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Epidemiology of Hepatitis C Virus Infection in Egypt

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Authors' contributions

This work was carried out in collaboration between all authors. Author Fatma A. selected the subject of study, did the design and contacted the publisher. Authors Fatma A. collected the majority of materials used to develop the manuscript and was helped by author Maha G. Fatma A. wrote the manuscript which was then reviewed by authors Maha G. and Monkez Y. After discussion, all authors approved the final manuscript.

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ABSTRACT

Hepatitis C virus constitutes an epidemic in Egypt having the highest prevalence in the world of 14.7%. The reasons behind this unique epidemic may be dated back to iatrogenic role of parenteral antischistosomal therapy campaigns to control endemic schistosomiasis. Other routes of infection are contributing to the ongoing HCV transmission. The prevalent genotype in Egypt is type 4 (73%), the origin, evolution, and dynamics are difficult to determine. Risk factors for acquiring HCV infection include: History of antischistosomal injection treatment before 1986, old age, male gender, and residence in rural areas. Other risk factors include; injection therapy, blood transfusion prior to 1994, exposure to various facility-based medical procedures, and occupational transmission among health care workers. In community settings, a set of risk factors, mostly related to prevailing social and cultural conditions, are responsible for maintaining the high rates of HCV transmission. Chronic HCV is the main cause of liver cirrhosis and liver cancer in Egypt and, indeed, one of the top five leading causes of death. It kills an estimated 40,000 Egyptians a year.

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When talking about children, current HCV seroprevalenceis high, approximately 5-8%. It is to be emphasized that HCV infection is not always benign in the childhood period in Egypt. It has been shown that blood transfusion, surgical procedures, dental treatment, male circumcision and age above 10 years are important risk factors associated with anti-HCV antibody prevalence. In addition, vertical transmissions, and household transmission have been documented as routes of transmission.

Occult HCV infection is defined as elevated liver function tests and negative HCV antibodies in serum, while HCV RNA is detectable in liver tissue and peripheral polymorphonuclear cells (PBMCs). Interest in occult HCV has emerged recently in Egypt. Studies at a national level are being carried out, but no results have yet been released. Many small scale studies have been performed among particular patient groups, which have highlighted the importance of this disease entity.

Keywords: HCV; Egypt; risk factors; schistosomiasis; pediatric HCV; blood transfusion; occupational hazards; infection control; traditions.

1. INTRODUCTION

HCV currently infects nearly 2% of the world's population Fig. 1 [1]. In Egypt the situation is very critical. Hepatitis C virus constitutes an epidemic in Egypt which is having the highest prevalence in the world Fig. 2. Nowhere else is there an HCV epidemic that affects a whole country. In all other countries, the prevalence of HCV is between 1% to 2%. There are a few exceptions where the prevalence of HCV is 3%. In Egypt however, the prevalence of HCV is 14.7%. Just about every family in Egypt is touched by hepatitis C. The blood borne virus, which is highly infectious, infects at least 1 in 10 of the population aged 15 to 59 [2].

2. Magnitude of the Problem

In 1992, when HCV antibody testing became widely available, the prevalence of HCV in Egypt was reported to be 10.8% among first-time blood donors [4]. Since then, many prevalence estimates of HCV have been reported [5,6] including the Egyptian Demographic Health Survey (EDHS) [7]. The latter is a national probability sample of the resident Egyptian population, which concluded that, in general, anti-HCV antibody prevalence was 14.7%.

Fifteen percent of the EDHS respondents aged 15-59 had antibodies to the HCV virus in their blood, indicating that they had been exposed to the virus at some point and 10% were actively infected. Men were more likely to be infected than women; however, among both women and men, there was direct correlation between infection and age. Twelve percent of rural residents were infected versus, 7% of the urban ones. The prevalence was highest in rural Lower and rural Upper Egypt (19.5% and 28.4% respectively), while it was lowest in the Frontier Governorates and the Urban Governorates (5.9% and 8.2% respectively) Fig. 3.

The level of education as well as the wealth quintile had an impact on HCV prevalence, Fig. 4. Individuals with no or less than primary education (17 and 13 percent, respectively) were markedly more likely to be infected with the HCV virus than the more educated population (7-8 percent). Meanwhile, the likelihood of HCV infection also decreased with the wealth quintile from 12 percent among respondents in the lowest wealth quintile to 7 percent among respondents in the highest wealth quintile.

Reasons for this exceptional epidemic in Egypt are controversial. A generally accepted postulation is the iatrogenic role of the parenteral campaigns carried out some decades ago to control endemic schistosomiasis [10].

3. HCV Genotypes

There are seven major genotypes of HCV, which are indicated numerically from one to seven, [11]. The prevalent genotype in Egypt is type 4 (73%) followed by genotype 1 (26%), whereas mixed HCV genotypes infection was found in 15.7% in cases in Egypt, [12].

