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Hemodialysis Status in an Egyptian Coastal City, Alexandria: An Epidemiological Study with a 3-year Prospective Mortality Observation

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Authors' contributions

This work was carried out in collaboration among all authors. Author AFM gave the research idea and designed the study. Author AMF did the data acquisition. Author RMFS did the data analysis/interpretation. Author NSA supervised or mentored of the study. Author AFM took responsibility that this study has been reported honestly, accurately and transparently, and accepts accountability for the overall work by ensuring that questions pertaining to the accuracy or integrity of any portion of the work appropriately investigated and resolved. All authors read and approved the final manuscript.

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ABSTRACT

Backgrounds: Hemodialysis (HD) represents the main modality of RRT in Egypt and it constitutes a burden on the health care budget. In Alexandria province of Egypt, HD service is provided through fifty-seven HD units, which are categorized into twenty-one nonprofit units and thirty-six private for-profit HD units. Our aims were to study epidemiology and to assess the three-year survival of ESRD patients treated by HD in governmental hospitals in Alexandria province.
Methods and Design: In the year 2016; the data of the patients were collected from all the

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governmental hospitals in Alexandria province, which comprised seven HD units containing 687 patients. In a cross-sectional arm of the study, demographic data, vascular access, HIV, HBV and HCV serology, the possible etiology of chronic kidney disease (CKD), associated comorbidities, and the routine laboratory variables were included. Furthermore, in a prospective phase of the study, a three-year-survival rate of the studied HD patients was recorded.

Results: The total number of HD patients in Alexandria province during 2019 was totaled to be 3552 in all HD units, so the estimated HD prevalence rate would be around 710 ppm. Demographic data of the surveyed 687 patients in the governmental HD units showed their mean age; 50.78 years with more males, and their mean duration of HD; 55 months. It was also noted that there was no positive seroconversion regarding HCV, HBV nor HIV. Sixteen HCV antibody-positive patients received direct-acting antiviral drugs and were converted to HCV PCR-negative. HTN was more common etiology of CKD in males, while DM and combined DM and HTN were more common in females. The target hemoglobin level was present in around 37% of the studied HD patients. Most of the studied patients had serum calcium ranged from 8-10 mg /dl and 53% of them had serum phosphorus ranged from 3-5.5 mg /dl. Para-thyroidectomy was done for 2% of the studied patients while 4% of cases received cinacalcet. The 3-year, 5-year and 7-year survival rates were 92.5%, 87%, and 82% respectively.

Conclusion: The epidemiology of hemodialysis patients in Alexandria province is not different in many aspects from other published data about some Egyptian governorates however there is no published new epidemiology about the whole country. 11.2% of HCV Abs positive became PCR negative after antiviral management protocol.

Keywords: Epidemiology of HD; Alexandria; Egypt; mortality.

1. INTRODUCTION

CKD is emerging as an essential non-communicable disease worldwide. The three crucial risk factors of CKD are diabetes mellitus (DM), hypertension (HTN), and obesity, which are highly prevalent in developing countries including Egypt. Before 1996, the epidemiology of the ESRD in Egypt was not examined on a national scale [1]. CKD is a major health problem that leads to ESRD requiring RRT.

Regular dialysis treatment has been available at a national level in Egypt for more than three decades [2]. HD is a vital and lifesaving procedure so that many organizations, including governmental and non-governmental bodies, adopt it. HD service is usually provided by either non-profit- or profit-based bodies. Non-profit HD centers are divided into HD units related to university hospitals, military hospitals, and police hospitals, or those related to the ministry of health. The latter is further divided into insurance hospitals, teaching hospitals, and government hospitals. Egyptian government usually subsidizes the cost of HD in almost all sectors.

Only a few studies have systematically examined the epidemiology of HD population in Egyptian provinces; namely, Sohag [3], El-Minia [4], Kafr El Sheikh [5], Dakahlia [6], Menoufia [7] and [8], Assiut [9], Sharkia [10] and El Beheira governorate [11]. An Annual Report of the Egyptian Renal Data System (ERDS 2018), representing seventy-four dialysis units from 17 Egyptian governorates (cities) who participated with their data with a total number of 6,757 patients, was declared recently [12]. However, nation-wide Egyptian epidemiological data are still incomplete and need further study and proper registration.

Alexandria city, the capital of Alexandria province, is the second-largest and populous city, and the most important port in Egypt. In this province, HD service is provided through fifty-seven HD units, which are categorized into twenty-one nonprofit units (five universities, nine insurances, and seven governmental) and thirty-six private for-profit HD units. The well-designed health care service structure and limited distance between the governmental units in Alexandria pave the way for a systematic epidemiological examination of the HD patients in this coastal region.

1.1 Aim of the Work

The present work aims to study epidemiology and assess the three-year survival of ESRD patients treated by HD in governmental hospitals in Alexandria province.

