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Original Research Article

Gender differences in barriers for hepatitis C virus treatment access, uptake and adherence in Alexandria, Egypt, 2016

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Abstract

The objective of this study was to determine gender differences in barriers associated with HCV treatment access, uptake and adherence. A descriptive hospital based comparative cross sectional study was conducted between May 2015 and April 2016. The target population was 240 chronic infected HCV patients who met the inclusion criteria, attending 3 hospitals in Alexandria city. Data were collected through pretested pre-coded structured interview format. Two separate multivariate logistic regression models were fit for each sex. Generalized estimating equation logistic regression was used to evaluate factors contributing to 95% confidence access, uptake and adherence to HCV therapy. There were differences between males and females regarding specific demographic, clinical, individual, psychosocial and healthcare factors facilitating treatment access and uptake. Women had lower levels of HCV knowledge, self- efficiency, and social support, had higher prevalence of psychological comorbidity, felt more social stigma and healthcare discrimination. Treatment access was low for both sexes. Fewer women had access to diagnostic tests, medication and continued care compared to men. Many patient, provider, healthcare and community barriers were significantly perceived by women that impact HCV treatment. Our findings indicated that social, behavioral, clinical, and health service characteristics associated with HCV treatment access, uptake, and adherence are potentially different among women and men. Early gender-based intervention strategies to improve treatment access should focus on these differences.

Key words: Hepatitis C virus (HCV), Gender differences, barriers, treatment access

INTRODUCTION

Hepatitis C is among the most common notifiable infectious diseases and the majority of those affected develop chronic illness (Smith et al., 2007). Worldwide 180 million people are estimated to live with chronic HCV (World Health Organization, 2012). Each year, over 350000 die from HCV (World Health Organization, 2010). The 2014 Egyptian Demographic Health Survey (EDHS) measured HCV prevalence to be 14.7% among a nationally representative sample of 11,126 Egyptians aged 15–59 years old. Accordingly, Egypt suffers from a particularly high morbidity and mortality rate, with 40,000 dying from the disease each year (El-Zanaty and Way, 2014). It is estimated that roughly 15 million Egyptians currently suffer from Hepatitis C (El-Zanaty and Way,

2014). In Egypt, there are 170,000 to 200,000 new HCV cases every year due to inadequate infection control practices and injection therapy such as blood transfusions (El Sherbini et al., 2007). Today, HCV infection and its complications are among the leading public health challenges in Egypt (Abdel-Ghaffar et al., 2015).

Fortunately in Egypt, the HCV treatment landscape is changing; pegylated interferon, ribavirin and protease inhibitor regimens of 6–12 months duration, which generate serious adverse effects in about 10 % of people and achieve cure in only 70 % are being replaced by all oral, well tolerated interferon free, direct acting antiviral (DAA) therapy, often for 12 weeks duration, with cure in more than 95%. Egypt has embarked on a government-sponsored mass treatment program using several combinations of DAAs (El-Fishawy et al., 2016).

Evidence documents successful HCV treatment outcomes. Maximizing HCV treatment can be an effective HCV preventative measure. However, HCV treatment remains substandard. Barriers to accessing medical care for HCV have been receiving more attention in the last few years, with the realization that only a small percentage of those infected with HCV undergo antiviral treatment (Grebely, 2008). Barriers to HCV treatment access may occur at the patient, provider and healthcare system levels (Lettmeier, 2008). In addition to the above mentioned barriers, another evidenced barrier to antiviral treatment for patients and providers alike are co-occurring psychosocial problems. Poor self-efficacy and depression will give rise to low self-esteem, low self-worth, reduced motivation, reduced adherence, poor social support, greater perceived stigmatization, pessimism, hopelessness and reluctance to healthcare seeking (Krüsi et al., 2010).

Gender is an important factor that may explain barriers to effective HCV access and uptake. There is emerging evidence describing how gender intermediates the experience of HCV. Women may experience stigma associated with HCV more strongly than men (Smith et al., 2007). However, there is a lack of research investigating how gender affects HCV treatment access specifically (Krüsi et al., 2010; Swan, 2010; Lowry et al., 2011; Kurtz et al., 2005; Bourgois et al., 2004; World Health Organisation Regional Office for Europe, 2012). Swan 2010 found that women's concerns about confidentiality, stigma, treatment side effects and intolerance, all were barriers that impacted their HCV treatment uptake decisions more than men. HCV treatment knowledge has been also found to be particularly low among women, with women having higher HCV treatment refusal and/or premature interruption rates than men (Swan, 2010). Although, Krüsi et al, 2010 reported a significantly higher rate of dropout from pre-HCV treatment management among men (Lowry et al., 2011). Evidence more broadly suggests that women's treatment access decisions are situated alongside their caring responsibilities and lack of engagement with services (due to fear of child removal (Kurtz et al., 2005), incidences of physical, sexual, emotional violence (Bourgois et al., 2004), and the demands of funding a regular drug supply) (World Health Organisation Regional Office for Europe, 2012). Further research is needed to investigate how gender shapes barriers and facilitators to HCV treatment access, uptake and adherence.