Genotype 4 is also the most common genotype in Central and West Africa and the Middle East. Currently, HCV 4 infection is spreading beyond its strongholds in Africa and the Middle East. It has recently spread in several Western countries, particularly in Europe Fig. 5, due to variations in population structure, immigration, and routes of transmission [13].

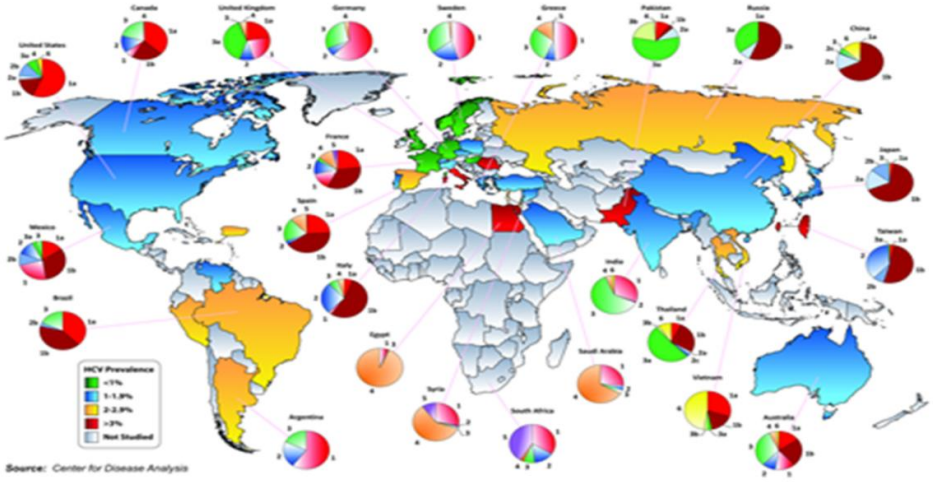

Fig. 1. HCV global prevalence among adults and genotype distribution [3]

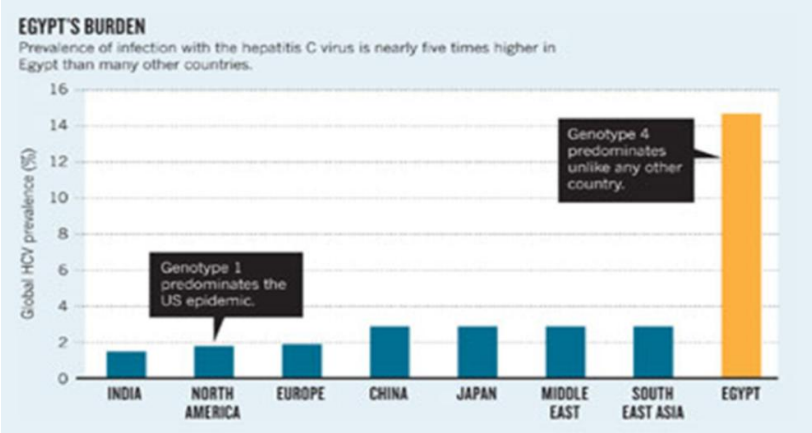

Fig. 2. Prevalence of HCV worldwide [8]

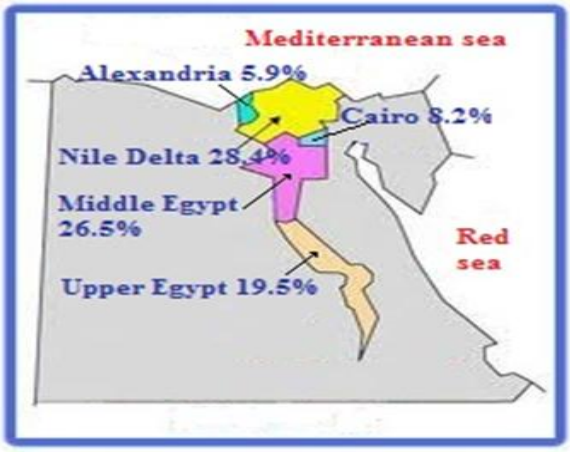

Fig. 3. HCV spread ratios across Egypt [9]