2. PATIENTS AND METHODS

The current work was instigated in the year 2016. The data of the patients were collected from all the governmental hospitals in Alexandria province of Egypt, which comprised seven HD units containing 687 patients. In a cross-sectional arm of the study, treating physicians and residents as well as qualified nurses collected the patients' data by a questionnaire form, which included demographic data, vascular access, HIV, HBV and HCV serology, associated comorbidities, possible etiology of CKD and the routine laboratory variables. All laboratory investigations were done through sample withdrawn pre-hemodialysis session. The possible etiological diagnosis of CKD was recorded subjectively according to the opinion of the treating consultants. Furthermore, in a prospective phase of the study, a three-year-survival rate of the studied HD patients was recorded. On the other hand, the total number of HD units and the total number of HD patients throughout the whole province was retrieved from the Alexandria Directory of health affairs in June 2019.

The seven governmental HD units surveyed included; Abo Keir Hospital (127 patients), El Gomhorya Hospital (109 patients), Alexandria Fever Hospital (114 patients), Borj El Arab Hospital (58 patients), El Agamy General Hospital (48 patients), Ras El Tin General Hospital (72 patients), El Amrya Hospital (159 patients).

2.1 Statistical Analysis and Data Interpretation

Data were collected, revised, verified then edited on a personal computer and analyzed using IBM SPSS software package version 22.0. Qualitative data were described using numbers and percentages. Quantitative data were described using mean ± standard deviation for parametric data, or median (minimum-maximum and/or interquartile range) for non-parametric data after testing for normality using the Kolmogorov-Smirnov test. The significance of the obtained results was judged at the (0.05) level. For qualitative data, the Chi-Square test with or without correction maneuvers was used for comparison of the distribution of observation(s) between 2 or more groups of patients. Kaplan-Meier test was used to calculate overall survival and disease-free survival by using log-rank $\chi 2$ to detect the effect of risk factors affecting survival.

3. RESULTS

The number of HD patients in Alexandria province during 2019 was totaled to be 3552 in all HD units. Since the province has a population of around five-million individuals, then, the estimated HD prevalence rate would be around 710 ppm. The newly admitted patients over the three years of the study observation were found to be 473 patients, giving an estimated mean frequency of newly admitted cases of ~158 patients/year (data were not shown).

According to the regulations of the prevailing rules, all patients were offered regular HD sessions three times per week, four hours each, utilizing bicarbonate-based dialysate with a blood flow rate of 300 ml/min and a dialysate flow rate of 500 ml/min. Dialysis-related water treatment in all of the included HD units was carried out following the Egyptian MOH guidelines [13]. Dialysis adequacy was assessed utilizing the urea reduction ratio (URR); being targeted to be above 60%.

Demographic data of the surveyed 687 patients in the governmental HD units in Alexandria province are shown in Table 1. Their mean age was 50.78 years and around 63% of them were between 19-55 years of age, with more males than females, and their mean duration of HD was 55 months. The mean BMI of the total studied group was 27.5±5.3. Most of the HD patients received HD through arterio-venous (A-V) fistulae (92.1%) and only 1.2% of total patients had previous kidney transplantation.

Table 2 shows the status of seroreactivity to hepatitis C virus antibodies (HCV-Abs), hepatitis B surface antigen (HBsAg) and antibodies to human immunodeficiency virus (HIV-Abs). During the period of the study, it was noticed that the frequency of HCV-antibody-positive patients and that of HBsAg changed from 142 and 19 out of the 687 patients (20.6% and 2.76%, respectively) to 129 and 30 out of the 801 patients (16.1% and 3.74%, respectively), in the years 2016 and 2019, respectively. Moreover, sixteen HCV antibody-positive patients received direct-acting antiviral drugs (Qurevo) and were converted to HCV PCR-negative. (data were not shown), In 2019, the study included three HIV antibody-positive cases who were dialyzed in the Fever Hospital; being the only place that accepts this type of patient in the province (data were not shown). It was also noted that there was no positive seroconversion regarding HCV, HBV nor HIV.

The routine Laboratory variables of the studied HD patients are shown in Table 3, while Table 4 shows the relation between one-year mortality and different variables denoting that males had statistically significantly higher mortality than females.

The distribution of possible etiologies of ESRD in both genders is illustrated in Graph 1, revealing that while HTN was more common in males, DM and combined DM and HTN were more common in females. While HTN represented the most common possible cause of CKD, followed by DM, pregnancy-related factors were the least cause for ESRD. However, in a significant proportion of cases, the cause of ESRD was unknown. Similarly, the frequency of commonly associated comorbidities is shown in Graph (2) denoting that the commonest comorbidities were HTN and Ischemic heart disease (IHD).

