

## Review Article

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## Major Risk Factors in the Onset of End-Stage Renal Disease

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### Abstract

**Aims:** The incidence of chronic End-Stage Renal Disease (ESRD) is rapidly increasing among the Palestinian population in the last few years. Therefore, it is important to study the factors that influence this increase. This study is aimed to investigate the major risk factors that led to increased ESRD that requires hemodialysis in Northern West Bank.

**Methods:** A literature review was conducted to determine the causes of ESRD, treatment, complications, incidence and prevalence in developing and developed countries.

**Results:** The major risk factors that are significantly associated with the onset of ESRD include diabetes mellitus, hypertension, cardiovascular disease, recurrent taken analgesic drugs and infection of the urinary tract.

**Conclusion:** Identifying major risk factors affecting ESRD is an important topic. There should be more attention to improve the quality of renal replacement therapy and facilities. This could be achieved through increasing the number of qualified staff and the dialysis machines. Furthermore, knowing the causes will help to focus on prevention and early treatment. This will reduce health system costs associated with ESRD.

**Keywords:** ESRD; Causes of ESRD; ESRD treatment; Complications of ESRD; Risk factors for ESRD; Risk factors for diabetes

### Introduction

This study focuses on one of the most common health problem in both developed and developing countries, namely End-Stage Renal Disease (ESRD) which is a term used when kidney reaches a complete, or almost complete failure to function; kidneys can no longer remove wastes, regulate and concentrate urine [1].

ESRD is the irreversible loss of kidney function. At the point where kidneys fail to sustain life, renal replacement therapy is required. Dialysis is the process of cleaning the blood and removing excess fluids artificially with a special equipment called the dialysis unit [2].

The Palestinian Ministry of Health is the main health care provider for the ESRD management program in Palestine. The dif-

ferent treatment modalities of ESRD are free of charge. Patients with ESRD belong to group of Patients with "Special Diseases" and are eligible for a government health insurance. In northern West Bank, there are 8 dialysis centers serving 585 patients. In each city there is one dialysis center. In North of West Bank there are four dialysis centers (while there are no dialysis centers in Salfeet and Tubas. Therefore, patients from Tubas have to go to Jenin government's hospital while Salfeet patients receive dialysis services in Al-Waitany hospital in Nablus city).

ESRD may result from many different causes, and it is often asymptomatic until severe renal damage develops. Moreover, there are many risk factors that lead to the onset of ESRD. This study aims at identifying the main risk factors that led to the onset of ESRD in Northern West Bank.

### Problem Statement

ESRD is a common health problem in Palestine. It is rapidly increasing among Palestinians. Moreover, ESRD is considered to

be a burden on the health system in Palestine, there are rare studies that aim at identifying the main risk factors that lead to the onset of ESRD in Palestine. Since the researchers work in health care, they see the necessity of conducting a study that could give a vivid idea of the main risk factors that lead to the onset of ESRD in Northern West Bank.

## Significance of The Study

Northern West Bank is undergoing transition characterized by rapid urbanization and life style changes, as well as an epidemiological transition characterized by resisted burden of infectious diseases, raises in chronic disease such as chronic renal failure.

Although ESRD is one of the leading causes of morbidity and mortality worldwide, there are limited studies reported in Palestine. Chronic diseases are responsible for 81% of the total deaths in Palestine, and the ESRD is responsible for 4% [3]. Furthermore, ESRD is a growing problem in northern West Bank and renal replacement therapy is exerting an increasing pressure on health systems. No studies or research have investigated the risk factors of the ESRD in Palestine to date. Similar to other developing countries, these types of studies are nearly neglected. Therefore, the early intervention for patients with diabetes, hypertension and other risk factor is necessary to prevent kidney damage.

Patients of ESRD require ongoing dialysis or kidney transplantation to survive. Underdeveloped organ donor and transplant programmers, health system and financing issues, the cost of pharmaceuticals commonly pose additional barriers to the delivery of efficient and cost-effective renal replacement therapy.

## Literature Review

### Diagnosis of ESRD

Diagnosis of ESRD typically requires the physician's review of the patient's medical history as well as a physical examination. A patient with a history of chronic kidney disease that has progressed may be suspected of having ESRD. The physical examination includes tests to determine the advancement of the kidney disease and will likely include a measurement of a patient's blood pressure. Additional tests that may be performed [4].