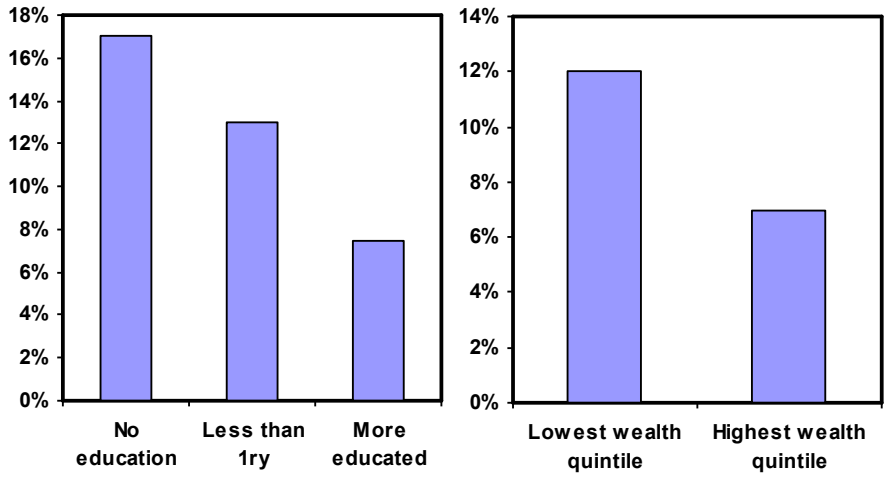

Fig. 4. The impact of level of education and the wealth quintile on HCV prevalence

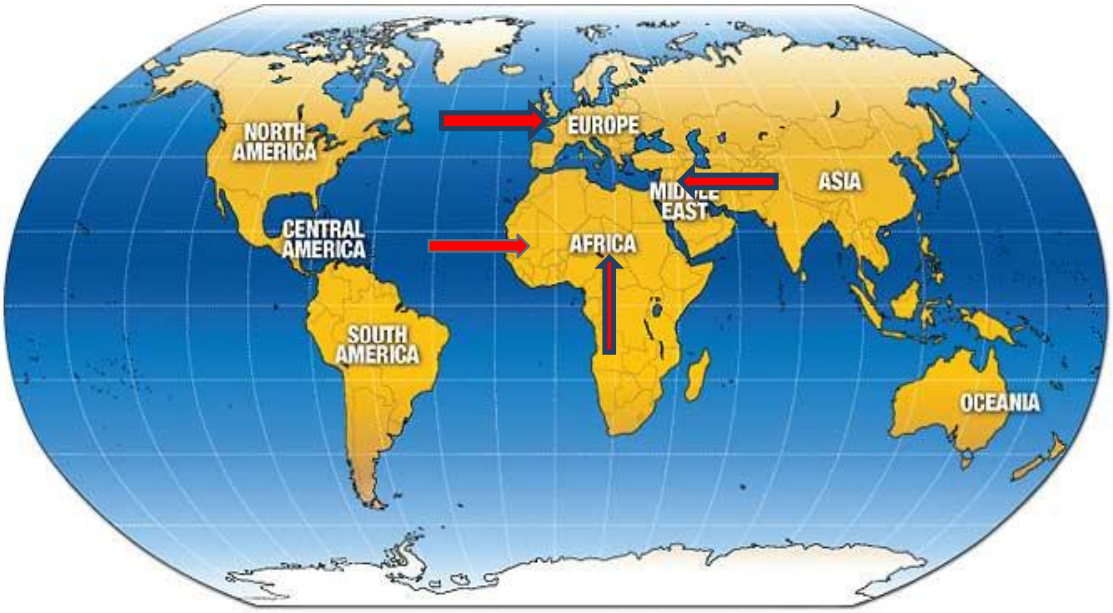

Fig. 5. Global origin and spread of HCV 4 infection [1]

The origin, evolution, and dynamics of HCV 4 are difficult to determine given the limited population-based epidemiological studies and phylogenetic analysis of this genotype in the geographic regions in which it is endemic. The information available from small-scale field surveys from Central African countries (Zaire, Gabon, Central African Republic, and Tanzania) and Cameroon in addition to sequence analysis studies indicate that HCV 4 strains circulating in Central Africa and Cameroon are extremely heterogeneous, and suggesting that it probably has been endemic for a long time [14-23]. Between 1920-1960 during the mass vaccination campaign against trypanosomiasis in Cameroon, a great spread of genotype 4 occurred [24]. The excessive genetic variety in sub-Saharan Africa might lead to the assumption that HCV 4 was initiated and circulated in Central and WestAfrica before spreading to other regions [16,20].

However, it is not clear how HCV infection was maintained for a long period in these areas even in the absence of the known routes of transmission as blood transfusion and injection. Perhaps other ways of infection transmission like

scarification, circumcision practice and sexual contact may be responsible for persistence and propagation of infection in tropical and subtropical regions [13].

In Egypt several combined population genetics and epidemiological analyses were conducted to determine the origin and the historical changes in Egyptian HCV prevalence [10,15,19,20,25,26].