The type of HD vascular access in both genders is demonstrated in Graph 3, showing that permanent HD catheters were more commonly used in females, while the graphs for distribution of their hemoglobin level, corrected serum calcium, and serum phosphorous are depicted in Graphs 4 and 5a, b respectively. Graph 5c shows the frequency of distribution of the parathyroi*d hormo*ne levels in these patients. Thirteen patients (1.9%) were noticed to have had Para thyroidectomy performed before the study, whereas 4% of the cases were maintained on calcimimetics (data were not shown).

Graph 6 and Table 5 show that the median survival after initiation of HD among the studied cases was 17.67 months with a confidence interval ranging from 15.25 to 20.09, while the 3-year, 5-year, and 7-year survival rates were 92.5%, 87% and 82%, respectively.

4. DISCUSSION

The prevalence of ESRD requiring RRT is believed to be increasing in Egypt and it constitutes a burden on the health care budget in our country since all the health care needs of these patients are subsidized by the Egyptian ministry of health (MOH). It is well known that HD represents the main mode of RRT in Egypt, and Alexandria is not an exception. The epidemiology of ESRD in Alexandria has not been formally examined before 2016. Alexandria, a coastal city on the Mediterranean Sea in the north of Egypt, with a total area of 2833 km^2, has a population of around five million individuals (National institute of urban planning, [14,15], and [16]. As registered in the records of Alexandria's Directory of health affairs, the number of HD patients was known to be 3523, which means 710 pmp. Lack of data on the previous frequency of patients on HD in Alexandria province makes accurate identification of the changing prevalence of ESRD not feasible. Only eight cases out of 687 HD patients, who were treated in governmental hospitals, had had kidney transplants before the study.

Table 1. Demographic data of patients in Alexandria governmental hemodialysis units*

		Mean±SD
Age in years (N=687)		50.78±12.75
BMI in total population (N=302)kg/m^2		27.5±5.3
BMI in females (N=144)kg/m2		28.2±5.7
BMI in males (N=158) kg/m2		26.8±4.9
Duration of Dialysis (N=673) in months		55.06±50.76
Pre-sessional systolic blood pressure. (N=583)		129.7±18.5
Pre-sessional diastolic blood pressure (N=584)		81.09±10.05
Gender: Male/total [N (%)]		357/687 (52.0%)
Previous kidney transplantation [N (%)]		8/687 (1.2%)
Vascular access	Fistula [N (%)]	606 (92.1%)
N=658	Permanent catheter [N (%)]	33 (5%)
	Graft [N (%)]	1 (0.15%)
	Temporary Vascular access[N (%)]	18 (2.7%)

**N represents the number of available data*

Table 2. Frequency of viral serology in hemodialysis patients in Alexandria governorate*

Viral serology (N=687)	N(%)
Negative viral serology (HCV, Hepatitis B,HIV)	534(77.7)
HCV - antibody-positive	134(19.5)
HBs - antigen-positive	11(1.6)
Both HBs antigen and HCV-antibody-positive	8(1.16)

** N represents the number of available data*

Table 3. Laboratory variables in hemodialysis patients in Alexandria governorate*

	Mean ±SD
HB (N=585)	9.49±1.55
Albumin (N=133)	3.24±0.58
Urea reduction ratio(URR) (N=522)	0.59±0.11
pre-dialysis session blood-urea (N=591)	133.84±38.79
Serum creatinine (N=527)	7.76±5.1
Serum potassium (N=170)	5.05±1.12
Serum calcium (N=385)	8.58±1.22
Serum phosphorus(N=380)	5.3±1.5
Parathyroid hormone level (N=167)	560.86±566.8
Serum ferritin (N=79)	468.73±375.3
Transferrin saturation (N=96)	28.07±10.65

**N represents the number of available data*

Table 4. Relation between one-year mortality from June 2016 until May 2017 and different variables*

	Mortality		Test of significance
	Alive N (%)	Dead N (%)	
Sex	616(89.7%)	71(10.3%)	
Female (N=330)	305 (92.4)	25 (7.6)	χ^2=5.22
Male (N=357)	311 (87.1)	46 (12.9)	P=0.02
Vascular access			
A-V Fistula (N=606)	545 /606(89.94)	61/606(10.06)	Monte Carlo test
Permanent catheter	28/33(84.8)	5/33(15.2)	P=0.57
Temporary catheter	16/18(88.9)	2/18(11.1)	
***Possible etiology**			
Unknown	144/155(92.9)	11/155(7.1)	χ^2=2.26 P=0.13
Hypertension(HTN)	245/269(91.1)	24/269(8.9)	χ^2=0.952 P=0.329
Diabetes (DM)	63/75(84)	12/75(16)	χ^2=2.92 P=0.087
Combined DM and HTN	32/45(71.12)	13/45(28.88)	χ^2=17.89 P<0.001*
Pyelonephritis	31/35(88.57)	4/35(11.43)	χ^2=0.047 P=0.83
Obstruction and stones	26/29(89.66)	3/29(10.34)	χ^2=0.0 P=1.0
Glomerulonephritis	18/20(90)	2/20(10)	χ^2=0.0025 P=0.96
Polycystic kidney disease	15(100)	0(0.0)	χ2=1.77 P=0.18
Interstitial nephritis (Drug induced)	7/8(87.5)	1/8(12.5)	χ2=0.041 P=0.84
Urinary Reflux	7/8(87.5)	1/8(12.5)	χ2=0.041 P=0.84
Hereditary	23/23(100)	0(0.0)	χ2=2.74 P=0.09
Pregnancy related	6/6(100)	0(0.0)	χ2=0.041 P=0.84

