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## Prevalence, Associating factors and Impact of fatigue-- A Systematic critical review on maintenance Hemodialysis patients

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### Abstract

End stage renal disease patients need to undergo hemodialysis lifelong to prolong their survival. Fatigue is the commonest and multifactorial problem among patients on hemodialysis. There are many factors leading to physical and mental fatigue among patients on hemodialysis which has a detrimental effect on their day-to-day activities and health related quality of life. This critical review is aimed at exploring the prevalence, the associating factors, and the impact of fatigue on health-related quality of life of patients undergoing hemodialysis. Online databases such as PubMed index, Web of science, PsycINFO, CINAHL, Google Scholar, etc., were scrutinised to get the full text articles. The prevalence of fatigue is high among patients on hemodialysis and estimated to be between 41% to 83.8%. Existing studies have listed out the several factors associated with fatigue into different aspects such as Physiological factors, Psychological factors, Social factors, Dialysis/ Disease related factors, Changes in Biochemical Parameters. Ageing, comorbidities, feminine gender, poor sleep quality are the common associating factors of fatigue. Depression and anxiety are also more frequently associated with fatigue. High prevalence of fatigue impairs the daily activities of the patients and leading to decreased working capacity, restricted functioning, mood instability, sleep disturbances, impaired family and social functioning. These consequences decrease the health-related quality of life and increases the morbidity and mortality of the patients on hemodialysis. Therefore, this critical review helps to expand the knowledge of the health care professionals to assess, identify and intervene the fatigue as early as possible.

### Keywords

**Fatigue, Hemodialysis, End stage renal disease, Systematic Review**

## INTRODUCTION

End stage renal disease (ESRD) is a debilitating illness with a deteriorating renal function. Hemodialysis is the main life supporting treatment option for ESRD patients. A report by Global Burden of Disease, Injuries and Risk Factors in 2017 estimated that approximately 3 million patients are treated by hemodialysis worldwide and this will increase to 5.4million by 2030. <sup>1</sup>

Patients undergoing maintenance hemodialysis often complain of many issues which affect their quality of life. Fatigue is one of the commonest and a chronic, burdensome, and a most dreaded symptom experienced by patients when undergoing maintenance hemodialysis.<sup>2</sup> 60 – 97 % of patients on hemodialysis reportedly have fatigue as a frequent, severe, distressing, and troublesome symptom. An online survey conducted during pandemic reveals the prevalence of fatigue was around 53.7% among patients on hemodialysis.<sup>6</sup> Old age and female patients were independently associated with a higher burden of fatigue when undergoing hemodialysis. There are multiple causes leading to fatigue like poor nutritional status, repeated and long-time exposure to hemodialysis, anemia, uremia, dialysis inadequacy, advancing age, sleep disorders, inflammation, pain in bones and muscles and comorbid diseases which also have an adverse impact on the quality of their life.<sup>3,4</sup> Fatigue leads to physical, emotional, and/or cognitive exhaustion and tiredness which is not relieved by rest particularly following haemodialysis.<sup>5</sup>

Fatigue patients frequently become tired, weak and have lack of energy to do the daily activities. Stress and frustration induced by lack of energy leads to declined cognitive function, ability to work and achieve personal goals. Chronic fatigue negatively affects the physical, cognitive, and social activities that leads to poor life satisfaction. Restless leg syndrome among renal insufficiency patients has highest levels of fatigue. <sup>3</sup>

A qualitative study revealed that the chronic experience of fatigue adversely affects not only the patient's daily basic activities but also participating in other social activities ultimately leading to social isolation and poor quality of life as a marked consequence. Approximately one in two patients reported fatigue clinically, which further increases the pervasiveness of symptoms of fatigue among maintenance hemodialysis patients. Functional impairment produced by fatigue among hemodialysis patients increases 3% risk of death.<sup>5</sup>

However, fatigue is mostly assessed by a subjective expression of the patients: It is often under-recognized and under-treated by healthcare providers and negatively affects the physical, cognitive, and social wellbeing of the patients undergoing hemodialysis thus ultimately affecting their quality of life and life satisfaction.<sup>3</sup> In a cross-sectional study it was reported that the presence of a number of comorbidities represented as one of the important cause of fatigue and acted as a barrier in maintaining the quality of life of hemodialysis patients.<sup>3,4</sup> Poor quality of life leads to the complications like depression and malnutrition and even increased mortality.<sup>4</sup> Patients are often found struggling to maintain the health related quality of life and fatigue is an important predictor of increased risk of death among patients on hemodialysis.<sup>5</sup> They often feel helpless in identifying and controlling the symptoms induced by fatigue. Mostly fatigue has been underrated and poorly studied among patients on hemodialysis and this knowledge gap decreases their capability in controlling their fatigue related symptoms. Hence this study is aimed at exploring the systematic review on prevalence, associating factors and impact of fatigue on health-related quality of life of patients undergoing maintenance hemodialysis.