### Causes of ESRD

ESRD has many causes that varies from one patient to another. The key risk factors for chronic kidney disease are the increasing age of the population, diabetes mellitus II and hypertension. The most common causes include the following [5].

- Uncontrolled hypertension can damage the kidneys over time.
- Glomerulonephritis is the inflammation and damage of the filtration system of the kidney and can cause kidney failure.

- Polycystic kidney disease is an example of a hereditary cause of chronic kidney disease where both kidneys have multiple cysts.
- Medications such as the use of some analgesics regularly over long durations of time can cause analgesic nephropathy and kidney damage.
- Atherosclerosis leading to ischemic nephropathy, can cause kidney damage.
- Obstruction of the urinary tract by stones or cancer can lead to the enlargement of the prostate and then strictures that may cause kidney damage.
- Diabetes mellitus type I and type II cause diabetic nephropathy, that leads to kidney failure. Diabetes is the largest single cause of ESRD in the United Kingdom, accounting for 30-40% of all cases [6].
- Obese American people have up to a seven times greater risk of kidney failure than non-obese people, suggesting that obesity should be considered a risk factor for ESRD [7].

### ESRD Treatment

The treatment alternatives for ESRD include hemodialysis, peritoneal dialysis, and kidney transplantation.

### Kidney Transplantation

Is the surgical procedure of placing a fully functioning kidney into a person with ESRD? This procedure is usually an elective one, performed in patients who have undergone careful preoperative assessment and preparation. The transplanted kidney may originate from a deceased donor or from a related or unrelated person [8].

### Dialysis

Dialysis is the most common treatment for End Stage kidney failure, replacing the impaired filtering ability of the kidneys. Eventually, most patients with End Stage kidney failure require a kidney transplant. Dialysis is a procedure that is performed routinely on persons who suffer from acute or chronic renal failure, or who have ESRD [4].

The process involves removing waste substances and fluid from the blood that are normally eliminated by the kidneys. Dialysis may also be used for individuals who have been exposed to or ingested toxic substances to prevent renal failure from occurring [9]. There are two ways to perform dialysis: Peritoneal dialysis and Hemodialysis [4]. Peritoneal dialysis is performed by surgically placing a special, soft, hollow tube into the lower abdomen near the navel. After the tube is placed, a special solution called dialysis is instilled into the peritoneal cavity. The peritoneal cavity is the space in the abdomen that houses the organs and is lined by

two special membrane layers called the peritoneum. The dialysis is left in the abdomen for a designated period of time which will be determined by physician. The dialysis fluid absorbs the waste products and toxins through the peritoneum.

Hemodialysis can be performed at home or in a dialysis center or hospital by trained healthcare professionals. A special type of access, called an Arteriovenous (AV) fistula, is placed surgically, usually, in the patients' arm. This involves joining an artery and a vein together. An external, central, Intravenous (IV) catheter may also be used. A dialysis machine pumps small amounts of blood out of the body and through a filter called an artificial kidney or dialyzer. This kidney filters extra fluid and wastes from the blood. The blood is then pumped back into the body and special medication will be given to patient to prevent blood from clotting.

## Complications of ESRD

As kidney function deteriorates, loss of excretory, regulatory, and endocrine functions takes place, and complications develop in virtually every organ system [10].

**Systemic Complications:** The onset of uremia is slow and dangerous, starting with rather nonspecific symptoms such as malaise, weakness, insomnia, and a general feeling of being unwell. Patients may lose their appetite and complain of morning nausea and vomiting [11]. Systematic complications encompass the following:

**Gastrointestinal Complications:** This is a common problem in ESRD patients, and nutritional support is important (Gastrointestinal disturbances include anorexia, nausea, vomiting, and hiccups). Peptic ulcer disease and symptomatic diverticular disease are common in patients with chronic renal failure. These symptoms usually developed with dialysis [12].

**Cardiovascular Complications:** The most common cause of death in patients with ESRD is cardiovascular disease. Volume overload may cause CHF and pulmonary edema. Hypertension contributes to cardiovascular disease. Dyslipidemia is a primary risk factor for cardiovascular disease and a common complication of ESRD [13].

**Hematological Complications:** Anemia is inevitable in CRF because of loss of Erythropoietin production. Abnormalities in white cell and platelet functions lead to increased susceptibility to infection and easy bruising. It occurs mainly because of erythropoietin deficiency and, to a lesser degree from hemolysis, presence of uremic inhibitors, blood loss, and deficiency in iron, folate, or vitamin B12 [14].