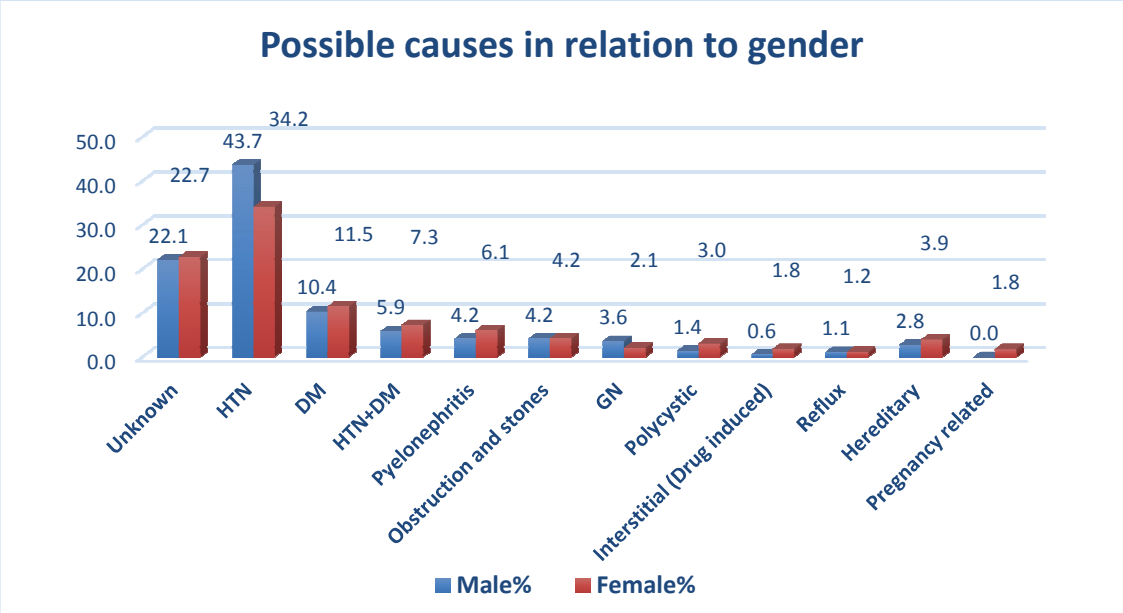
**N: represents the number of available data*

**Possible etiology: the suspected etiology according the treating team*

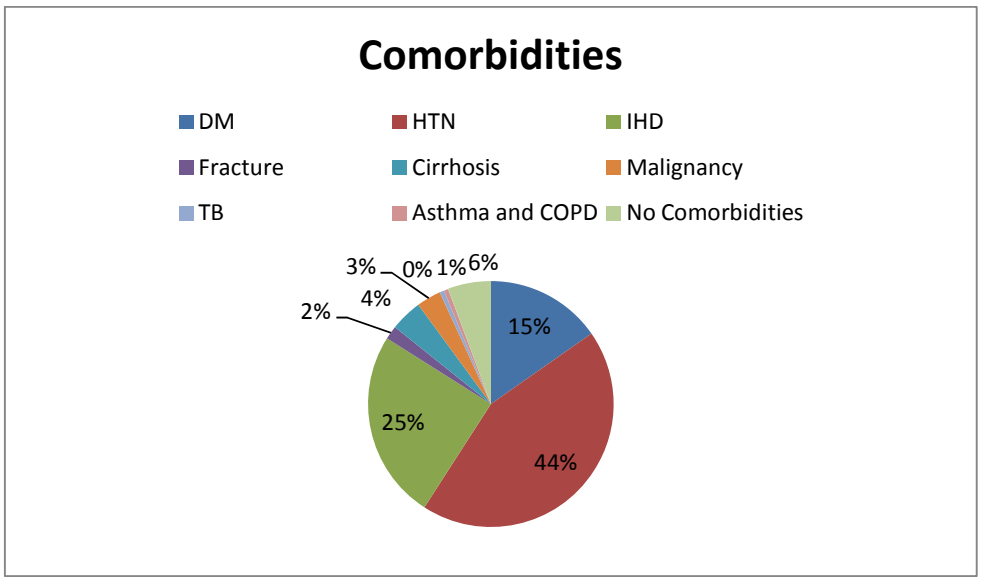
Table 5. Median overall survival time

Median overall survival time/years	Std. error	95% confidence interval	
		Lower bound	Upper bound
17.67	1.235	15.246	20.087