## **METHODS**

An online search done on fatigue and hemodialysis through various search engines like PubMed index, Web of science, PsycINFO, CINAHL, Google Scholar, etc., Abstract, and

full text articles have been browsed and scrutinised according to the objective of the review and included in the study. A narrative review approach has been followed for this systematic review.

The key terms used to search the databases online are the combination of words like “Fatigue”, “Hemodialysis” and “Quality of Life”. The search was limited to the original full text online articles published from 2015 to 2023 to allow for adequate appraisal of the findings. Inclusion criteria were: (1) Observational studies encompassing cohort, cross-sectional, analytical and correlational studies, (2) Participants aged 18 years or older with end stage renal disease and on maintenance hemodialysis, (3) The articles that had explicit findings related to prevalence, impact of fatigue and its associated factors among hemodialysis patients and (4) The articles published in English literature only. Exclusion criteria were: (1) The articles that discussed the factors affecting the quality of life other than fatigue, (2) The articles discussed only the fatigue among peritoneal dialysis patients and renal transplant patients, (3) To focus only on prevalence, associated factors, and impact of fatigue, coping strategies and interventional measures to curtail fatigue among hemodialysis patients related articles were excluded. The full text articles that fit the above criteria only were adopted to be included in the review. Out of total 1149 abstracts, 142 non duplicated abstracts were reviewed. 33 full text articles that fulfil the criteria of the study were completely scrutinised to incorporate into the study. Finally, 16 full text articles were selected according to the PRISMA guidelines and reviewed in this study.<sup>(Fig: 1)</sup> The extracted data includes the following items (Table 1): (1) First Author name and year of Publication, (2) Aim, (3) Design, (4) Population / Age Criteria, (5) Fatigue grading tool, (6) Inclusion and Exclusion criteria, (7) Prevalence of Fatigue, (8) Results found.

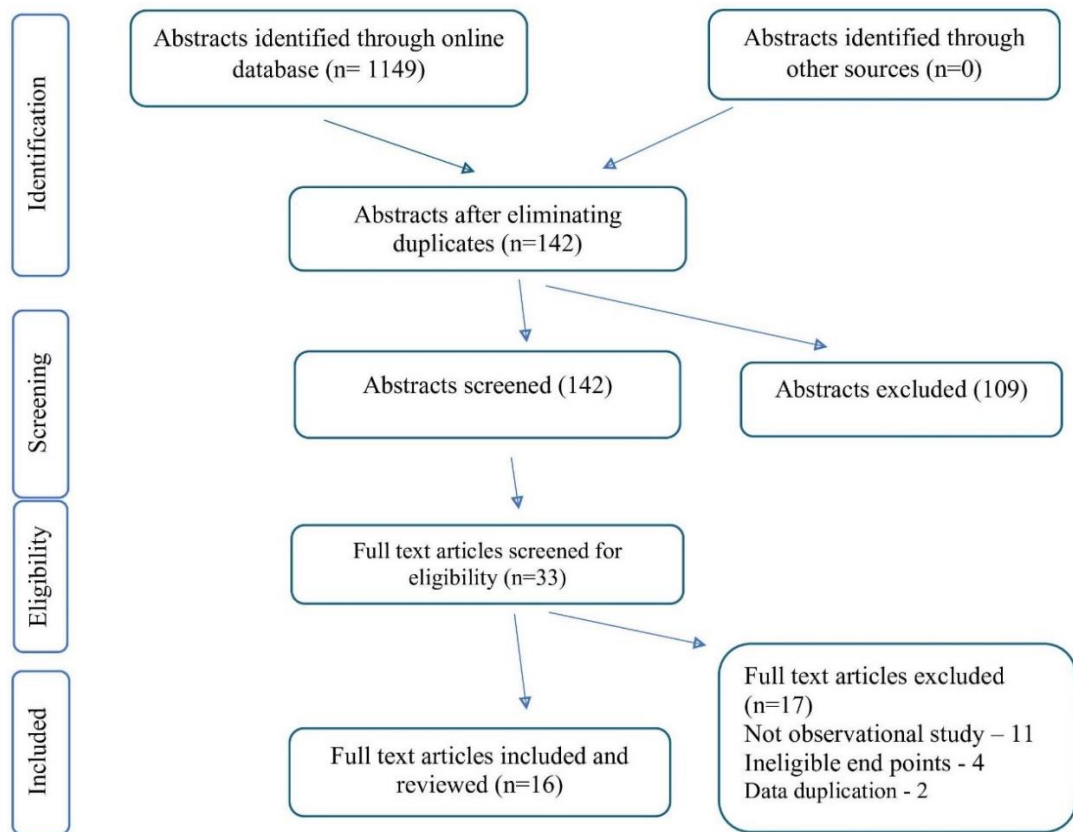


Fig 1: PRISMA flow diagram of the different phases of the systematic review

Table 1: Prevalence, Associating factors and Impact of fatigue among patients on haemodialysis