**Dermatologic Signs:** Pruritus is a common dermatologic complication assumed to be secondary to accumulation of toxic pigments in the dermis [14].

**Bone Disease:** Metabolism of calcium and phosphorus is abnormal in patients with ESRD and is associated with the development of bone disease. Phosphate retention occurs as GFR declines. Both hyperphosphatemia and reduction in the active form of vitamin D lead to hypocalcaemia [15].

## Neuralgic Complications

Both the central and peripheral nervous systems are affected by ESRD. Early symptoms that affect the central nervous system include decreased ability to concentrate or think abstractly. Later symptoms include apathy, lethargy, and insomnia. Severe symptoms include increased deep tendon reflexes, decreased coordination, coma and death may follow when the BUN level rises to 150 to 200 mg/dL. Psychological features that may follow during the course of ESRD include delusions, depression, mania, and euphoria. The cause of the central nervous system symptoms is not clear but may be due to a toxic increase in parathyroid hormone or a decrease in brain metabolism secondary to impaired neurotransmission and inhibition of various enzymes [16].

**Vascular Signs:** Vascular access complications are similar to those seen in any patient with a vascular surgical procedure (e.g.: bleeding, intravascular infections, vessel occlusion) [11].

**Dialysis Catheters:** A peritoneal dialysis catheter subjects patients to the risks of peritonitis and local infection. The catheter acts as a foreign body and provides a portal of entry for pathogens from the external environment [10].

**Infection/Immunologic:** Patients who have received renal transplants may experience recurrent renal failure due to rejection or other graft complications. In addition, chronic immunosuppressant makes them prone to infection [10].

**Electrolytes Disturbances:** ESRD prompts a variety of disturbances in electrolytes (sodium and potassium), water balance and metabolic acidosis [11]. Electrolyte disturbances contain the following:

## Metabolic Acidosis

Most patients with chronic kidney disease develop metabolic acidosis because of their reduced ability to excrete hydrogen ions generated mainly from the metabolism of sulfur containing amino acids. As patient condition approaches ESRD, serum bicarbonate concentration often falls to between 12-20 mEq/L and the anion gap increases [17].

**Sodium Balance:** Sodium balance remains virtually normal until very late in the course of ESRD, because the kidney can markedly increase the amount of sodium excreted per nephron by reducing tubular sodium reabsorption. Although sodium balance maintained, the kidney loses its ability to adapt to large variations in salt intake. Indeed, intake of large amounts of sodium can easily

overwhelm the excretory capacity of the failing kidney and result in fluid retention, edema, and hypertension [17].

**Potassium Balance:** Hyperkalemia may occur in association with dietary indiscretion, use of potassium containing salt substitutes, increased catabolism, or metabolic acidosis. Hypokalemia may occasionally occur in patients with ESRD, and it is usually due to gastrointestinal losses or excessive use of the anion exchange resin sodium polystyrene sulfonate [17].

**Water Balance:** The ability to concentrate or dilute urine is impaired in patients with chronic kidney, which makes them more susceptible to hypernatremia. Hypernatremia may occur if water consumption is not sufficient to replace fluid loss [11].

### Incidence and Prevalence of ESRD Worldwide

ESRD (ESRD) is increasing worldwide. Renal replacement therapy and kidney transplantation are an increasing burden on health systems. This condition is particularly serious in developing countries where health resources are inadequate [18]. Worldwide, the number of patients receiving Renal Replacement Therapy (RRT) is estimated at more than (1.4) million, with an annual incident rate growing to 8% [19].

The average of incidence of new patients treated due to ESRD in EU during years (1995) was (120) persons per million populations, ranging (68) in Finland, (163) in Germany. These figures are higher in the US with (262) person per million populations, Japan (210) person per million populations, but lower in Canada (140) person per million populations during the same year [20]. In 1998, the incidence of treated ESRD in Europe ranged (110) person per million populations with Netherlands at (192) person per million populations. Higher incidence rates were recorded in the same year in countries outside Europe, such as the USA (>300 person per million population) and Japan (200) person per million populations [21].

The reported annual incidence of patients with ESRD varies widely, from as low as (4) person per million populations in Bolivia. Higher numbers (254) person per million populations in Puerto Rico. Incidence rates of (52) person per million populations and (200) persons per million populations were reported in Turkey and Egypt, respectively [21]. India has an estimated incidence of ESRD of (100) person per million populations. Approximately (100,000) patients develop ESRD each year [21].