Regardless of the high occurrence of HCV in Egypt, studies have proposed that the epidemic form of type 4a infection was more recent and fairly dissimilar from the endemic form in sub-Saharan Africa [15,21]. The absence of genetic variety in Egypt matched with the sub-Saharan African strains and the preponderance of genotype4a assume a somewhat common cause for the epidemic not a lengthy endemicity and dissemination. Molecular evolutionary investigations on Egyptian type 4a isolates specifies that the Egyptian HCV epidemic was originated and promulgated by widespread anti schistosomiasis mass treatment campaigns [10,15,19,21,25,26]. The spread of HCV 4a was largely augmented in rural areas between 1930s to1980s, parallel with the mass campaigns, with the most rapid enlarged progression between 1930 to1955 [19,21]. Even though the anti-schistosomal campaigns ended in the early 1980s, the occurrence of HCV remains high in Egypt. Considering that HCV currently is more than 30% of the annually reported acute hepatitis cases [27], it appears that the existing prominence of HCV in Egypt is caused by new infections developed further than the era of anti-schistosomal campaigns [13].

4. RISK FACTORS AND TRANSMISSION

4.1 History of Anti schistosomal Injection Treatment Before 1986

Schistosomiasis was a common parasitic disease in Egypt contracted by swimming or walking in polluted channels. It can produce urinary tract or liver damage over many years. Before 1986 the strategy of treatment was tartar emetic given by intravenous injection. Extensive campaigns were done to fight schistosomiasis in the rural areas of Egypt 1960's- 1970's and early 1980's, [28,29].

Egypt's hepatitis C epidemic dates back decades when glass syringes used during mass vaccination campaigns were not properly sterilized between uses. This reservoir of infection was continued for years due to lack of both awareness and efforts to control the spread. Overall, despite improvement in schistosomiasis-related morbidity between 1980-1990 [30,31], it appears to have caused widespread infection with HCV, which by the 1990s, had replaced schistosomiasis as the primary cause of liver disease in Egypt [30]. Active infection rates are particularly high among individuals who reported receipt of at least one injection to treat schistosomiasis compared to those who had not received such an injection [7].

4.2 Age

Different studies have shown a dramatic increase in HCV prevalence with age; a cohort effect that may be explained, at least in part, by the early association between parenteral antischistosomal therapy campaign and HCV transmission [32-34].

4.3 Gender

Higher HCV prevalence rates are observed in males compared to females. These differences may also be in part attributed to the parenteral anti schistosomasis campaigns (PAT), as males were more affected by the schistosomiasis disease burden and hence were main targets of these campaigns [35-38].

4.4. Geographical Differences

Higher prevalence was observed in rural dwellers compared to individuals living in urban areas. These differences may also be in part due to the PAT campaigns, as rural areas were more affected by the schistosomiasis disease, consequently, were more involved by these campaigns [35-39].

4.5 Injection Therapy

For any other indication, like for hemorrhoids, or urinary incontinence [38].

4.6 Hospital-based Procedures

4.6.1 Blood transfusion

Prior to 1994, blood transfusion was a common route for HCV transmission in Egypt [40]. After that date, blood and blood products were screened for HCV which eliminated the possibility of HCV transmission via this route [10,27].

4.6.2 Other procedures

Experiencing various facility-based medical procedures however minor they are, contributes to susceptibility to HCV [7]. Surgical procedures, perinatal care, and dental treatment have been incriminated in HCV transmission in many studies [6,33,41].

4.6.3 Occupational hazards

Transmission among health care workers through needle sticks and sharp injuries is common in Egypt and contributes to the high rates of HCV infection, given that needleless systems are not adopted in all Egyptian hospitals and health care units [42,43].

4.7 Community-based Risk Factors

4.7.1 Social and cultural factors

A group of risk factors, having intimate relations with dominant community and cultural aspects are the cause of the documented high rates of HCV transmission in Egypt. On rural areas, during many big community-based studies, wound treatment, excision and dentistry carried out by informal health care providers were reported as significant risk features [42-44]. Furthermore, nearly half of deliveries are manipulated by old-fashioned birth assistants who do not stick to sound infection control procedures [43,44]. Traditional scarification and tattooing practices may also contribute to HCV transmission in these settings [13,43].

4.7.2 Intrafamilial and sexual transmission

Play a role in the high prevalence of HCV in Egypt [45,46]. The household contacts of HCV seropositive patients had been shown to have an elevated risk of HCV infection [47,48] Recently in 2014, El-Bendary et al. [49] conducted a pilot study of the epidemiological aspects of intrafamilial spread of HCV infection in Egyptian population. They concluded that intrafamilial contact is an important factor in the transmission of HCV in Egypt. Transmission might occur during family contact, sexual behavior, and the shared use of personal items. The investigators recommended a wide scale national study to clarify this important entity.

4.8 Intravenous Drug Using (IDU)

Whereas intravenous drug using is the main drive of HCV incidence and prevalence in many countries [50], it is not so in Egypt. This is attributed to the specific context of the Egyptians [10,27,51]. However, in terms of absolute measure, IDU has an impact on HCV transmission [52] comparable to other countries. El-Ghazzawi, [53] reported an HCV prevalence amongst IDUs of 63%. Based on the prevalence rate of 14.7%, injecting drug use may contribute to a maximum of about 1% of the national HCV prevalence in Egypt [54].