FIRST AUTHOR AND YEAR OF PUBLICATION	AIM	DESIGN	POPULATION/ AGE CRITERIA	FATIGUE GRADING TOOL	INCLUSION /EXCLUSION CRITERIA	PREVALENCE OF FATIGUE	RESULTS FOUND
Ricardo Eugenio, et. al (2023) <sup>7</sup>	To assess the prevalence and the predisposing factors of fatigue.	Cross-sectional study/ Brazil	95/ 24 - 87 years	The Chalder Questionnaire.	Inclusion criteria -Stage 5 CKD and on HD Exclusion criteria: - Patients undergoing peritoneal dialysis. -Age < 21 years - Dialysis for < 12 months - Those with Psychiatric disorders, active infectious or autoimmune disease, liver failure, and	The prevalence of fatigue in patients undergoing haemodialysis was 51.6%	Fatigue was associated with depression 34.7% (65.9% vs. 34.1%, P = 0.001) and poor sleep quality 69.5% (59.1% vs. 49.9% P = 0.027) and it lowers the quality of life in terms of physical and general health than non-fatigue patients. 50% of patients have depression. Women have more frequent depression than men. 2% improvement in physical health and 3% improvement in general health will reduce the probability of fatigue.

					metastatic malignant neoplasms.		
Stavros Tsirigotis, et.al (2022) <sup>3</sup>	To identify the factors associated with fatigue	Cross-sectional study/ Greece	100/20 - 85 years	Modified Fatigue Impact Scale (MFIS)	Inclusion: - Aged 20 years or older - At least three months on haemodialysis. - Ability to speak, read, and write Greek Exclusion: -Insufficient language ability -Age above 85 years -Cognitive deterioration -Drug or alcohol abuse.	High level of Physical fatigue (p=0.001) was reported among haemodialysis patients aged over 70 years.	Patients with Ageing (73%), Comorbidity (44%), sufficient anxiety about the dialysis regimen (66%), Insomnia (15%), Divorced/ Widowed patients, those with primary education, inadequate information about the disease, those perceived tired after dialysis, those perceived changes in their body image have high level of physical and mental fatigue that leads to poor quality of life.
Yu-Hui Wu, et. al (2022) <sup>8</sup>	To associate fatigue, anxiety and depression with physical activity among patients with and without comorbidities.	Cross-sectional survey design/ China	120/20 years to - no upper age limit	Brief Fatigue Inventory —Taiwan version (BFI-T)	Inclusion criteria: -Aged 20 years and older -At least 3 months on HD with three weekly sessions. -Had sufficient cognitive function and accepted to participate. -Able to read and communicate in Chinese. Exclusion criteria: -Patients with cognitive disabilities or mental illness -Those who could not complete the questionnaire, lack self-care ability and hospitalized.	-	Hemodialysis patients with comorbidities exhibited more severe levels of depression (p<0.001), anxiety (p<0.001), and fatigue (p<0.001), than patients without comorbidities. Fatigue restricts the patients from doing physical activity that leads to depression and anxiety and the study found that regular physical activity level reduces fatigue severity and fatigue interference.
Jona Sakiqi, et al (2022) <sup>9</sup>	To assess the factors related to depression and the impact of insomnia and fatigue on depression.	Cross-sectional study/ Greece	100/18 - 85 years	Modified fatigue impact scale	Inclusion criteria: -Age 18-85 years old -on hemodialysis for at least three months -Able to speak, read, and write in Greek. Exclusion criteria: -Inadequate language skills -Aged over 85 years old -Cognitive decline -Drug or alcohol abuse	--	Depression is strongly associated with Insomnia and fatigue. An increase in physical and mental fatigue score increases insomnia that ultimately increases depression level of the HD patients. Insomnia also a predicting factor for fatigue.
Subrata Debnath, et. al (2021) <sup>2</sup>	To characterize and compare fatigue severity and fatigue interference with daily activities between dialysis and non-	Observational study/ United states	209/ No age criteria	9-item Brief Fatigue Inventory	Inclusion: (i) On thrice weekly hemodialysis for at least six months Exclusion (i) Patients with malnutrition and anaemia (ii) With Comorbidities such as acute cardiovascular events, refractory psychiatric disorders, and significant neurological disorders.	Severe fatigue was highly prevalent on a hemodialysis day than non hemodialysis day (P = < 0.001). 49% of patients have reported	Fatigue severity and interference is high on dialysis day than non-dialysis day. It positively associated with Age and depression. Negative Impact of fatigue affects the daily activities such as general activity, mood, walking ability, normal work, relations with other people and enjoyment of life (P < 0.0001) of hemodialysis patients on dialysis day.