The issue of gender difference has not previously been explored for HCV treatment access. Previous studies of self-reported health status have shown that women have poorer health profiles than men across a range of chronic conditions. Early social and medical research on HCV indicated inappropriate treatment and ineffective prevention strategies for women (Berg et al., 2004). Chronic illnesses could be managed most effectively when gender-specific health education and support is offered (World Health Organisation Regional Office for Europe, 2012). The present study aimed at exploring gender differentials in barrier factors associated with accessibility and adherence to treatment for HCV from patients' perspectives. This is important in order to develop gender-based guidance regarding HCV treatment access improvement, and the provision of psycho-social interventions targeting patients and providers.

The following research questions were addressed

1. What are the gender variations in the pattern of accessibility, uptake and adherence to HCV treatment?
2. What are the gender differences in demographic, personal, psychological, socio cultural and healthcare factors affecting accessibility and adherence to HCV treatment?
3. What are the gender variations in the most common perceived barriers to accessibility and adherence to treatment for HCV?

Subjects and Methods

We did descriptive, hospital-based comparative cross-sectional study in three hospitals of Alexandria city between May, 2015 and April, 2016. Patients with chronic HCV infection were recruited from HCV treatment settings (Hepatology clinics) in numerous locations serving rural and urban areas of Alexandria city as well as outside regions to ensure that the study subjects are diverse. The selected hospitals were the Main University Hospital, Insurance hospital (Gamal abed el Naser), and government hospital (Fever Hospital).

Inclusion criteria of the study subjects were patients; who had HCV infection that was diagnosed by serologic methods with confirmation by HCV RNA testing, aged 18 years and over, of disease duration not less than one year

and were able to provide informed consent for involvement. Exclusion criteria were pregnancy, advanced liver disease (decompensated cirrhosis), and cognitively impaired or mentally ill patients.

Sample size and sampling strategy

A qualified statistician determined the sample size using statistical program Epi-info. The number of patients (n) to be included in the study was estimated using the following equation: $n = (Z^2 \times p \times q) / D^2$ [18].

Since the actual prevalence of chronic hepatitis C infection is 14.7% (EDHS 2014) (World Health Organization, 2010), the probability of its occurrence was estimated to be nearly (p = 0.15), the probability of non-occurrence (q = 1-p = 0.85) and a value of 0.03 was chosen as the acceptable limit of precision (D) at 95% confidence intervals where (Z = 1.96). Based on these assumptions, the sample size is estimated to be 200 patients. To compensate for non-response, the sample size is suggested to be 240 patients with chronic HCV infection.

The sample was randomly invited from the three selected hospitals. Number of studied patients in each hospital was proportionally allocated in the sample according to the total number of patients registered in the hepatology records for each hospital (2015).

Data collection

Data were collected using a pretested, precoded structured interview format. In-depth interviews were conducted by trained data collectors in a quiet place at the outpatient clinic or in the patient ward and lasted up to 40 minutes. All participants completed the interviews. During the interviews, the following data were collected:

• Participant's characteristics: age, sex, marital status, level of education, residence, occupation, insurance coverage, health-related behaviors such as smoking, alcohol consumption, injectable drug use as well as reasons for treatment seeking.

• Clinical data were retrieved from patient's medical record: HCV diagnosis, disease duration, viral load (IU/ml), ALT value (U/L), symptoms, disease severity, presence of comorbid conditions, ever uptake of HCV medication (treatment could include pegylated interferon and ribavirin, with or without direct antiviral agents or interferon-free), and self-reported adherence to treatment. Access to healthcare was the patient's attainment of timely and appropriate healthcare. Treatment uptake was defined as proportion of HCV infected patients at service that received a prescription for HCV treatment (Lettmeier, 2008).

• Psychosocial factors related to access and adherence to treatment: An interview guide was developed based on a review of the literature and was grouped into 4 domains:

Personal factors

Knowledge of HCV and its treatment (16 questions; score range 0–16; α-reliability = 0.90), attitudes towards heath care use (7 statements; score range 0–35; α-reliability = 0.90) and gender perception (6 statements; score range 0–6; higher scores indicated stronger gender perception; α-reliability = 0.93).

Psychological factors

Depression is measured with the Beck Depression Inventory (BDI–II, NL), a 21-item self-report rating inventory (Richter et al., 1998). The total score ranges between 0 and 63, with scores <14 considered normal, a score of 14 and more indicating depressive symptoms. Anxiety is measured by Generalized Anxiety Disorder Questionnaire (GAD-7) (Swinson, 2006) (7 statements; score range 0–21 with scores <5 considered normal; α-reliability = 0.89). Self-efficacy was assessed using Hepatitis C Treatment Self-Efficacy Survey (17 items) (Bonner et al., 2012). Responses range from 0 to 10. Global Self-Efficacy is calculated by averaging the items with a higher score indicating more self-efficacy.

Sociocultural factors

Perceived availability of social support was captured using the 12-item Interpersonal Support Evaluation List (Brookings and Bolton, 1988). Higher scores indicate higher social support level. Stigma was measured using the modified Berger scale (Berger et al., 2001). This 40-item four-point scale groups stigma into the following 4 categories, personalized stigma (self-stigma); perceived public attitude (concern with public attitude about people with HIV); disclosure concerns and negative self-image (internalized negative self-image). The scores are scaled in the positive direction (higher the score higher the stigma). The scale was pilot tested for its reliability in this cultural setting. The internal reliability (Cronbach's Alpha) was 0.79. Cronbach's alpha for self, public attitude, disclosure and negative stigma was 0.76, 0.79, 0.62 and 0.85 respectively.