### Incidence and Prevalence of ESRD in the Middle East

The population of the Arab countries is (350) million, with a growth rate of (3%) (range 2.3-4.7), this considered as one of the highest growing rates in the world. Compared to world growth

estimates with an average of (1.7%) [22]. Table 1 shows the incidence of ESRD in the Arab world [23]. The incidence of ESRD ranged from (64) patients per million populations in Yemen, (212) patients per million populations, Qatar, (93) patients per million populations. In the light of these estimates, it is expected to have nearly (20,000) new cases of ESRD every year.

The prevalence of ESRD is increasing at an alarming rate. Higher prevalence rates are reported in Japan (1149.9) person per million population and the United States of America (975) person per million population). In Europe, the prevalence rate varies from one country to another, with an average of (283) person per million population) [24]. A cross-sectional, descriptive study conducted in France in 2003 showed that the prevalence of dialysis patients was (513.1) person per million populations, and total of number of patients treated with renal dialysis is 30,882 [25]. Table 2 shows the prevalence of ESRD in the Arab world [23] Table 3.

Country	ESRD Incidence (per million population)
Egypt	200
Qatar	212
Saudi Arabia	120
Jordan	70
Lebanon	120
Kuwait	72
Yemen	64

**Table 1:** Incidence of ESRD in the Arab world 2006.

Country	ESRD Prevalence (per million population)
Egypt	235
Qatar	262
Saudi Arabia	462
Jordan	120
Lebanon	243
Kuwait	80
Yemen	320
Average	352

**Table 2:** Prevalence of ESRD in the Arab world 2006.

City	No. of patients	No. of nurses in kidney unit	No. of nephrologists doctor	No. of dialysis machines
Jenin	81	9	1	11
Rammalh	75	8	1	12
Nablus	136	12	2	22
Tulkarem	43	6	0	9
Qalqilia	34	6	0	9
Jericho	23	5	0	6
Bethlehem	31	6	0	7
Hebron	142	12	2	24
Total	565	64	6	100

**Table 3:** Number of Cases of ESRD, Nurses in Kidney Unit, Nephrologists Doctors, and Dialysis Machines in West Bank, 2006. **Source:** Hospital Kidney Unit in West Bank. 2010

## ESRD in West Bank

The Palestinian Ministry of Health is the main health care provider for the ESRD management program in Palestine. The different treatment modalities of ESRD are free of charge. Patients with ESRD belong to group of Patients with “Special Diseases” and are eligible for a government health insurance.

In northern West Bank there are 8 dialysis centers serving 565 patients (at present). Patients usually do three dialysis sessions/week, each dialysis session last between 3-4 hours. Dialysis machines are old and not enough to cover for the increasing numbers of patients. And this situation keeps technicians working under pressure. In addition, some centers lack nephrologists doctor and in general the nurse patient ratio is 1:5, while the international standard recommends 1:3 [26], dialysis units are crowded with patients and most of unites have small working areas.

## Morbidity and Mortality in ESRD

ESRD causes a high rates of morbidity, mortality. Moreover, is responsible of many social and financial implications. This in fact lead to major public health problem. These problems could be seen clearly not only on different modalities of treatment like dialysis (hemodialysis and peritoneal dialysis),but also on existing co-morbidities, age, duration on dialysis, supportive therapies and infection control strategies [27].

The mortality rate in the US due to ESRD is 24% per year. Other leading causes of death in patients with ESRD are cardiac related which accounts for (43%) of all deaths in this population [28]. A study conducted in Turkey showed that mortality ratio of ESRD patients was 14.1%, while the mean age of patients was 60 years. The most common cause of mortality was cardiovascular diseases, and the most common cause of co-morbidity was infec-

tions, older age, anemia, absence of residual renal function, hypoalbuminemia, inflammation, and metabolism [29].

Another study conducted in Saudi Arabia showed that Diabetes Mellitus (40%), hypertension (39.2%), cardiovascular diseases (32.8%), hepatitis C (18.4%), and hepatitis B (8.8%) were the major co-morbidity causes of ESRD. The main reasons for patient with ESRD hospitalization were the vascular access problems (33.6%), infections (31.2%), cardiovascular disease (18.4%) and bleeding (6.4%)(40). The case fatality rate who started hemodialysis during the first year is (20%) in Jordan [30].