	dialysis days.					fatigue.	
Zakariya Al Naamani, et.al (2021) <sup>6</sup>	To determine the prevalence of fatigue, anxiety, depression, and sleep quality.	A cross-sectional and descriptive correlational design/ Oman	123/18 years - No upper age limit	Functional Assessment of Cancer Therapy- Fatigue (FACT-F), Scale	Inclusion: -Adult aged over 18 years -On haemodialysis for at least three months -No known psychiatric or neurological disorders Exclusion: -Patients with cancer or dementia.	The study found the prevalence of fatigue is 53.7% among hemodialysis patients.	The predicting factors of fatigue are Ageing, being female, depression (7.9 times, $p > .001$ ), anxiety (6.3 times $p > .001$ ) and poor sleep (3.8 times $p > .001$ ).
Yukio Maruyama, et. al (2021) <sup>10</sup>	To compare the prevalence and severity of fatigue among patients receiving different dialysis modalities.	Cross-sectional study/ Japan	194/18 years - No upper age limit	Profile of Mood States (POMS), Visual Analogue Scale (VAS), and original scale of fatigue	Inclusion: -Adult aged over 18 years -Patients receiving Hemodialysis, Online Hemodiafiltration, Peritoneal Dialysis and combined therapy with PD and HD. Exclusion Criteria: -Under 18 years of age - Those with terminal cancer and any mental disorder, such as schizophrenia, depression or dementia.	The prevalence of severe fatigue was high on dialysis days for patients on Hemodialysis and Hemodiafiltration than dialysis free days.	The study found that the fatigue is the commonest symptom, and the different modality of dialysis treatment did not affect the presence of fatigue. Ageing, employment status, increased BMI and creatinine are the influential factors of fatigue. More than 80% of patients felt that the fatigue affected their work or daily life.
Astrid D.H. Brys, et.al, (2021) <sup>11</sup>	To assess in-depth understanding of diurnal fatigue patterns and related variables using a mobile Health (mHealth) ESM application	Prospective observational study / The Netherlands	40/18 - 84 years	Fatigue severity scale & PsyMate mHealth App	Inclusion Criteria: - On haemodialysis for at least six months. Exclusion Criteria: - Adults less than 18years of age -Insufficient understanding of the Dutch language. -Inability to handle the mHealth application independently because of hearing problems, vision problems or insufficient cognitive skills -Diagnosed dementia; chronic fatigue syndrome; fibromyalgia -Actual instability of clinical condition requiring hospitalization.	68% of participants experiencing at least some fatigue.	The momentary predictors of Fatigue are HD treatment days, Less physical activity, depressed mood, and poor sleep quality.
Federica Picariello, et. al (2019) <sup>5</sup>	To evaluate fatigue severity.	Prospective Study/ UK	174/18 years - No upper age limit	The Chalder Fatigue Questionnaire	Inclusion criteria: - Adults aged 18 or older. - In-centre haemodialysis patients for 90 days or longer. - Able to speak or write English, - Willing patients. Exclusion criteria:	47.1 % of hemodialysis patients were clinically reported fatigue.	Fatigue was the predictive factor for increased risk of death (6% for one point of increased fatigue) due to distress, impaired functioning, and its consequences and it reduces the likelihood of transplantation (8% reduction one point of increase in fatigue) among haemodialysis patients.

					-Those with significant visual or physical impairment. -Any known cognitive impairments, serious mental health conditions (e.g. psychosis, personality disorder)		
Marit S. van Sandwijk, et al (2019) <sup>12</sup>	To compare fatigue, anxiety depression and Quality of life in patients with ESRD versus patients with a haematological malignancy undergoing chemotherapy.	cross-sectional cohort study/ Netherlands	168/18 years to - No upper age limit	The Checklist Individual Strength (CIS).	Inclusion criteria: -Age above 18 years of age. - On HD for at least 6 months. - Patients who undergone kidney transplant at least 1 year ago -Patients undergoing chemotherapy Exclusion criteria: -Active psychiatric or neurologic disease, previously diagnosed chronic fatigue syndrome, liver cirrhosis and an inability to understand the questionnaires. -For patients undergoing chemotherapy with brain metastases	53.3% of patients undergoing hemodialysis had very high severe fatigue than chemotherapy and kidney transplant patients.	High prevalence of severe Fatigue strongly impairs the quality of life of haemodialysis patients. (Correlation coefficient -0.58, P<0.001). HD patients have 23.4% of less quality of life. Anxiety and depression also impair the quality of life of HD patients. (Correlation coefficient -0.44, 0.57, P<0.001).
Astrid D.H. Brys, et.al (2019) <sup>13</sup>	To assess fatigue diurnal changes and its relation with depression	Prospective, observational study/ Italy	51/18 years - No upper age limit	Fatigue Severity Scale	Inclusion criteria: -All HD patients aged above 18 years. Exclusion criteria: -<18 years of age -Hearing or reading problems, -Dementia, actual instability of clinical condition requiring hospitalization, or active cancer.	-	The study found that fatigue increased significantly during the dialysis session. Patients also reported higher fatigue immediately before hemodialysis in the hospital environment than postdialysis day (F(1, 47) = 9.34, P =0.004, partial $\eta^2$ =0.166) and found that individuals with high fatigue have higher depression than low depressive people before HD and on non-dialysis days.
Hanaa Hamdy Ali, et.al (2017) <sup>14</sup>	To assess the fatigue, depression, and sleep disturbances	Descriptive cross-sectional design/ Egypt	105/18 - 65 years	Fatigue Severity Scale (FSS)	-All adult patients undergoing hemodialysis for at least 3 months. Exclusion criteria: - Patients with concomitant diseases that prevent cooperation - Patients with history of psychiatric disease.	83.8% of hemodialysis patients had total fatigue symptoms.	HD patients have high prevalence of fatigue, sleep problems and depression symptoms and the study reported that fatigue (89.5%) affects the family and social duties of HD patients.37.1 % of patients also had severe depression. Aging and lower income are the positive predictors of fatigue. Fatigue and sleep latency are also positively correlated.
Zeinab Faried Bahgat. et.al	To assess the effect of fatigue on daily	Descriptive cross-section	100 / No age criteri	Fatigue Symptom Inventory (FSI) –	Inclusion criteria: - Adults both sexes undergoing HD Exclusion criteria:	41% of the patients have severe fatigue in	The study found that fatigue is negatively correlated with degree of daily living activities. Higher level of fatigue leads to decrease