Healthcare factors

Such as easiness to have healthcare services, affordability of diagnostic tests, HBV vaccination, availability and

accessibility to a specialized doctor, availability and accessibility to medication, continuity of care. Healthcare discrimination scale (14 items) was worded based on thorough literature review. Each item was rated on a 5-point Likert scale ranging from 5=strongly agree to 1=strongly disagree. Higher scores indicating higher perceived discriminatory behavior (α-reliability = 0.86). The validated 26-item Medical Interview Satisfaction Scale (MISS) (Wolf et al., 1978) was used to assess patient satisfaction with medical care. The MISS contains four subscales: Distress Relief, Communication Comfort, Rapport and Compliance intent as well as a global satisfaction score. Survey respondents were instructed to 'consider all medical professionals seen at hepatology clinic when filling out the instrument. Scores ranged from 1 (most satisfied) to 7 (least satisfied) (α-reliability = 0.82).

- The perceived barriers for non-treatment access and adherence is a 17-item scale (based on a though review of the related literature). Participants rated the extent to which each item was perceived as a barrier to HCV treatment. A four-point Likert scale was used: 1 (No problem at all), 2 (Very slight problem), 3 (Somewhat of a problem), and 4 (Major problem). The 17 items are collapsed into four subscales: patients' barriers (4 items), provider barriers (3 items), healthcare barriers (4 items) and community barriers (6 items) (α-reliability = 0.87).

Ethical considerations

The research is in accordance with the ethical guidelines of the modified 1975 Declaration of Helsinki. Personal details of the professional background of the researchers were given to assure participants of the confidentiality of the research and help allay fears of talking about the personal and sensitive topic of HCV. The research ethics committee of the University of Alexandria, Faculty of Medicine granted ethical approval.

Statistical analysis

SPSS 20.0 program was used for analysis. As the scores were not normally distributed for most of study variables (except for age, disease duration, ALT value, and knowledge), the chi-squared and Mann–Whitney tests were used to determine significant differences between the sexes. Median percentage scores were calculated as (total score/maximum possible score) × 100. We hypothesized that gender differences in treatment access and adherence for HCV would not be explained only by socio demographic, and clinical factors, but also some important psychosocial and healthcare factors of the respondents as well. To test the hypothesis, two separate multivariate logistic regression models were fit for each sex.

The dependent variable in *multivariate logistic regression* model is dichotomous (treatment access: present or absent) and the independent variables are of any type; socio demographic, and clinical psychosocial and healthcare factors (discrete or continuous). The independent (observed) variables, X_i are related to the dependent (outcome) variable, Y by the following equation:-

$$\text{Logit } (p)=\beta 0+\beta 1X1+\ldots+\beta nXn$$

Where $p = Pr\{Y=1\}$ and $\text{Logit}(p)=\ln(p1-p)$ and p can be calculated by taking the inverse of the Logit (p) as shown in the following equation:

$$p=e\beta 0+\beta 1X1+\ldots+\beta nXn1+e\beta 0+\beta 1X1+\ldots+\beta nXn$$

Where p represents the probability of the presence of outcome (treatment access) when the findings $X_1, X_2,\ldots X_n$, are identified. β_i is the coefficient of the independent variable X_i that is estimated using the available data (training set). Only significant variables (p-value ≤ α) are included in the model. Variables were added by stepwise selection method. Odds ratio is used to interpret the effect of independent variables on the dependent variable, which is estimated by exp (β_i). An α-level of 0.05 was used to determine statistical significance (Bagley et al., 2001).

RESULTS

Patient characteristics

Characteristics of the 115 women and 125 men with chronic HCV infection who participated in the study, stratified by gender (not adjusted for hospital setting), are summarized in Table (1). Compared with the men, the women had older age (mean age 55.2 versus 52.1 years), higher rates of illiteracy (66.1% versus to 37.6%), unemployment (58.3% versus to 20.0%), and at least one comorbid condition (65.2% versus 52.8%). However, men more likely than women to have insurance coverage (44.0% versus 23.5%), being smokers (52.0% versus 2.6%), consuming alcohol (5.6% versus none) and had higher mean ATL value (151.8 versus 112.8 IU/ml). These gender differences in patient characteristics were statistically significant ($p<0.05$).

Only 36.0% of men and 22.6% of women had ever received HCV medication and the difference was statistically significant (p=0.021) (Figure 1). Of these, women were less commonly to adhere to HCV treatment than men (30.8% compared to 33.3%). However, this gender difference was not statistically significant (p=0.395). Male and female participants displayed similar demographic and clinical characteristics regarding marital status, residence, socio economic status, injectable drug use, time since diagnosis of HCV, median viral load, HCV-related symptoms, and disease severity where (p>0.05 for all).