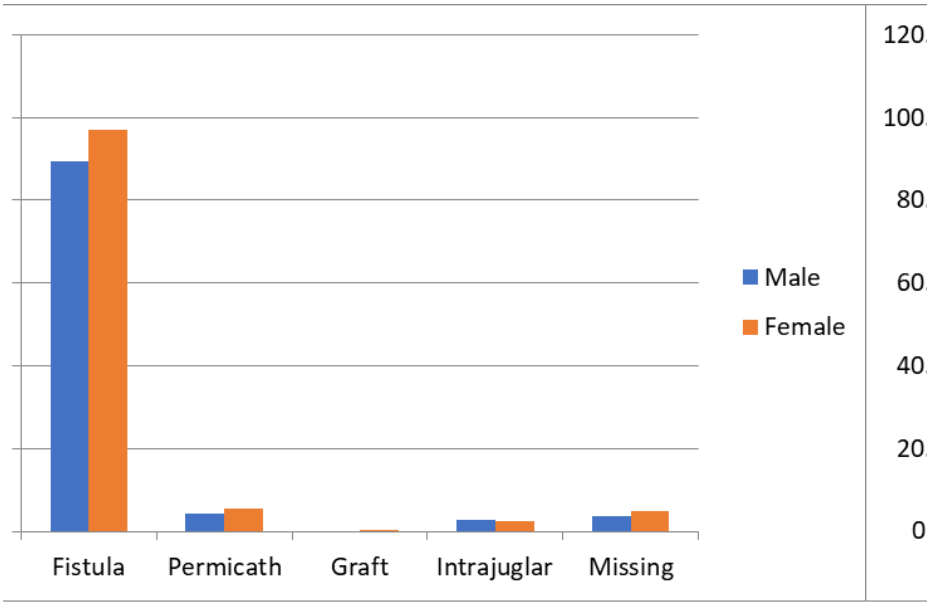
a. Estimation is limited to the largest survival time if it is censored



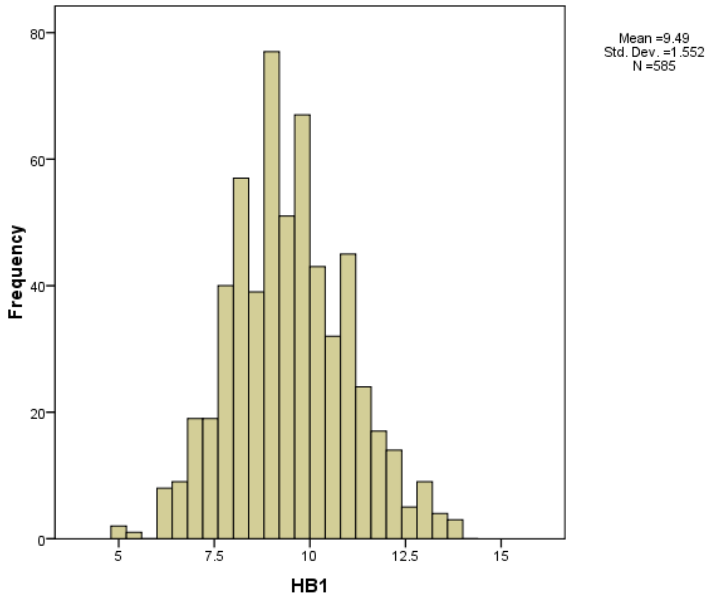
Graph 1. Relation between gender and possible etiology of CKD