## Risk Factors of ESRD

### Diabetes Mellitus and Hypertension

A study was conducted in Canada to determine the prevalence of ESRD showed that the increases prevalence and incidence were estimated, particularly among people with diabetes mellitus. In 1996, there were (17,807) patients receiving renal replacement therapy in Canada. This number jumped to (32,952) by 2005, for a relative increase of (85%) and a mean annual increase of (5.8%) [31]. Over (90,000) of Americans developed ESRD with diabetes II. Current population of patients on dialysis therapy is (300,000). More than (80,000) patients are living with transplanted kidneys. Both prevalence and incidence of ESRD are approximately twice that were 10 years ago [32].

A study was conducted in UK showed that ESRD is common. The main risk factor for impaired kidney function is diabetes mellitus. About (30%) of patients with diabetes II develop some degree of diabetic nephropathy. In addition, a follow-up study conducted in South Africa showed that diabetes mellitus is a major risk factor of ESRD [33].

Across sectional study conducted in Egypt in order to determine the prevalence of diabetic nephropathy as a cause of ESRD showed that the prevalence of diabetic nephropathy increased gradually from (8.9%) in 1996, to (14.5%) in 2001. average age of patients with diabetic nephropathy was significantly higher than other causes of patients with ESRD. Mortality was also significantly higher in diabetic patients with ESRD [34].

A retrospective analysis study conducted in Saudi Arabia to determine Risk Factors for Developing ESRD. Results showed that diabetes II is the main risk factor [35]. In Jordan, another study about epidemiology of dialysis showed that prevalence of hemodialysis was (312) person per million population. ESRD incidence in 2002 was (111) person per million population. Therefore, diabetes mellitus was leading cause of hemodialysis (29.2%) of cases [30].

Hypertension is a main risk factor for increasing incidence of ESRD in men in the US. A follow-up study showed that elevation of blood pressure is a strong independent risk factor of ESRD [17]. Hypertension is considered one of main risk factors of ESRD in Kuwait especially in old age [36]. Both hypertension and diabetes mellitus are main risk factors for increasing incidence of ESRD in black men in USA. Studies showed that (30- 40%) of all patients with diabetes develop nephropathy, ESRD, and necessitating dialysis or kidney transplantation [37]. Another study demonstrated that the high prevalence (13%) of ESRD among adult American population is due to the rise in the number of people with diabetes and hypertension [38].

A cross-sectional study carried out to determine the causes of chronic renal failure among Iranian hemodialysis patients showed that hypertension (20.8%) and diabetes mellitus (36.6%) were the most common causes of ESRD in Iran. Main causes of ESRD did not differ significantly between men and women [39]. In Palestine, a study conducted in 2008 at An-Najah National University to determine the prevalence of reduced renal function among diabetic hypertensive patients showed that hypertension and diabetes mellitus are the most common causes of ESRD [40].

A case control study conducted in USA confirmed that kidney stones increased the risk of chronic kidney disease especially interstitial nephritis, diabetic nephropathy, and hypertension. Chronic kidney disease is frequently seen among patients with kidney stones, an estimated percent of (10% - 15%) of patients eventually develop chronic kidney failure [27].

A cross sectional study conducted in Caribbean showed that Hypertension, chronic Glomerulonephritis and diabetes mellitus were the common causes of ESRD [41]. Another cross sectional study conducted in Saudi Arabia to determine epidemiology and causes of ESRD showed that dialysis patients increase in the (KSA). Patients' average age was (55) years. Main causes of

(ESRD) include diabetic nephropathy(28%), hypertension(24%), unknown(23%) and obstructive uropathy (8%) [42]. A study conducted in Egypt showed that hypertension was responsible for (28%) of the cases of renal failure in Egypt. Other significant causes were: chronic Glomerulonephritis (16.6%), ESRD of unknown etiology (16.2%), obstructive uropathy (9.3%), and diabetic nephropathy (8.9%) [24].

Another study conducted in Jordan confirmed that diabetes mellitus is the major leading cause of Hemodialysis. Other risk factors like hypertension and Glomerulonephritis are second and third risk factor, respectively [43].