Injecting drug use is unlikely to contribute much to HCV prevalence among women, again given the context of Egyptians. Moreover, injecting drug use among women in the Middle East and North Africa region is believed to be marginal with only about 10% or less of IDUs being females [55,56].

5. COMPLICATIONS

HCV infection most often leads to an asymptomatic chronic state, which can later progress to active liver disease and grave compilations. An important characteristic of HCV disease is that the majority of patients are unaware of their disease status until they develop severe liver disease that may present several years later [2]. Chronic HCV is the main cause of liver cirrhosis and liver cancer in Egypt and, indeed, one of the top five leading causes of death [28]. HCV kills an estimated 40,000 Egyptians a year [2].

6. HCV INFECTION IN CHILDREN

6.1 Magnitude of the Problem

In the Western world the prevalence of HCV infection is relatively low in children, with an anti-HCV prevalence rate of 0.2%-0.4% [57]. In Egypt, although mass campaigns to control schistosomiasis that took place decades earlier may have been responsible for much of seropositivity in the old-age people, current seroprevalence is also high in children too young to have been involved in those campaigns [10,26]. The prevalence in those under age 20 is approximately 5-8%, demonstrating the continued presence of significant hepatitis C transmission in modern-day Egypt [35].

The magnitude of HCV infection in children has been studied by many authors. In 2000 and 2002 two community-based cross sectional studies to determine the prevalence of HCV among Egyptian children were carried out. The first was in Lower Egypt [40] and the second was in Upper Egypt [58]. In 2007,El-Raziky et al. [59]

concluded that asymptomatic HCV infection was present in 2.02% of 1042 children studied. In 2010, Khalil et al. [41] from Assiut situated in Upper Egypt, measured the rates of anti-HCV positivity among children at the age of 1-9 years. On the next year [60], researchers from Alexandria, located on the Mediterranean Coast of Egypt estimated the prevalence of HCV infection among healthy children. The most recent work published was that of Farghaly et al. in 2014 [61] who studied the frequency of HCV infection among children with type 1 diabetes mellitus (T1DM) in Upper Egypt. Summary of the most recent studies performed is shown in Table 1.

It is worth mentioning that HCV infection is not always benign in the childhood period in Egypt as reported by El-Raziky et al. in 2004 [62]. They found that ALT levels were elevated in up to half of the HCV RNA-positive children. Symptoms such as diarrhea, abdominal pain, history of fatigue and school absence because of illness were also common among pediatric patients studied by El-Raziky et al. in 2007 [59]. Whereas the first group of authors reported histological abnormalities in three quarters of the HCV RNA-positive children they evaluated, the second investigators found that none of the HCV positive children was diagnosed as having signs of advanced liver disease upon clinical or ultrasonographic examination. Regarding children with T1DM examined by Farghaly et al. in 2014, [61] HCV infection was not associated with significant changes in hepatic biochemical parameters and there were no significant impact on serum levels of liver biochemical profile.

6.2 Risk Factors

In the Western World, blood transfusion is the principal route of transmission of HCV in children [62]. Earlier evidence suggested that new cases are due to perinatal (vertical) transmission [63].

Studies in Egypt suggest that children are exposed to HCV vertically through mother-to-child transmission [64-68]. High RNA prevalence was documented among infants of HCV positive mothers, ranging between 3.8% and 11.1% [69,70]. Moreover, Egyptian children are at high risk of being horizontally infected with HCV by their parents, or household exposure [70]. The latter can occur either directly or indirectly through shared needles or other possible fomites [5]. Analysis of data gathered during studies of countryside communities' demonstrated parents who had anti-HCV were more likely to have children with anti-HCV antibodies than parents who lacked antibodies. The relationship was larger with mothers than fathers and when the parent had HCV RNA [71]. Sequencing isolates from 13 families with parent(s) and children having HCV RNA, showed that10 of 18 had genetically similar viruses.

In Egypt also, medical exposures to HCV at a very young age have been incriminated [72-75]. High HCV levels were reported among thalassemic children [72,76,77], children on hemodialysis [73,74] and diabetic children [72,73,75]. Residence in rural area and low socioeconomic class are also significant risk factors [61]. Barakat and Elbashir in 2011, concluded that history of previous blood transfusion (odds ratio[OR] = 34.8, 95% CI=4.39-272.95), intravenous injections (OR=4.68, 1.89-11.59), surgical intervention (OR=5.64, 2.55-12.52), dental treatment (OR = 6.81, 2.64-17.39), [54] injection (OR=2.29, 1.08-4.89) and circumcision for boys by informal health care providers (OR=2.6, 1.0-6.73), age above 10 years (OR=6.83, 2.44-19.07), are the most significant risk factors for HCV infection [60].