Table 1. Background characteristics of men and women with chronic HCV infection attending hospitals of Alexandria

Characteristics	Men (n=125)		Women (n = 115)		P value
	No.	%	No	%	
Age (mean ± SD), years	**52.1 ± 11.1**		**55.2 ± 10.1**		0.023 *
Marital status					
Never married	3	2.4	4	3.5	^{FE}p = 0.713
Ever married	122	97.6	111	96.5	
Educational level					
Illiterate	47	37.6	76	66.1	0.000 *
Low education (basic/middle)	67	53.6	31	27.0	
High education (high school/university)	11	8.8	8	7.0	
Employment status					
Currently employed	100	80.0	48	41.7	0.000 *
Unemployed/housewife/retired	25	20.0	67	58.3	
Residence					
Rural	82	65.6	77	66.9	0.867
Urban	43	34.4	38	33.1	
Socio economic status					
Low	103	82.4	89	77.4	0.377
Middle	14	11.2	20	17.4	
High	8	6.4	6	5.2	
Insurance coverage					
No	70	56.0	88	76.5	0.001 *
Yes	55	44.0	27	23.5	
Smoking status					
Smoker	65	52.0	3	2.6	^{FE}p = 0.000 *
Non-smoker	60	48.0	112	97.4	
Alcohol consumption					
No	118	94.4	115	100.0	^{FE}p = 0.015 *
Yes	7	5.6	0	0.0	
Injectable drug use					
No	123	98.4	115	100.0	^{FE}p = 0.499
Yes	2	1.6	0	0.0	
Disease duration, mean ± SD (years)	21.2 ± 10.6		20.7 ± 9.7		0.078
Median viral load (IU/ml) (n = 60)	345,000		341,000		^{Z}p= 0.431
ALT value (U/L) mean ± SD	151.8 ± 47.6		112.8 ± 33.5		0.012 *
Experiencing HCV-related symptoms					
No	141	77.0	133	76.9	0.970
Yes	42	23.0	40	23.1	
Disease severity (cirrhosis)					
No	133	72.7	137	79.2	0.151
Yes	50	27.3	36	20.8	
Co- morbidity					
No	59	47.2	40	34.7	0.004 *
Yes	66	52.8	75	65.2	
Patient self-report good adherence to treatment (≥ 80%)	(n = 45)		(n = 26)		
No	30	66.7	18	69.2	0.395
Yes	15	33.3	8	30.8	

HCV = Hepatitis C Virus FEp= p value of Fissure Excat test Zp = p value fo Mann Whitney U non-parametric test * significant at < 0.05 Reference interval of ALT for women was 9 to 52 (U/L) and for men was 21 to 72 (U/L). Symptoms: depression, fatigue, weakness, and abdominal pain. The most prevalent comorbidities identified in the HCV study population were musculoskeletal disorders, hypertension, lipid metabolism disorders, anemia and diabetes mellitus

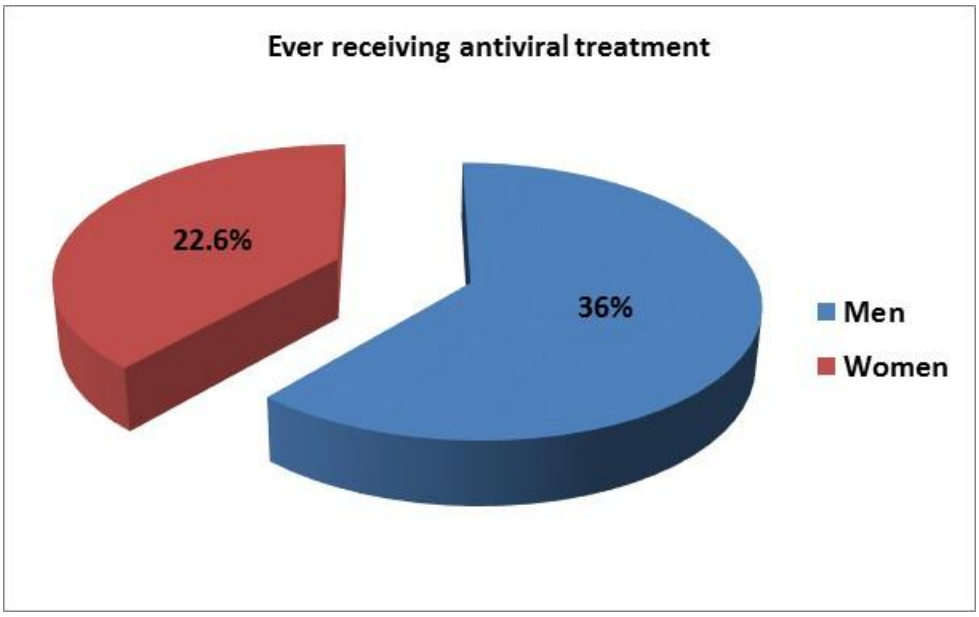

Figure 1. Women and men patients' access and uptake to antiviral medication for HCV infection

Factors contributed to accessibility, uptake and adherence to HCV treatment

Individual factors

Women with HCV reported significantly lower mean score % than men regarding knowledge about the disease (41.5 % versus 70.6%), knowledge about the treatment (50.3 % versus 71.4%) as well as overall knowledge (47.4 % versus 70.9%), $p<0.05$ for all. Gender difference was noted a reason for treatment-seeking (p=0.001). Higher proportion of women than men (72.2% as versus to 24.0%) would likely to resume their daily life activities. The median gender perception score % for men were significantly higher than that for women (87.6% versus 62.3%, p = 0.001). There was no gender difference in attitudes towards healthcare use (p =0.219) (Table 2)

Psychological factors

Women were significantly more likely than men to have depressive symptoms (67.0 % versus 48.8%, p=0.000), and anxiety (47.0 % versus 29.6%, p=0.001). However, women tended to have significantly lower median score of perceived self-efficiency than men (4.5 as versus to 8.8, p=0.007).