### **Demographic Factors: Gender, Age, Smoking and BMI**

A descriptive study conducted in Iran showed that the prevalence of Chronic Renal Failure (CRF) is high in Iran. The age group with high risk of ESRD is (61-75) years old which constitute 38.5% [44]. A cross-sectional study was conducted in Korea. It showed that the prevalence of Chronic Renal Failure (CRF) increases with ageing. Particularly after (50) years in both genders [45]. Other cross-sectional surveys conducted in Japan showed that the prevalence of chronic kidney disease increased significantly in men not in women [46]. A prospective study conducted in French urban area showed incidence of ESRD in males and a dramatic increase of incidence with age in both genders [47].

A follow up study in the US evaluated the prognostic value of several potential risk factors for ESRD confirmed that the two most common risk factors were proteinuria and obesity [48]. Another study in the USA determined that obesity is a risk factor for kidney failure, whereas hyperlipidemia and smoking were not significant risk factors for ESRD [37]. A cross-sectional study conducted in Singapore showed that higher BMI levels were positively associated with chronic kidney failure among men but not in women [49]. A cohort study conducted in USA showed that overweight and obesity are important independent risk factors for chronic kidney failure and ESRD [50].

Another cohort study conducted in USA to determine the association between increased (BMI) and risk for ESRD showed that higher baseline BMI remained an independent predictor for ESRD. After additional adjustments for baseline blood pressure level and presence or absence of diabetes mellitus [51]. In addition, cross-sectional health survey conducted in Norway showed that obesity, smoking, and physical inactivity were significantly associated with ESRD [52]. A retrospective multicenter matched case-control study conducted in nine centers in Germany, Italy and Austria to assess whether tobacco consumption increases the risk of ESRD showed that in men with inflammatory or non-inflammatory renal disease cigarette smoking significantly increases the odds ratios to ESRD. Adverse effect of smoking on renal failure prognosis in the women were found to positive [53].

## Analgesic Drugs

A survey study conducted in USA confirmed that frequently taken analgesic drug (acetaminophen or non-steroidal anti-inflammatory drugs) have an increased risk of ESRD, aspirin is excluded [54].

## Polycystic Kidney Disease and Cardiovascular Disease

A study conducted in Egypt showed that adult with polycystic disease of the kidney responsible for (4.3%) of the cases of ESRD [24]. A cohort study conducted in the US showed that Atherosclerosis is independently associated with an increased risk for incident chronic kidney failure in non-diabetic adults [55].

## Other Risk Factors

A community-based medical screening program conducted in Taiwan showed that Hypertriglyceridemia is an independent risk factor for chronic kidney failure in adults [56]. A cohort study conducted in Norway to determine the association between Preeclampsia in one or more pregnancies and the subsequent development of ESRD showed that preeclampsia is a factor of an increased risk of subsequent ESRD [57].

Another study conducted in USA to determine association between family history and incidence of ESRD showed that large proportion of incident ESRD cases have close relatives with ESRD in whom preventive actions might be directed. Genetic analyses in multiply affected families may identify the inherited factors contributing to progressive renal failure [58].

A case control study conducted in Israel showed that Amyloidosis is the most significant complication of familial Mediterranean fever (FMF), leading to ESRD. Recently, (MEFV) gene responsible of this disease was cloned and more than 18 mutations have been identified [59].

## Economic Costs of ESRD

Dialysis treatment takes up 0.7 to 1.8% of the health care budget in European countries [60]. Consequently, economic costs of ESRD are high. In 1999, more than 400,000 Americans required dialysis therapy and/or transplantation for kidney failure, and Medicare medical expenditure for ESRD care was more than \$11 billion [61]. With the current rate of population growth, there will be 172,667 incidents and 661,330 prevalent patients by the year 2010. The Medicare costs for care of ESRD will increase from \$ 12 billion to 28 billion over this time period [61]. The costs of medication and patient care are also growing. Between 1994 and 1999 spending on recombinant human erythropoietin treatment increased by 100% in the USA, the cost of intravenous iron supplementation increased by 50% and cost for Calcitriol or other vitamin supplements increased by 200% [61].

A prospective study was conducted in Canada to estimate direct health-care costs and productivity losses from short- and long-term ESRD disability [62]. The study showed less than 0.1% of Canadians have ESRD; however, the disease generated direct health-care costs of \$1.3 billion in the year 2000. The amount of direct spending per person with ESRD is much more than the average spending per person for all health-care conditions. Adding indirect morbidity and mortality cost brings the total burden associated with ESRD to \$1.9 billion. This economic impact is higher than that for skin or infectious diseases, about the same as for genitourinary or endocrine diseases, but lower than that for conditions such as cancer or a stroke [62].