(2016) <sup>15</sup>	living activities.	al design/ Egypt	a	Arabic version	-Patients with cancer, tuberculosis, human immune deficiency syndrome (AIDS), chronic heart diseases, liver diseases and patient on temporary HD.	first week of assessment.	level of daily activities such as loss of work motivation, difficulty of starting and finishing daily activities, loss of concentration, headache, and disturbance of sleeping. Females reported severe fatigue. Ageing, Longer duration of HD and three weekly sessions also increases fatigue.
Si Yuan Wang (2016) <sup>16</sup>	To assess and identify the risk factors of fatigue.	Multicentred cross sectional study/ China	345 /18 - 82 years	Functional assessment of chronic illness therapy fatigue scale (FACIT-Fatigue)	Inclusion criteria: -Chinese citizens aged over 18 years who underwent routine hemodialysis for more than twice a week for at least 3 months. Exclusive criteria: -Patients with advanced or severe infection or malignancy, uncontrolled heart failure, intellectual problems or refused to participate	- High level of fatigue was reported among hemodialysis patients aged over 60 years.	The common significant predictors of fatigue among maintenance hemodialysis patients are Aging, poor sleep quality, bad social and family functioning, doing physical exercise less than an hour per day, comorbidity, Kt/V < than 1.2, and high serum creatinine level. (All p<0.05)
Sofia Zyga, et. al (2015) <sup>17</sup>	To investigate the demographic factors and the levels of fatigue.	Analytic study design/ Greece	129/ 18 years to No upper age limit.	Fatigue Assessment Scale (FAS) - Greek Version	The inclusion criteria: -Aged above 18 years -Undergoing hemodialysis for at least 6 months -Ability to write and read the Greek language fluently. Exclusion criteria: -Patients with history of mental illness -Patients with serious mobility or eye problems.	The prevalence of fatigue was reported to be 61% and among that 13.7% were extremely fatigue.	HD patients residing in urban areas, patients dealing with domestic work, low educational status, unemployment are the predictive factors of fatigue.
Tsiamis Georgios, et.al (2015) <sup>18</sup>	To investigate and correlate the levels of fatigue and quality of life.	Cross-sectional design/ Greece	134/ 18 years to No upper age limit	Fatigue Assessment Scale (FAS)	The inclusion criteria: -Aged above 18 years old or more. -Able to communicate in Greek -Diagnosed with end-stage renal disease. -Cooperative patients Exclusion criteria: -Aged less than 18 years and not able to communicate in Greek	The prevalence of fatigue was 52.9% (10 <FAS <= 20) and among that 15% of patients had high to very high levels of fatigue. (30 <= 50).	The study proved that patients who experience high levels of fatigue had worse quality of life (MVQOLI total score 2.90) than patients with low fatigue ((MVOQLI total score 3.67) (p<0.005). Women have reported higher fatigue (0.19%) and most poor quality of life than men.

## RESULTS

In this systematic review, the characteristics of 16 full text eligible articles published between 2015 to 2023 were discussed. These studies have been conducted in various