Graph 2. Associated comorbidities in the studied group

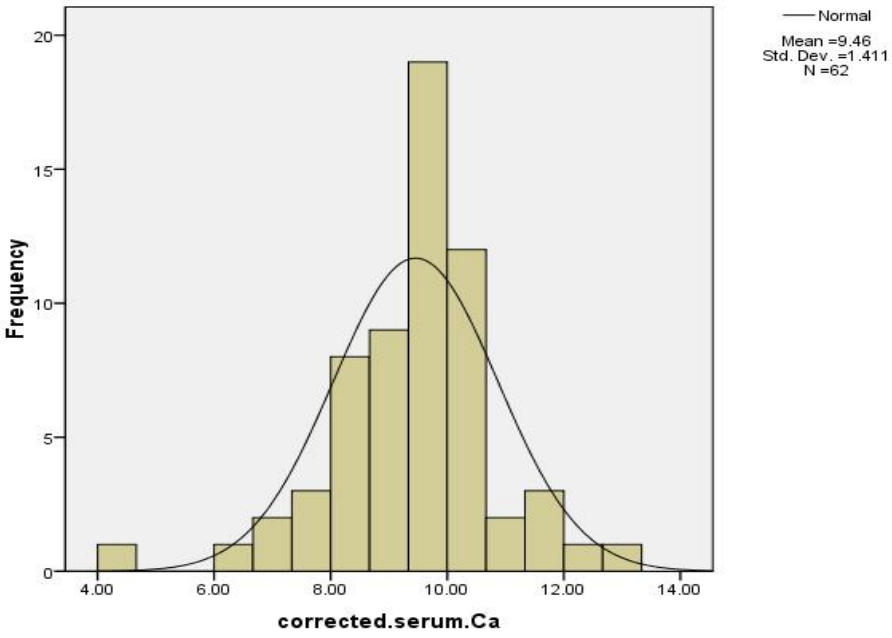


Graph 3. Relation between gender and vascular axis

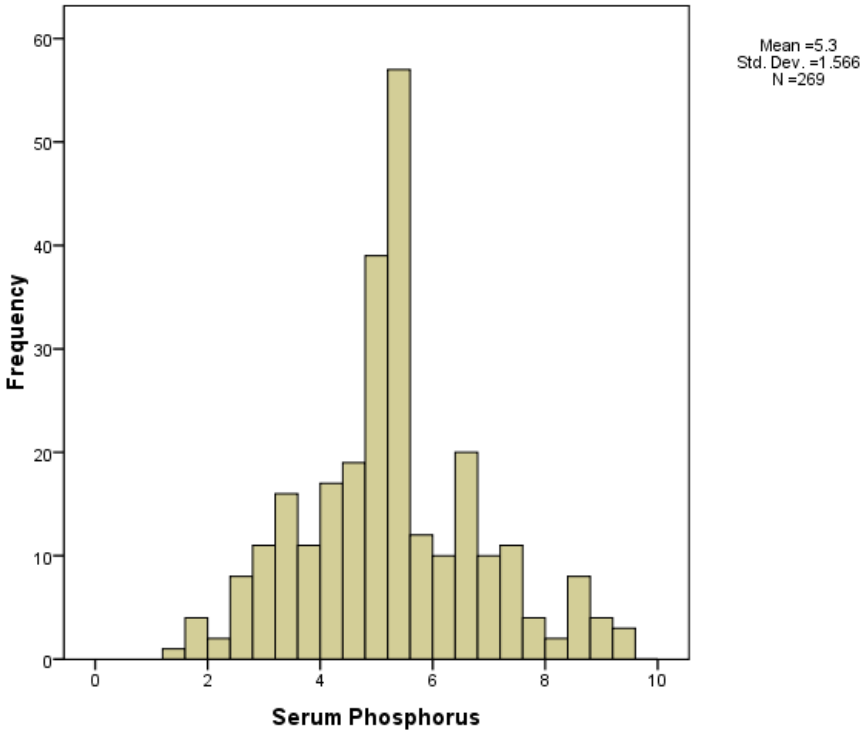


Graph 4. Histogram for hemoglobin

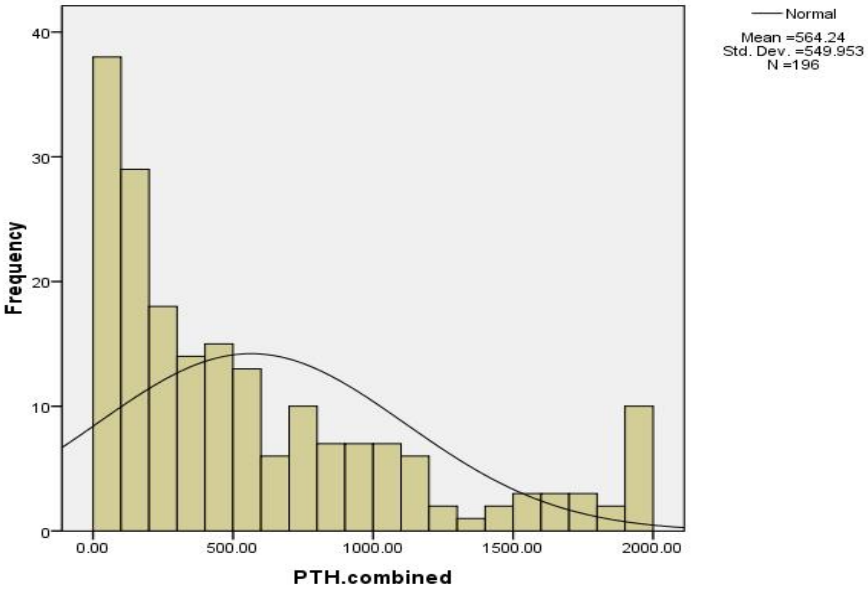
The prevalence of ESRD worldwide differs significantly; the highest prevalence was found in Taiwan (0.16%), [17], while the lowest prevalence was 230 pmp in the Philippines [18]. In the USA, the prevalence was; 2,160.7 pmp, during the year 2016 [19], while in Europe, the prevalence increased from 889 pmp in 2008 to 924 pmp in 2014 [20,21]. In Egypt, there have been no published studies, until now, that covers the prevalence of ESRD all over the country. Nevertheless, a Ministry of Health official stated that the total number of HD patients during the year 2016 was 56,000 from a total population of over ninety-four million; giving a prevalence rate of ~593 pmp [22,16].