Sociocultural factors

Women tended to receive less social support than men. This was indicated as median social support score % for women (40.3%) was significantly lower than that for men (66.7%), ^{z}p=0.001. The distribution of types of stigma by gender is presented in Table (2). Significantly higher proportions of women felt disclosure stigma (48.7% versus 27.2%, p=0.008), public attitude stigma (33.9% versus 13.6%, p=0.002) as well as overall stigma (39.9% versus 24.0%, p=0.004) as compared to men. No significant differences by gender was noted regarding personalized (p=0.119) and negative self-image stigma (p=0.515).

Healthcare factors

Significantly higher proportion of men than women were more affordable to HCV diagnostic tests (50.4% versus 30.4%, p=0.005). Moreover, significantly more men than women stated that medications were available for them (35.2% versus 30.4%, p = 0.031) and continuity of care was maintained (58.4% versus 31.3%, p=0.002). Women tended to be less satisfied with the clinical consultation and care as compared to men. This was indicated as median satisfaction score % for women (39.5%) was significantly lower than that for men (63.7%), p=0.000.

No statistical significant differences were observed based on gender regarding easiness to get healthcare services, HBV vaccination, availability and accessibility to a specialized doctor and experiencing discrimination from a health care worker where (p>0.05 for all).

Table 2. Factors associated with accessibility and adherence to treatment in men and women with chronic HCV infection attending hospitals in Alexandria

Factor	Sub-item	Men (n = 125)		Women (n =115)		P value
		No.	%	No	%	
Personal	**Knowledge about disease** Mean ± SD (score %)	70.6 ± 4.8		41.5 ± 3.2		0.000 *
	Knowledge about treatment Mean ± SD (score %)	71.4 ± 5.2		50.3 ± 3.8		0.001 *
	Total HCV Knowledge score Mean ± SD (score %)	70.9 ± 4.6		47.4 ± 3.4		0.002 *
	Reason for treatment seeking					
	Health improvement	49	39.2	20	17.4	0.001 *
	Avoid infection of others	46	36.8	12	10.4	
	Resuming daily life activities	30	24.0	83	72.2	
	Attitude towards health care use Median score % (Q1 – Q3)	58.5 (30.5 – 72.4)		67.4 (53.9 – 84.2)		^{Z}p = 0.219
	Gender perception Median score % (Q1 – Q3)	87.6 (63.7 – 92.7)		62.3 (48.2 – 83.1)		^{Z}p = 0.001 *
Psychological	**Depression**					
	Normal (< 14 score)	64	51.2	38	33.0	0.000 *
	Depressive symptoms (≥ 14 score)	61	48.8	77	67.0	
	Anxiety					
	Normal (GAD-7 score < 5 score)	88	70.4	61	53.0	0.001 *
	Anxious (GAD-7 score > or =5)	37	29.6	54	47.0	
	Perceived self-efficiency Median score (Q1 – Q3)	8.8 (7.7–9.6)		4.5 (2.8–7.3)		^{Z}p =0.007 *
Socio cultural	**Social support** (Median score %) (Q1 – Q3)	66.7 (25.0 – 83.3)		40.3 (20.2 – 60.6)		^{Z}p =0.001 *
	HCV Stigma #					
	Personalized	32	25.6	32	27.8	0.119
	Disclosure	34	27.2	56	48.7	0.008 *
	Negative self-image	40	32.0	33	28.7	0.515
	Public attitude	17	13.6	39	33.9	0.002 *
	Overall HCV stigma	30	24.0	39	39.9	0.004 *
Healthcare #	Easiness to have healthcare services	72	57.6	61	53.0	0.384
	Affordability of diagnostic tests of HCV.	63	50.4	35	30.4	0.005 *
	HBV vaccination	20	16.0	17	14.8	0.391
	Availability and accessibility of specialized Doctor.	93	74.4	81	70.4	0.095
	Availability of medication	44	35.2	35	30.4	0.031 *
	Access to medication	45	36.0	26	22.6	0.021*
	Continuity of care	73	58.4	36	31.3	0.002 *
	Discrimination, Mean ± SD (score %)	72.9 ± 11.7		74.1 ± 11.7		0.193
	Satisfaction with clinical consultation (Median score %) (Q1 – Q3)	63.7 (38.9 – 72.8)		39.5 (28.6 – 61.8)		^{Z}p = 0.000 *

Categories are not mutually exclusive Z of Mann Whitney non parametric test * Significant at 0.05 level

Table 3. Multivariate logistic regression analysis of factors associated with accessibility and adherence to treatment for men and women with chronic HCV infection attending hospitals of Alexandria