countries such as Greece, Brazil, China, United States, Oman, Japan, Netherlands, UK, Italy, and Egypt. Among these countries 4 studies have been conducted in Greece,<sup>3,9,17,18</sup> 2 from China<sup>8,16</sup>, 2 from Egypt<sup>14,15</sup> and 2 from Netherlands<sup>11,12</sup>. Majority studies used Cross-sectional design. Prospective observational<sup>2,5,13,11</sup>, Correlational<sup>6</sup>, Analytical<sup>17</sup> and cohort<sup>12</sup> design were also used. Various fatigue assessment tools were utilised in these 16 full text articles. Three studies used the Fatigue Severity Scale<sup>11,13,14</sup>, two studies used the Modified Fatigue Impact Scale (MFIS)<sup>3,9</sup>, The Chalder Fatigue Questionnaire<sup>5,7</sup>, Brief Fatigue Inventory<sup>2,8</sup>, and Fatigue Assessment Scale (FAS)<sup>17,18</sup> to assess the fatigue level. Other studies used the various fatigue scales like Functional Assessment of Cancer Therapy-Fatigue (FACT-F) scale<sup>6</sup>, Profile of Mood States (POMS), VAS and original scale of fatigue<sup>10</sup>, The Checklist Individual Strength (CIS)<sup>12</sup>, Fatigue Symptom Inventory (FSI)<sup>15</sup> and Functional assessment of chronic illness therapy fatigue scale (FACIT- Fatigue)<sup>16</sup>. PsyMate mHealth App was also used in a study to assess the fatigue level.<sup>11</sup> The study subjects ranging from 40 to 345, encompassing total 2187 patients, out of which 1881 patients received maintenance hemodialysis. The age variability of the patients was between 18 to 91 years, minimum age limit is 18 years and in most of the studies upper age limit was not specified. The mean age of individuals was between 49.5 to 67.3. Majority of the participants were males. Inclusion and exclusion criteria were varied based on the study purpose.

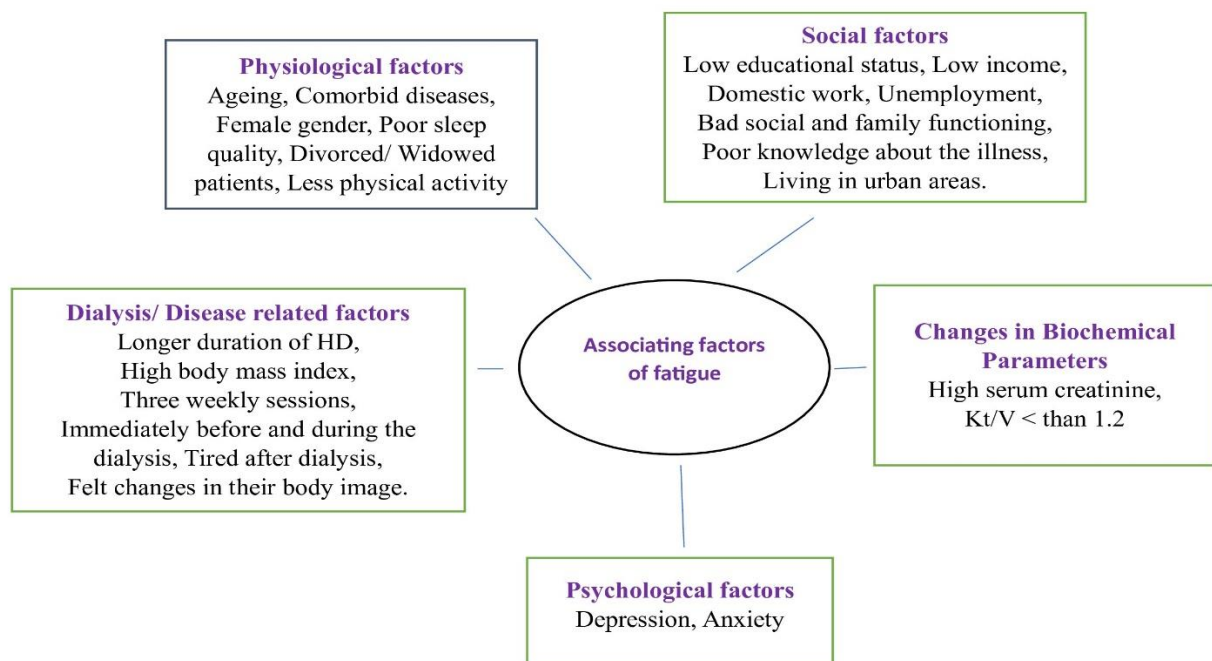
### Prevalence of Fatigue

As fatigue is considered to be one of the commonest and a most complex symptom among patients undergoing hemodialysis, in this review its prevalence was found in the ranges between 41% and 83.8%<sup>14,15</sup>, denoting a moderate to high level of prevalence. One study revealed that a high level of physical and mental fatigue was reported among patients over 70 years of age<sup>3</sup> and another study reported the same in patients over 60 years of age<sup>16</sup>. Two of the studies have reported that many patients suffer from severe fatigue on dialysis

days than non-dialysis days.<sup>2,10</sup>. One article discussed that patients undergoing hemodialysis reported very high fatigue than renal transplant or chemotherapy patients.<sup>12</sup>

### Associating Factors of Fatigue

Based on the reviewed articles the associating factors have been listed out under five different aspects: Physiological factors, Psychological factors, Social factors, Dialysis/ Disease related factors and Changes in Biochemical Parameters. Physiological factors include Ageing, comorbid diseases, female gender, poor sleep quality, divorced/ widowed patients and less physical activity. Psychological factors are depression and anxiety. Social factors revealed to be low educational status, low income, domestic work, unemployment, bad social and family functioning, poor knowledge about the illness and living in urban areas. Dialysis/ Disease related factors are longer duration of hemodialysis, high body mass index, three weekly sessions, immediately before and during the dialysis, those feeling tired after dialysis and those who perceived changes in their body image. Changes in Biochemical Parameters include high serum creatinine and  $Kt/V < \text{than } 1.2$ . (**Fig. 2**)