7. HAS HCV INCIDENCE RATES DECLINED OR NOT?

Some studies have concluded a decline in HCV incidence, while others did not. Barban et al. [78] have recently suggested that it seems plausible that HCV incidence rate has declined drastically in the last two decades since the discovery of the epidemic in 1991–1992. That is because some of the potential drivers of this epidemic, such as the PAT campaigns and contaminated blood, are no longer present. However, results of the time trend analysis of Mahmoud et al. [38], suggested that, contrary to expectations, there appears to be a small decline, though statistically not significant, in HCV prevalence over time in the general population and high risk population in Egypt, a finding that goes in accord with other authors. A possible reason is the very high baseline HCV prevalence in the country.

For example, the transmission risk for reuse of unclean needles or syringes, depends on the likelihood that the needle/syringe was used before on an HCV patient, which is HCV RNA prevalence. The high background prevalence can drive much more incidence. In the neighboring Libya for instance, having less than 1% HCV RNA prevalence [55], a reuse of a contaminated needle is nearly ten-fold less likely to lead to an HCV spread than in Egypt [51].

Table 1. Summary of the most recent studies performed in Egypt, with regard to the prevalence of HCV among children

Year	Age	Study sample	location	ELISA	+ve no (%)	PCR	+ve no (%)	Others + Veno(%)	Reference
2000	<19	2010	Lower Egypt		178 (9%)	-			[40]
2002	<19	2967	Upper Egypt	+	84 (3%)	-			[58]
2007	1-9	1042	Hospital-based	+	15 (1.4%)	+	5	ALT(6)	[59]
2010	2m-15y	465	Assuit University	3rd gen	121(26%)	+	87 (72%)		[41]
2011	6-15	500	Alexandria	+	5.8%	+			[60]
2014	3-16	150(T1DM)	Assuit	3rd gen	18(12%)	+	12(75%)	Total bilirubin, direct bilirubin, protein, ALT, AST	[61]

8. OCCULT HCV

8.1 Background

The role of occult HCV infection in chronic liver ailment was first described by Castillo et al. in January 2014 [79]. When patients have neither HCV antibodies nor RNA in their sera, but have elevated liver function tests. They may have detectable HCV RNA in their liver tissue and PBMCs [80]. In fact, OCI is a very controversial issue, [81].

8.2 Occult HCV in Egypt

Due to the unique situation as regards incidence/prevalence of HCV infection in Egypt, Egyptian investigators are too much interested to know whether OCI may have a role different from that in other parts of the world. Studies at a national level are being carried out, but no results have yet been released. Many small scale studies have been performed among particular patient groups, [82-84].

9. CONCLUSION AND CLOSING REMARKS

HCV infection is a major health problem in Egypt. The beginning was iatrogenic, however, other routes of transmission led to continuation of the problem up till now. Both adults and children are affected by this disease. Routes of transmission and risk factors for this infection are well established. Studies of OCI for special groups of patients have been conducted. All efforts should be exerted to bring HCV disease to an end.

CONSENT

It is not applicable.

ETHICAL APPROVAL

The study was approved by Zagazig University Institutional Review Board (IRB).

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COMPETING INTERESTS

Authors have declared that no competing interests exist.

REFERENCES

1. Alter MJ. Epidemiology of hepatitis C virus infection. World J Gastroenterol. 2007; 13(17):2436–2441.
2. Egypt steps up efforts against hepatitis C; 2014. (Accessed 23 September, 2014).
3. Available:http://lloydbelcher.org/2011/07/28/hepatitis_c_hongkong_2011/. /(Accessed 15 September, 2014).
4. Kamel MA, Ghaffar YA, Wasef MA, Wright M, Clark LC, Miller FD. High HCV prevalence in Egyptian blood donors. Lancet. 1992;340(8816):427.
5. Mohamed MK, Abdel-Hamid M, Mikhail NN, Abdel-Aziz F, Medhat A, Magder LS, et al. Intrafamilial transmission of hepatitis C in Egypt. Hepatology. 2005;42(3):683–687.
6. Saleh DA, Shebl F, Abdel-Hamid M, Narooz S, Mikhail N, El-Batanony M, et al. Incidence and risk factors for hepatitis C infection in a cohort of women in rural Egypt. Trans R Soc Trop Med Hyg. 2008; 102(9):921-928.
7. El-Zanaty F, Way A. Egypt demographic and health survey 2008. (Egyptian: Ministry of Health and Associates and Macro International, Cairo); 2009.
8. Available:http://www.natureasia.com/en/nmiddleeast/article/10.1038/nmiddleeast.2011.83. Published online 7 July 2011. (Accessed 2October, 2014).
9. Available:http://www.hcv-egypt.net/encyclopdeia/transmission/index.htm (Accessed 5 September, 2014).
10. Millera FD, Abu-Raddad LJ. Evidence of intense ongoing endemic transmission of hepatitis C virus in Egypt. Natl Acad Sci U S A. 2010;107(33):14757–14762.
11. Nakano T. An updated analysis of hepatitis C virus genotypes and subtypes based on the complete coding region. LiverInt. 2011; 32(2):339–45.
12. Zekri AR, Bahnassy AA, Shaarawy SM, Mansour OA, Maduar MA, Khaled HM, El-Ahmadi O. Hepatitis C virus genotyping in relation to neu-oncoprotein overexpression and the development of Hepatocellular carcinoma. J Med Microbiol. 2000;49(1):89-95.
13. Kamal SM, Nasser AI. Hepatitis C genotype 4: What we know and what we don't yet know. Hepatology. 2008;47(4): 1371–1383.
14. Xu LZ, Larzul D, Delaporte E, Bréchot C, Kremsdorf D. Hepatitis C virus genotype 4