The typical annual direct dialysis cost per capita is basically the same between countries [63]. It is noteworthy that peritoneal dialysis is the more expensive modality in countries that still import the dialysis solutions. For example, costs of dialysis modalities are approximately \$22,644 million for Hemodialysis and \$22,350 for peritoneal dialysis in Turkey [63]. The estimated total annual cost of Hemodialysis in Jordan was US\$ 29 million. Hemodialysis sessions accounted for about three-quarters of the total cost while medications and investigations accounted for an additional 20% [43].

## Discussion and Implications

This study was an effort to highlight the main factors that lead to ESRD. Identifying major risk factors on the onset of ESRD is an important part in preventing complications of developing ESRD. Based on our literature findings, our next step will be to conduct a cross sectional study of ESRD patients in the northern West Bank to determine the association between these major risk factors we identified through the literature and ESRD. Based on our literature, several international studies that were conducted in Japan, France, Iran, and Korea showed that ESRD dramatically increases with age, particularly after the age of 50 in both genders and males develop ESRD more than females [44-47]. Furthermore, studies conducted in the US showed that there is a positive association between BMI and ESRD [64]. Studies show that there is no association smoking on the onset of ESRD. Several other studies conducted in USA, Singapore, Norway, Germany, Italy and Austria showed that obesity and smoking are important independent risk factors for chronic kidney failure and ESRD [37,40,48,50-52,64].

Studies on the impact of gender and age could be due to genetic or social differences between the Palestine community and other communities. Other studies conducted in the US that indicates an association between family history and incidence of ESRD [58]. Family history of renal disease, diabetes, cardiovascular disease, and hypertension have a high probability of developing ESRD [30-32,34]. Studies were conducted in the world show that elevations of blood pressure are a strong independent risk factor for ESRD [17,36].

Other studies conducted USA, Caribbean, Iran, Saudi Arabia,

Egypt, Jordan, Palestine showed that hypertension and diabetes mellitus were the most common causes of ESRD [24,27,37,39,40-43]. Studies show that there is significant association between patients who have diabetes mellitus and hypertensive with onset of ESRD. This can be explained on the light of rapid urbanization, transformation into sedentary life style, increase in prevalence and incidence in diabetes mellitus and hypertension lead to the increase in number of cases of chronic kidney disease. There were significant effects of diabetes mellitus, hypertension and cardiovascular diseases on onset ESRD. When a patients suffers from a total of pathology chronic disease (diabetes mellitus, hypertension and cardiovascular diseases) are more likely to get kidney failure. Changes in the pattern of living, increase in incident chronic diseases lead to a high complication.

Several study conducted in different country confirm that there is a significant association between glomerulonephritis and other urinary tract infection with incident of ESRD [24,27,41-43]. A study in the US confirmed that frequently taken analgesic drug (acetaminophen or Non steroidal Anti-inflammatory Drugs) have an increased risk of ESRD. Polycystic Kidney Disease is the main genetic disease that causes ESRD. A study in Egypt show that polycystic disease of the kidney is responsible for (4.3%) of the cases of ESRD [3].

## Conclusion

This study was an effort to highlight the main risk factors that lead to ESRD. Identifying major risk factors in the onset of ESRD is vital to focusing on prevention of ESRD and the complications associated with the disease. There should be more attention needed to improve the quality of renal replacement therapy and facilities, this could be achieved through increasing the number of qualified staff and the dialysis machines. Furthermore, knowing the causes also makes advancements on prevention and early treatment. This will reduce overall health system costs associated with ESRD. The need to conduct and improve national programs of kidney transplantation in Palestine, and also to increase community awareness about kidney donors is critical. Furthermore, since renal replacement therapy is costly, the necessity of initiating preventive health programs especially among high-risk group such as patients with diabetes mellitus, hypertension, cardiovascular is highly essential. Moreover, increasing public awareness of taking medications without doctor's prescriptions is another important area. It should be noted that monitoring patients' access to medications and pharmacies are necessary. Another area of focus is the necessity of conducting other research in the field of renal failure and ESRD risk factors. Our research highlights the importance of identifying major risk factors that affect ESRD from international perspectives. Based on the evidence we gathered, we hope to shed on light on making changes and improvements to prevent and treat those with ESRD in Palestine.

## Special Note

This paper is excerpted from the thesis of Kazem Nazme Basheer. The full thesis is available online at the An-Najah National University website.

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