Independent factors		Men (n = 125)		P	Women (n = 115)		P
		aOR	95% CI	value	aOR	95% CI	value
Socio Demographic & clinical	Age (years)	0.9	0.4 – 2.6	0.642	1.1	0.6 – 3.1	0.805
	Educational level (high=0, low=1)	1.2	0.5 – 3.2	0.248	3.6	1.1–5.8	0.000*
	Employment status (employed = 0, unemployed=1)	2.3	0.9 – 4.8	0.082	2.6	0.7 – 4.9	0.072
	Insurance coverage (yes=0, no=1)	1.5	0.4 – 4.8	0.649	2.9	1.3 – 4.8	0.007*
	Smoking (no=0, yes=1)	0.6	0.2 – 1.9	0.853	0.9	0.3 – 3.9	0.724
	Alcohol consumption (no=0, yes=1)	0.7	0.3 – 1.4	0.934	-----	----	----
	ALT value (IU/ml)	1.5	0.3 – 6.6	0.825	2.1	0.4 – 9.6	0.710
	Comorbidity (no=0, yes=1)	2.7	1.4 – 6.9	0.003*	1.9	0.8 – 3.8	0.138
Individual	Knowledge about HCV & treatment (score %)	2.1	0.6 – 8.9	0.709	6.10	2.4 –8.11	0.000*
	Reason for treatment seeking (avoid infection of others=0, health improvement or resuming daily life activities=1)	2.1	0.7 – 9.1	0.693	2.1	0.7 – 7.6	0.634
	Gender perception (score %)	1.3	0.8 – 7.9	0.596	0.6	0.3 – 0.8	0.002*
Psychosocial	Depression (no=0, yes=1)	1.9	0.4 – 7.7	0.642	4.2	1.8 – 12.5	0.001*
	Anxiety (no=0, yes=1)	1.8	0.6 – 6.3	0.593	1.6	0.3 – 3.8	0.691
	Perceived self–efficiency (Score %)	0.6	0.1 – 0.8	0.007*	0.8	0.3 – 2.8	0.496
	Social support availability (score%)	2.2	0.7 – 8.5	0.721	0.6	0.1 – 0.9	0.021*
	Overall HCV stigma (no=0, yes=1)	3.6	1.4 – 7.9	0.001*	10.2	3.7 – 20.5	0.000*
Healthcare	Affordability of diagnostic tests for HCV infection (yes=0, no=1)	1.6	0.3 – 6.9	0.836	2.2	0.5 – 9.2	0.810
	Availability of medication (yes=0, no=1)	3.8	1.5 -8.6	0.000*	5.3	1.3 – 12.9	0.000*
	Continuity of care (yes=0, no=1)	0.8	0.2 – 6.7	0.431	1.2	0.4 – 10.4	0.832
	Satisfaction with clinical consultation and care (score %)	2.4	0.8 -7.9	0.284	6.5	1.6 – 12.9	0.000*

Dependent: received HCV infection treatment (no=0, yes=1) R2 = 82.6%.
*aOR = adjusted odds ratio; CI = confidence interval. * Significant at 0.05 level*

Determinants of HCV treatment accessibility and adherence

In table (3), several factors were significantly contributing to non-treatment access and adherence. High social support and gender perception scores were independently associated with women's access for HCV treatment. However, illiteracy, lack of insurance coverage, lack of knowledge about HCV & treatment, depressive symptoms, felt stigma, unavailability of medication as well as dissatisfaction with HCV health care were determinants that adversely affected women's HCV treatment access. In men, the facilitating factor for treatment access was high perceived self-efficiency scores. However, treatment seeking was adversely associated with the presence of comorbid conditions, felt HCV stigma and unavailability of medication. For both genders, age, employment status, smoking, alcohol consumption, ALT value, anxiety, affordability of diagnostic tests and continuity of care were not determinants of treatment access and adherence. These variables together explained 82.6% of the variability in treatment access and uptake (R^2 = 82.6%) with significant overall model X^2 = 29.496, p=<0.001.

Perceived Barriers to accessing and adherence of HCV treatment

Table (4) provides the percentages of the individual barrier items perceived. When the endorsement of an item as 'somewhat of a problem' or a 'major problem' is combined, barriers that significantly different perceived between women compared with men were as follows: patient level barriers; lack of awareness about HCV (62.05 versus 40.0, p=0.001) and lack of personal financial resources (57.0% versus 45.0%, p=0.003), provider level barrier;

Table 4. Perceived barriers to accessing, uptake and adherence to treatment for men and women with chronic HCV infection attending hospitals of Alexandria

Barrier		Men (n = 125) (%)			Women (n = 115) (%)			P value
		No problem at all	Very slight problem	Somewhat / Major problem	No problem at all	Very slight problem	Somewhat / Major problem	
Patient	*Lack of awareness about HCV and treatment*	45.0	15.0	40.0	30.0	8.0	62.0	0.001 *
	Experience side effects of medication	70.0	10.0	20	69.0	13.0	18.0	0.751
	Lack of personal financial resources (transport cost, cost of investigations and treatment)	27.0	18.0	45.0	23.0	20.0	57.0	0.003 *
	Presence of comorbid conditions	58.0	13.0	29.0	50.0	17.0	33.0	0.387
Provider	*Lack of medical professionals who are trained and competent in HCV care*	50.0	20.0	30	49.0	21.0	30.0	0.543
	Communication difficulties	61.0	22.0	17.0	33.0	39.0	28.8	0.018 *
	Patient non-adherence to clinic visits	35.0	32.0	33.0	38.0	30.0	32.0	0.731
Health care	*Lack of medical coverage*	29.0	30.0	41.0	32.0	33.0	35.0	0.382
	Long distance to the facility	70.0	20.0	10.0	29.0	38.0	33.0	0.001 *
	Lack of transportation	40.0	30.0	30.0	36.0	32.0	23.0	0.832
	Lack of psychological counseling	68.0	20.0	12.0	60.0	24.0	16.0	0.531
Community	*Lack of HCV knowledge in the community*	40.0	22.0	38.0	15.0	20.0	65.0	0.000 *
	Lack of support group for persons with HCV	65.0	15.0	20.0	42.0	18.0	40.0	0.003 *
	Lack of adequate and affordable housing	60.0	25.0	15.0	57.0	23.0	20,0	0.647
	Community stigma against person with HCV	38.0	27.0	35.0	21.0	15.0	64.0	0.001 *
	Lack of understanding work environment for people with HCV	50.0	30.0	20.0	66.0	29.0	5.0	0.019 *
	Lack of work opportunities for persons with HCV	55.0	15.0	30.0	50.0	17.0	33.0	0.321