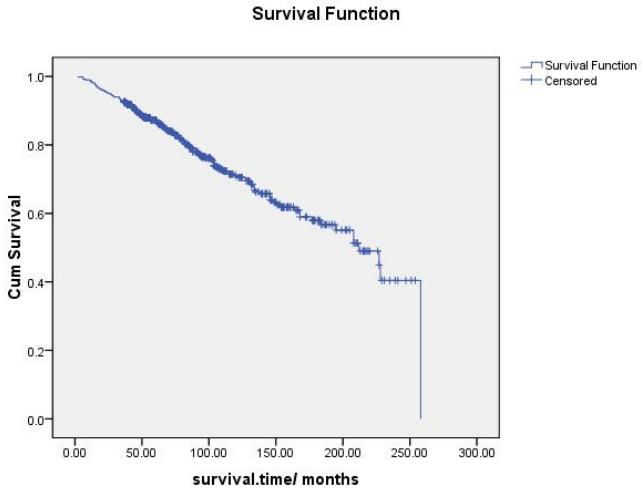
Graph 5a. Histograms of corrected serum calcium in the studied group



Graph 5b. Histograms of serum phosphorus in the studied group



Graph 5c. Histograms of parathyroid hormone in the studied group



Graph 6. Kaplan-meier curve for 3-year survival

Additionally, few studies have been published tackling such an issue in some Egyptian localities. In Upper Egypt, several studies were published: A study in El-Minia governorate during the year 2006 reported a prevalence rate of 308 pmp [4]. In Sohag during the year 2010, the prevalence was 316 pmp [3], while in Assiut it was 366 pmp during the year 2014 [9]. On the other hand, in Lower Egypt, the prevalence in Kafer El Sheikh during the year 2012 was 283 pmp [5], in Menoufia during 2013 it was 330 and increased to 483 pmp during 2016 [7,8], while in Dakahlia governorate, the prevalence was 462 pmp and 503 pmp during the years 2013 and 2014, respectively [6]. In the El Beheira governorate, the prevalence during the year 2018 was 571 pmp [11]. This relatively low prevalence of ESRD-HD in Egypt is felt to be an underestimation of the real problem taking into consideration relatively poor data registration and documentation in this respect. Another explanatory issue might be a possible relatively higher mortality of HD patients compared to the developed countries.

In our study, the mean age of HD patients is 50.78 with male to female ratio 1.1:1 and the mean duration of HD is 55.06 months. In this respect, the mean duration of HD was previously reported to be 3.78±3.372 years in Menofia province during 2016 [8], while Afifi (2008) reported that the mean age in Egypt had increased from 45.6 years in 1996 to 49.8 years in 2008 [23]. The increasing mean age of ESRD patients on HD, together with the increase in the mean duration of HD, might reflect the potential progressive improvement in the healthcare services in Egypt in recent years. Recently, the Egyptian Ministry of Health has launched several steps and measures to increase the awareness of CKD, advising the treating medical practitioners on testing kidney function routinely, and early referral to a nephrologist. However, there is still a window for improvement of health care service and prevention of CKD, as the mean age of the HD patients in our country is much lower than that in the USA (69.1 years; [24] and Europe (64.4 years; [23]).

In this study, the prevalence of hepatitis C was 19.5% in the studied HD population in governmental HD units and showed a decreased prevalence of HCV Abs +ve from 20.6% in 2016 to 16.1 in 2019. This decrement in the prevalence of HCV might, at least partially, be in harmony with an overall significant reduction of 32 and 29% in the prevalence of HCV-antibody- and HCV-RNA-positive individuals, respectively, between the Egyptian Health Demographic Survey, carried out in 2008 and the Egyptian Health Issue Survey conducted during 2015, had been published [25]. The prevalence of HCV in Egyptian HD patients might have decreased, at least in part, due to the protocol of isolation of HCV patients and infection control programs that have been implemented in all HD units, as well as the initiation of the protocol of management of HCV in HD patients that was carried out all over the country. On the other hand, the worldwide prevalence of HCV in HD patients showed wide variations, with estimates ranging from 5% to approximately 60% depending on geographic location ([26] [DOPPS in 3 continents], [27] [Italy], [28] [China] and [29] [Iran]). In 2002, the prevalence of HCV infection across HD centers of the United States was approximately 8%, nearly five times greater than that of the general population in that country [30].