is highly prevalent in central Africa (Gabon). J Gen Virol. 1994;75(9):2393–2398.
15. Angelico M, Renganathan E, Gandin C, Fathy M, Profili MC, Refai W, et al. Chronic liver disease in the Alexandria governorate, Egypt: Contribution of schistosomiasis and hepatitis virus infections. J Hepatol. 1997;26(1):236–243.
16. Smith DB, Pathirana S, Davidson F, Lawlor E, Power J, Yap PL, et al. The origin of hepatitis C virus genotypes. J Gen Virol. 1997;78(2):321–328.
17. Ray SC, Arthur RR, Carella A, Bukh J, Thomas DL. Genetic epidemiology of hepatitis C virus throughout Egypt. J Infect Dis. 2000;182(3):698–707.
18. Ndjomou J, Pybus OG, Matz B. Phylogenetic analysis of hepatitis C virus isolates indicates a unique pattern of endemic infection in Cameroon. J Gen Virol. 2003;84(9):2333–2341.
19. Pybus O, Drummond A, Nakano T, Robertson BH, Rambaut A. The epidemiology and iatrogenic transmission of hepatitis C virus in Egypt: A Bayesian coalescent approach. Mol Biol Evol. 2003; 20(3):381–387.
20. Simmonds P. Genetic diversity and evolution of hepatitis C virus—15 years on. J Gen Virol. 2004;85(11):3173–3188.
21. Tanaka Y, Agha S, Saudy N, Kurbanov F, Orito E, Kato T, et al. Exponential spread of hepatitis C virus genotype 4a in Egypt. J Mol Evol. 2004;58(6):191–195.
22. Genovese D, Dettori S, Argentini C, Villano U, Chionne P, Angelico M, et al. Molecular epidemiology of hepatitis C virus genotype 4 isolates in Egypt and analysis of the variability of envelope proteins E1 and E2 in patients with chronic hepatitis. J Clin Microbiol. 2005;43(4):1902–1909.
23. Njouom R, Nerrienet E, Dubois M, Lachenal G, Rousset D, Vessière A, et al. The hepatitis C virus epidemic in Cameroon: Genetic evidence for rapid transmission between 1920 and 1960. Infect Genet Evol. 2007;7(3):361–367.
24. Ntagirabiri R, Poveda JD, Mumana A, Ndayishimiye H. Genotypes and subtypes of hepatitis C virus in Burundi: A particularity in Sub-saharan Africa. The Pan African Medical Journal. 2014;19 (401):69.
25. Simmonds P, Holmes EC, Cha TA, Chan SW, McOmish F, Irvine B, et al. Classification of hepatitis C virus into six major genotypes and a series of subtypes by phylogenetic analysis of the NS-5 region. J Gen Virol. 1993;74(11):2391–2399.
26. Kamal SM, Madwar M, Bianchi L, Tawil AE, Fawzy R, Peters T, et al. Clinical, virological and histopathological features: Long-term follow-up in patients with chronic hepatitis C co-infected with *S. mansoni*. Liver. 2000;20(4):281–289.
27. Zakaria S, Fouad R, Shaker O, Zaki S, Hashem A, El-Kamary SS, et al. Changing patterns of acute viral hepatitis at a major urban referral center in Egypt. Clin Infect Dis. 2007;44(4):e30–e36.
28. Available:http://hcvadvocate.org/hcsp/articles/Egypt_06.html (Accessed 15 September 2014)
29. Available:http://www.freerepublic.com/focus/f-news/3136777/posts (Accessed 20 September 2014).
30. Darwish NM, Abbas MO, Abdelfattah FM, Darwish MA. Hepatitis C virus infection in blood donors in Egypt. J Egypt Public Health Assoc. 1992;13(3–4):223–236.
31. Selim O, El-Zayadi AR. Prevalence of hepatitis C virus among non-A, non-B-related chronic liver disease in Egypt. J Hepatol. 1992;13(2–3):416–417.
32. Abdel-Aziz F, Habib M, Mohamed MK, Abdel-Hamid M, Gamil F, Madkour S. Hepatitis C virus (HCV) infection in a community in the Nile Delta: Population description and HCV prevalence. Hepatology. 2000; 32(1):111 - 115.
33. Arafa N, El Hoseiny M, Rekacewicz C, Bakr I, El-Kafrawy S, El Daly M, et al. Changing pattern of hepatitis C virus spread in rural areas of Egypt. J Hepatol. 2005;43(3):418-424.
34. DossW, Mohamed MK, Esmat G, El Sayed M, Fontanet A, Cooper S, El Sayed N. Egyptian national control strategy for viral hepatitis; 2008-2012.
35. Mohamed MK. Epidemiology of HCV in Egypt 2004. The Afro-Arab Liver Journal. 2004;13(2):41–52.
36. Awadalla HI, Ragab MH, Nassar NA, Osman MA. Risk factors of hepatitis C infection among Egyptian blood donors. Cent Eur J Public Health. 2011;19(4):217–221
37. Abdelwahab S, Rewishac E, Hashem M, Sobhy M, Galal I, Allam WR, et al. Risk factors for hepatitis C virus infection among Egyptian healthcare workers in a National Liver Diseases Referral Centre.