Percentages of responses to somewhat of a problem and major problem are combined together. ^{MC}p *= p value of Monte Carlo test* ** Significant at 0.05 level*

communication difficulties (28.8% versus 17.0%, p=0.003). Long distances to a treatment facility was the only healthcare barrier significantly different between the two sexes, with 33.0% of women endorsing this barrier as problematic, compared to 10.0% of men (*P* =0.001). Women more commonly rated community factors as problems compared with men such as lack of HCV knowledge in the community (65.0% versus 38.0%, p=<0.001); lack of support group for persons with HCV (40.0% versus 20.0%, p=0.003) and feeling stigmatized for having HCV (64.0.0% versus 35.0%, p=0.001. However, men significantly endorsed more lack of understanding work environment for people with HCV as a barrier (20.0%) as compared to only 5.0% of women (p = 0.019).

DISCUSSION

This study offers a unique context on treatment access from the viewpoint of the patients infected with HCV. Recognizing and overcoming potential treatment barriers in relation to gender is crucial to improve HCV treatment uptake (Vlassoff and Garcia Moreno, 2002; McGowan and Fried, 2012).

Despite the availability and demonstrated efficiency in HCV medications and access to a dedicated viral hepatitis clinic-based within Alexandria hospitals, the present study indicated low treatment access and uptake for both genders. Hospital clinics often have rigid appointment scheduling and do not always provide multidisciplinary care that may have helped mitigate social factors associated with poor access and adherence to HCV treatment such as poor social functioning and ongoing drug use. Combination intervention approaches encompassing social as well as biomedical interventions are crucial for high efficacy of HCV therapy. HIV care should be integrated into accessible, non-stigmatizing services within national health systems (Robaeys et al., 2013).

Previous researches estimated the proportions of patients treated with HCV in tertiary care academic, community, and Veterans Affairs (VA) hepatitis C cohorts. Treatment rates ranged from 1.1% in a Vancouver inner-city population to 30% at a university-affiliated VA (Grebely et al., 2009; Rowan et al., 2004). Market research from the United States suggests that less than 10% of persons with known infection have been treated (Shiffman, 2007). Likewise, market uptake of interferon in Europe indicates an average treatment rate of 3.5% (Lettmeier et al., 2008). Treatment rates may be higher among countries where government sponsored surveillance and treatment programs are available, such as in France and other European countries (Delarocque-Astagneau et al., 2010; Hatzakis et al., 2011).

In this study, fewer women than men have accessed HCV treatment. Mc Nally et al in 2004 reported that men participants were more likely than women to be currently on HCV treatment. They explained a range of factors influencing decisions to commence treatment and to adhere to treatment including economic factors, concerns of side-effects, concerns about the impact of compliance requirements on family, children care and work commitments, and perceptions of community stigmatization and discrimination by treatment staff (Mcnally et al., 2004). For women especially, who may have additional barriers in accessing resources for transportation fees, childcare and more, providing treatment at no cost may substantially increase women's access (Walley et al., 2005).

While low uptake of older HCV antiviral regimens in HCV infected patients is well-documented in the literature especially in women, the reasons for low uptake are less clear (Khokhar and Lewis, 2007). The present study investigated potential barriers in women and men that are preventing treatment uptake as the burden of HCV morbidity and mortality increases.

Socioeconomic factors help to mediate the relationship between gender and healthcare access (World Health Organisation Regional Office for Europe, 2012). The present work investigated gender differences in socio economic determinants of treatment access. Multivariate analysis indicated that the differential socio-economic experiences of men and women in terms of educational status, knowledge level, and insurance coverage contribute to gender differences in HCV treatment access and uptake. A similar study in Scotland found stronger associations between socio economic deprivation and limited HCV testing and treatment uptake (Borg and Kristensen, 2000).

This study indicated that women had poorer HCV-related knowledge than men. Women recognized lack of knowledge as a significant barrier for HCV treatment. Previous research has revealed inadequate knowledge among HCV infected women (Stein et al., 2001). The need for more HCV-specific education is consistent with research suggesting that correct health knowledge is a prerequisite for behavioral harm reduction (Stein and Nyamathi, 2000). HCV patient education is associated with positive outcomes in various models of HCV care, including increased disease-specific knowledge, interest in treatment, willingness to accept treatment and increase liver specialty care clinic attendance (Gupta et al., 2007).

Interestingly in this study, despite higher prevalence of comorbid conditions among women as compared to men, yet men with comorbidity were less likely to have received definitive treatment. Clinical guidelines for management of HCV indicated severe depressive disorders, hyperthyroidism, hypertension, heart failure, coronary heart disease, diabetes, and pulmonary disease as contraindications for HCV treatment (Hilsabeck and Malek-Ahmadi, 2004). Effective strategies to manage these comorbidities are necessary to allow wider

access to HCV treatment.