The prevalence of HBsAg *s*eropositivity in the governmental hospitals was 2.76% in 2016 and increased to 3.7% in 2019 but without seroconversion. This prevalence was lower than that of most of the Arab countries: HBsAg was 5.88% among 81 Bahraini and 34 Saudi HD patients [31], 7.8%, in a Syrian study [32], and 8.1% in the Gaza Stripe [33]. There is a strict protocol for vaccination of HBV for all HD patients and staff in Egypt. Moreover, blood testing before transfusion for HBsAg-positive has been implemented as a strict routine rule since the last decade of the previous century. The rate of serum HBsAg seropositivity in patients on maintenance HD in the developed world is currently low (0–10%) while it appears higher (2–20%) in developing countries based on relatively few reports [34,35].

In the current study, the main identifiable potential cause of ESRD on HD was HTN (39.2%), followed by DM (10.9%), while the leading cause was unknown in around 22%. This is similar to previous local epidemiological studies performed in. El Beheira [11] and Sharkia [10] governorates, while unknown causes exceeded 30% in the epidemiological studies conducted in Dakahlia [6] and Menoufia [8]. Notably, HTN is the commonest leading cause of ESRD on HD in nearly all epidemiological studies all over Egypt. In accordance with that, the Egyptian Annual Report of ERDS (2018) nominated HTN (38%) followed by DM (18%), as the most common causes of ESRD. Patients with ESRD of unknown etiology represented the third common presentation (12%). However, in a few studies considering patients treated by HD, DM was the leading cause of ESRD, followed by HTN (34.7% and 21.5% in one study and 46% and 19% in another one, respectively; [36,37]. In the current work, interstitial nephritis, hereditary nephritis, and pyelonephritis were more common in the female gender as a leading cause of ESRD on HD; a difference that could be explained by more tendency for female gender to urinary tract infection, and the possibility of them using more analgesics.

Treatment of CKD-MBD targeted at lowering high serum phosphate and maintaining serum calcium [38], and management of anemia is an essential part of the care of hemodialysis patients [39]. In Egypt, drugs controlling the calcium/phosphorus axis (calcium carbonate, alfacalcidol, cinacalcet) and the use of ESA therapy are offered for HD patients through a fund by the MOH. Most of the studied patients of the current study had serum calcium ranged from 8-10 mg/dl and 53% of them had serum phosphorus ranged from 3-5.5 mg /dl. Parathyroid hormone level ranges were

less than 150 pg/ml in 30% of patients and more than 700 pg/ml in 32%, while 38% of them had a PTH range between 150 and 700 pg/ml. Para thyroidectomy had been performed for 2% of the studied patients while 4% of cases were receiving cinacalcet. These findings were similar to the Egyptian Annual Report [12] that declared that 2% of the Egyptian hemodialysis patients had para-thyroidectomy and 5% of them were receiving cinacalcet. The target hemoglobin level that set by KIDIGO guidelines, which ranged from 10 to above 11.5 g/dl, was present in around 37% of the studied HD patients [39]. This was nearly similar to the finding of a previous study that reported that 40% of the prevalent dialysis patients had a mean monthly target hemoglobin level of 11-12 g/dl, [40].

Mortality rates among HD patients vary greatly across regions and according to differences in age, gender, race, and comorbid conditions. The one-year mortality rate was 10.3% in the current study, while, according to the Dialysis Outcomes and Practice Patterns Study (DOPPS) the mortality rate was reported to be 6.6% in Japan, 15.6% in Europe, and 21.7% in the USA [41]. The median survival time among our studied cases was 17.67 months with a confidence interval ranging from 15.25 to 20.09. The 3-year, 5-year, and 7-year survival rates were 92.5%, 87% and 82%, respectively. Msaad et al. [42] reported that overall survival was 80.2% of their studied hemodialysis patients; their data were collected between January 2012 and January 2016.

5. CONCLUSION

The prevalence of ESRD on HD in Alexandria governorate, Egypt, was 710 ppm. Compared to previous Egyptian studies, there was an increasing age of HD patients and an increased duration of HD. HTN and DM were the most common possible etiologies of ESRD. Hepatitis C infection in dialysis patients have been decreasing and there was zero positive seroconversion as regard hepatitis B and C, while HCV Abs positive cases became PCR negative after antiviral management protocol in 11.2% of patients. The 3-, 5-, and 7-year survival rates, following hemodialysis initiation, were 92.5%, 87% and 82%, respectively. Future studies are recommended in other regions in Egypt to highlight the effect of different ecologic factors on the morbidity and mortality of hemodialysis patients.

ETHICAL APPROVAL AND CONSENT

Depending on Egyptian minister of health and population decree #95/year 2005 for Health Research and decree #539/year 2016 – ICH – Good Clinical Practice, Declaration of Helsinki and World Health Organization Guidelines, the Ethics Committee meet in the Central Directorate of Research and Health Development and review. The approval number is Com. No/Dec. No: 11-2017/ 27. Moreover, consent was taken from all the participants.

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COMPETING INTERESTS

Authors have declared that no competing interests exist.

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