**Fig 2: Associating factors of fatigue**

Ageing is considered to be one of the main predicting factors of fatigue. Ageing over 60 years of age decreases the energy and the level of performance of patients undergoing hemodialysis<sup>2,3,6,10,14,15,16</sup>. Ageing and comorbidity among patients on hemodialysis have statistically higher physical and mental fatigue. Physical fatigue often reported as tiredness, general muscle weakness, intense body pain, headache, poor sleep quality, low physical activity, decreased physical and general health, disturbances in daily activities, decreased working capacity, difficulty in walking ability, social activity limitations that all increases mortality, restricted functioning, distress and consequences whereas mental fatigue leads to declined cognitive function such as loss of memory, impaired family and social functioning, mood instability, lack of work motivation, poor concentration, inability to remain focused under certain conditions and psychological distress like depression, anxiety, etc.<sup>6,7</sup>

Patients on hemodialysis with comorbid diseases have decreased physical activity and more depression ( $p < 0.001$ ), anxiety ( $p < 0.001$ ) and fatigue ( $p < 0.001$ ).<sup>3,8</sup> Women perceives more depression than men, which has more probability for fatigue.<sup>7</sup> Biochemical variations such as high serum creatinine and  $Kt/V < 1.2$ , longer duration of HD, frequent dialysis session and high body mass index also leads to poor adherence of treatment by the patients undergoing hemodialysis which further worsens their condition.<sup>10,11,16</sup> Promising evidence suggested that negative factors like depression and anxiety also correlated with fatigue which furthermore leads to less physical activity and insomnia, which results in a cycle and further aggravates the depression and anxiety.<sup>8,9</sup>

### Impact of fatigue

The reviewed articles reported that the presence of physical and mental fatigue among patients undergoing hemodialysis lowers their health related quality of life.<sup>3,7</sup> Multifaceted and multifactorial problems of fatigue affecting the physical and general health of patients on

hemodialysis than non-fatigue patients.<sup>7</sup> Fatigue severity and interference restricts the day-to-day physical activity of patients on hemodialysis.<sup>2,8</sup> There is a negative correlation between fatigue and activities of daily living and higher fatigue leads to difficulty in starting and ending daily activities, headache, lack of concentration, lack of work motivation and sleep disturbances.<sup>15</sup> Fatigue has a negative influence on patients' mood, socializing with other people and life enjoyment. It also reduces the patient's walking ability, general activity, and normal working capacity.<sup>2</sup> More than 80% of the patients on hemodialysis reported fatigue have restricted daily life and work. It socially affects their role and ability to cope with their families, work setup and social behaviours.<sup>10</sup>

This high prevalence of fatigue increases mortality i.e., as one point of fatigue increased 6% increased risk of death. This occurs due to restricted functioning, distress and consequences produced by fatigue. It is also reported that one point increase in fatigue decreases the likelihood of transplantation to 8% among patients on hemodialysis.<sup>5</sup> 89.5% of patients on hemodialysis with fatigue have impaired family and social function and it decreases quality of life to 23.4% than normal people.<sup>12,14</sup> Many literatures in this review suggested that the prevalence of fatigue is one of the main predicting factor of quality of life and daily functioning of patients on hemodialysis. It often leads to a worse quality of life and increased risk of death.<sup>5,7,12</sup>

## **DISCUSSION**

This systematic review is mainly aimed at exploring the prevalence, associating factors and impact of fatigue on health-related quality of life of patients undergoing hemodialysis. As fatigue is the significant and multifaceted problem, this review identified the prevalence of fatigue was ranged between 41% and 83.8%. This result was consistent with the report of recent studies, revealed the prevalence of fatigue to be 69% to 77%<sup>19</sup> and

60-97%.<sup>20</sup> This more common general feeling of fatigue leads to general weakness, low physical activity, more dependency, and low functional capability of patients undergoing hemodialysis<sup>3</sup>.