In the present study, depressive symptoms and anxiety were reported significantly more in women than men. A study estimated that one-fourth of patients with HCV meet DSM-IV diagnostic criteria for major depressive disorder, while 45–60% of patients endorse some level (mild-to-severe) of depressive symptomatology (Kravitz and Ford, 2008). As depression is often under-recognized and under-diagnosed, the comorbid depression in many HCV patients may go untreated, and unstable depression is a contraindication to antiviral therapy. Depression is associated with poor self-efficacy will to function, low self-esteem, low self-worth, reduced motivation, reduced adherence, lack of or poor social support, greater perceived stigmatization, pessimism, hopelessness and reluctance to seek healthcare services (Ghany et al., 2009).

In the present study, women reported to experience social stigma associated with HCV more keenly than men. Felt and experienced HCV stigma impacted women participants' decisions regarding HCV commence of and adherence to treatment. Stigma and healthcare discrimination are well evidenced barriers to HCV testing and treatment access (Day et al., 2003). Stigma related to hepatitis C has been found to have negative effects on self-esteem, access to health care, employment and social support, and major deleterious effects upon health and well-being (Strauss et al., 2008). Service provider cognizance of the stigma about HCV, and steps to work against this in the treatment environment, is vital for encouraging HCV treatment access and uptake. Attention to the individual needs of service users enables innovative and personalized stigma reducing interventions such as the relocation of medication dispensing. There is a concomitant need to increase HCV literacy among the partners and families of affected individuals to create an enabling and socially supportive environment for care (Richmond et al., 2004).

Support from others was paramount not only from family and friends, but also from health professionals. Higher retention in treatment was evident when people were adequately prepared and well supported by an appropriate health service. In the present study, women reported that low practical, financial and emotional support from family, partners and/or service providers was a significant barrier for access and uptake of treatment. Gender-based social support interventions which may help treatment uptake among this population are recommended. Support and information about HCV treatment is also necessary for friends, family and carers of those undergoing HCV treatment (Monnet et al., 2006).

Geographic access is an important facilitator for treatment access. The present study found that long distance to the hospital was a significant barrier to women's access to treatment. Studies in France have found that poor geographic access to primary healthcare can have a negative influence upon HCV screening uptake (Hatzakis et al., 2011). A Dublin based qualitative study found that convenience was one of the most important facilitators to treatment appointment attendance, with geographic distance from the hospital discouraging attendance (Astell-Burt et al., 2011).

Given that effective communication with and trust in healthcare providers significantly influences treatment eligibility decisions in HCV. In this study, negative interactions with HCV treatment providers were reported as a barrier to treatment in women participants. In a cross-sectional study of 322 HCV patients treated at a tertiary care center, 41% reported communication difficulties with their physicians (Zickmund et al., 2004). Specifically, patients felt rushed, misled or not listened to. Patients may question a physician's competence, or feel stigmatized by these interactions. Because of these interactions, patients may feel discouraged, less likely to listen to physician recommendations and more inclined to defer therapy (Mitchell et al., 2010).

Although largely subjective, patient satisfaction is multi-determined and includes diverse aspects of care such as accessibility of services, quality of medical care, clarity of communication, and the interpersonal style of the health provider. A study demonstrated that patients who feel more actively involved in their health care decision-making process are more committed to their care, adhere better to positive health behaviors, and are more satisfied with their health care. (Ong et al., 1995). In the present study, women reported lower scores in global satisfaction with care compared with men. After controlling for multiple variables, women dissatisfaction with care was associated with poor access and uptake of treatment. Our data suggest that it is important for any practice to quantify their overall gender-based patient satisfaction and contributing factors so that they can continue to improve the quality of care they provide.

Obstacles arising at the government level are likewise important. Unavailability of medication was a significant factor adversely impact women uptake of HCV treatment. In an international study of HCV providers, lack of treatment promotion and insufficient funding were noted as significant government level barriers (McGowan et al., 2011). To address these issues, increased resource allocation and improved collaboration between government, healthcare, and educational stakeholders are needed.

CONCLUSION

In conclusion, this gender analysis indicated that social, behavioral, clinical, and health service characteristics associated with HCV access, uptake and adherence are potentially different among women and men. Whereas among men, these factors directly related to comorbidity,

availability of medication, perceived self-efficiency, and felt stigma. The treatment non-access among women was more clearly explained by socio demographic (i.e., educational level, insurance coverage) and individual (i.e., knowledge level and gender perception), psychosocial (depression, social support and social stigma) and healthcare factors (availability of medication and satisfaction with the clinical consultation). Early intervention strategies to improve treatment access, uptake and adherence should focus on these differences and on an integrated assessment of clinical, counseling, social, and work support, while facilitating access to health services.

Our study is subject to limitations. Some limitations of medical record data collection include missing data due to errors that occur during clinic visit narrative dictation and transcription, and lack of specificity for patient information. Listed barriers were based on patients' cited reasons for not initiating HCV therapy. These may differ from provider-reported barriers to care. As the study was descriptive, we were unable to make any causal associations between documented barriers and why patients were not treated. Lastly, patients captured in hospital clinics may be a biased selection of the HCV population as it does not reflect the general HCV population who do not have access to healthcare.

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Declaration of personal interests

The authors have no personal interests to declare.

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