefore, this can be associated with a lower prevalence of hypertension and better control of it (14). In 2011, a cohort study was conducted on 368 hemodialysis over 2 years and their BMI and blood pressure were measured showing that the mortality risk increased in patients with lower BMI. Also, in thinner patients, the prevalence of hypertension and its poor control and the volume of extracellular fluids were higher (8).

Some studies associated this paradox with the lack of muscular mass. To determine and estimate the muscular mass, the amount of creatinine serum was assessed (8, 15). For information and estimation of muscular mass, serum creatinine was evaluated (8, 15). These studies concluded that increased BMI and creatinine levels were less predictive for mortality. On the other hand, weight loss and lower serum creatinine levels were both associated with an increased risk of mortality and increased creatinine alone was associated with a reduction in mortality. Kalantarzadeh *et al.* conducted a cohort study on 121762 patients from the population of hemodialysis patients in which the association between mortality and dry weight and the changes of creatinine serum were determined and the patients were followed up for 5 years. They found a decrease in BMI, and muscular mass and weight loss, and a decrease in creatinine serum level were associated with an increase in mortality rate. Among patients who had inconsistent changes, those patients whose weight was reduced and their creatinine serum increased had less mortality in comparison to those whose weight increased and their creatinine decreased (11).

#### *Inflammation Role in BMI Paradox*

Although chronic inflammation is a common complication of uremia, the relationship with a high BMI has never been investigated. It was shown that in absence of inflammation, the inverse relationship between BMI and mortality in hemodialysis patients is significantly eliminated. Also, in patients with non-cardiovascular disease, the high BMI as a protective effect would be greater than patients with cardiovascular disease (12).

Some mechanisms explain why a high BMI plays a more effective role in patients with inflammation. Although a high BMI is associated with loss of

muscular tissue, it can be a sign of energy store and good appetite for the patients. Another point is that the production of uremic toxins is usually higher in subjects with less weight. In addition, endothelial cell density is associated with obesity, and it is likely that the internal restoration mechanism in these individuals would be better (16).

In this regard, a cohort study was conducted in which the association between BMI and mortality in 5904 hemodialysis patients with inflammation was investigated for more than 3 months. The mortality was higher in patients without inflammation and with a lower BMI, and no protective effect was observed in people without inflammation but with a high BMI. On the contrary, higher BMI was associated with a reduced mortality in patients with inflammation. Therefore, despite the high impact of BMI on patients with inflammation, these effects were far lower in patients without inflammation (17).

### Conclusion

This study suggests that there is a higher prevalence of hypertension in underweight patients who undergo dialysis. Also, underweight individuals who have a low BMI will suffer from less muscle mass and would have higher mortality rates. It can be concluded that in hemodialysis patients who are more obese and have a high BMI, the mortality rate would be lower, even we must try to prevent the progression of cardiovascular disease and muscular loss in these patients.

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### Conflict of Interest

None declared.

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