This review found that old age patients with comorbidity reported to have statistically significant higher physical and mental fatigue.<sup>3</sup> This may be due to ageing causes difficulty in adhering to the treatment which frequently deteriorates their physical condition.<sup>21</sup> Fatigue is commonly reported among feminine gender as they are easily exposed to more frequent depression.<sup>6,7,15,18</sup> Depression is the commonest and significant predictor of fatigue that increases the level of physical and mental fatigue among patients on hemodialysis.<sup>2,6,7,8,9,11,12,13,14</sup> The prevalence of Depression among ESRD patients are reported to be between 20% to 40%.<sup>27</sup> Depressive patients suffer from sadness, loss of interest, less interest to eat food, tiredness and less concentration.<sup>28</sup> Negative impact of Depression leads to Insomnia and fatigue. Insomnia is also a predicting factor for fatigue. As physical and mental fatigue increases insomnia also increases that leads to increased depression.<sup>9</sup> Depression, poor sleep quality and less physical activity are considered to be the momentary predictors of fatigue among hemodialysis patients.<sup>11</sup> High depressed people have higher fatigue than low depressed haemodialysis patients.<sup>13</sup> Depression along with anxiety increases fatigue that impairs the quality of life of hemodialysis patients.<sup>12</sup> They frequently have anxiety about their dialysis regimen (66%) that ultimately leads to fatigue.<sup>3,6,8,12</sup>

Changes in the biochemical parameters like high serum creatinine and  $Kt/V < 1.2$  are the influential factors of fatigue as it leads to increased uremic symptoms.<sup>10,16</sup> Poor sleep quality increases fatigue that lead the patients to use sleep medications which further worsens the fatigue, which may be the side effect of these medications.<sup>24</sup> The consequences of these physical and mental fatigue ultimately reduce their health-related quality of life, chances of

survival and even decreases the transplantation rate.<sup>5,18</sup> The transplant ineligibility occurs due to increased body mass index that is produced by the consequences of fatigue induced reduced functioning. Fatigue associated elevated levels of proinflammatory cytokines also reduces the chances of transplantation.<sup>5</sup>

Quality of life is the main predictor of determining health status of the patients on hemodialysis and it found to have negative correlation with comorbid diseases.<sup>22</sup> Aggravating fatigue may have effect on patient well-being and survival. It is also found that worsening fatigue have significantly high risk of all-cause mortality, first cardiac hospitalization, or cardiac death in maintenance hemodialysis patients.<sup>24</sup> This may be due to general cardiac causes like increased lipid metabolism, decreased heart rate, increased levels of proinflammatory cytokines and decreased fibrinolysis associated with fatigue among maintenance hemodialysis patients like general population.<sup>25,26</sup>

As many reviewed articles suggested that fatigue leads to impaired physical and mental functioning that reduces quality of life, but these studies lack detailed descriptions of its relationship with impact of fatigue. Studies also not been adequately explored with effect on family and social relationship, impact of post dialysis fatigue and the impact of other biochemical markers (Other than high serum creatinine and Kt/V) on fatigue. Improving fatigue in the end-stage renal disease population may positively impact patient well-being and survival. Longitudinal changes produced by fatigue also leads to increased mortality among maintenance hemodialysis patients.<sup>24</sup>

Highlights of this review on the prevalence, associating factors and impact of fatigue among patients undergoing hemodialysis, creates awareness of fatigue among patients and health care practitioners. Some of these risk factors are potentially modifiable, health care practitioners must need to recognize this earlier and complex problems created by it. The

interventions should be developed and implied clinically to find for coping measures to overcome the contributing factors. It further helps to evaluate and treat fatigue to reduce the prevalence. A multi-disciplinary approach to treatment and training for all renal providers is required to assess and address the impact of complexity of fatigue.

## **LIMITATIONS**

Majority of the studies involved in this review are cross-sectional study and therefore, conclusive interpretations on causality cannot be drawn. Only one longitudinal study compared the relationship of anxiety, depression, and quality of life with fatigue, but other domains have not been described and compared. Moreover, the reviewed studies were conducted in various countries and have different inclusion and exclusion criteria's limit our ability to draw conclusions on physiological and psychological variables.

## **RECOMMENDATIONS**

This review clearly states about the prevalence, associating factors and the impact of fatigue. This gives an overview to identify the different factors of fatigue and its impact among patients undergoing hemodialysis. Further reviews can be conducted on effect of Post dialysis fatigue, coping strategies to overcome the different contributing factors and complementary therapies of fatigue among patients undergoing hemodialysis.

## **CONCLUSION**

Fatigue is the highly prevalent, complex, and the troubling symptom of patients undergoing hemodialysis, its limited understanding of associating factors and its impact leads to delayed interventions and consequences. Patients on hemodialysis suffer from physical, psychological, and social problems due to fatigue. Physical and mental fatigue increases the risk of mortality due to detrimental effects on quality of life among patients on hemodialysis.



The promising evidence of this review helps the health care professionals for early identification of patients at risk and intervene as soon as possible to prevent the debilitating effects of fatigue and improve health related quality of life. Health care professionals can verify different associating factors of fatigue among each individual hemodialysis patients and treat them to reduce its impact to enhance their activities of daily living. Further research is necessary in this area of inquiry on fatigue related factors on different domains of life and its impact on daily life. It also may help deepen our knowledge on how fatigue correlates with quality of life of patients on hemodialysis and factors affecting the physical, psychological and social health. Also, very limited literatures focussed on coping strategies and complementary therapies to overcome the fatigue. Therefore, further research should be targeted to develop more appropriate interventions to overcome the fatigue among hemodialysis patients.

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