Trans R Soc Trop Med Hyg. 2012;106(2): 98-103.
38. Mahamoud YA, Mumtaz GR, Riome S, Miller DW, Abu-Raddad LJ. The epidemiology of hepatitis C virus in Egypt: A systematic review and data synthesis. BMC Infect Dis. 2013;(13):288.
39. Mostafa A, Taylor SM, El-Daly M, El Hoseiny M, Bakr I, Arafa N, et al. Is the hepatitis C virus epidemic over in Egypt? Incidence and risk factors of new hepatitis C virus infections. LiverInt. 2010;30(4): 560–566.
40. Habib M, Mohamed MK, Abdel-Aziz F, Magder LS, Abdel-Hamid M, Gamil F, et al. Hepatitis C virus infection in a community in the Nile Delta: Risk factors for seropositivity. Hepatology. 2001;33(1): 248–25.
41. Kalil KA, Farghally HS, Hassanein KM, Abd-Elsayed AA, Hassanein FE. Hepatitis C virus infection among paediatric patients attending University of Assiut Hospital, Egypt. Eastern Mediterranean health Journal. 2010;16(4):356-361.
42. Talaat M, Kandeel A, El-Shoubary W, Bodenschatz C, Khairy I, Oun S, et al. Occupational exposure to needlestick injuries and hepatitis B vaccination coverage among health care workers in Egypt. Am J Infect Control. 2003;31(8): 469–474.
43. El Katsha S, Labeeb S, Watts S, Younis A. Informal health providers and the transmission of hepatitis C virus: Pilot study in two Egyptian villages. East Mediterr Health J. 2006;12(6):758–767.
44. Stoszek SK, Abdel-Hamid M, Narooz S, El Daly M, Saleh DA, Mikhail N, et al. Prevalence of and risk factors for hepatitis C in rural pregnant Egyptian women. Trans R Soc Trop Med Hyg. 2006;100(2):102–107.
45. Kamal SM, Amin A, Madwar M, Graham CS, He Q, Al Tawil A, et al. Cellular immune responses in seronegative sexual contacts of acute hepatitis C patients. J Virol . 2004;78 (22):12252–12258.
46. Magder LS, Fix AD, Mikhail NN, Mohamed MK, Abdel-Hamid M, Abdel-Aziz F, et al. Estimation of the risk of transmission of hepatitis C between spouses in Egypt based on seroprevalence data. Int J Epidemiol. 2005;34(1):160–165.
47. Tibbs CJ. Methods of Transmission of Hepatitis C. Journal of Viral Hepatitis. 1995;2(3):113-119.
48. Minola E, Baldo V, Baldovin T, Trivello R, Floreani A. Intrafamilial Transmission of Hepatitis C Virus Infection. European Journal of Epidemiology. 2006;21(4):293-927].
49. El-Bendary M, Esmat G, Neamatallah M, Kamel E, Besheer T, Elalfy H, El-Setouhy M, Omran D. Epidemiological Aspects of Intrafamilial Spread of HCV Infection in Egyptian Population: A Pilot Study. Open Journal of Gastroenterology. 2014;4(5): 228-236.
50. Aceijas C, Rhodes T. Global estimates of prevalence of HCV infection among injecting drug users. Int J Drug Policy. 2007;18(5):352-8.
51. Mohamoud YA, Mumtaz GR, Riome S, Miller DW, Abu-Raddad LJ The epidemiology of hepatitis C virus in Egypt: A systematic review and data synthesis BMC Infectious Diseases. 2013;13:288.
52. Aceijas C, Friedman SR, Cooper HL, Wiessing L, Stimson GV, Hickman M. Estimates of injecting drug users at the national and local level in developing and transitional countries, and gender and age distribution. Sex Transm Infect. 2006;82 S(3):10-17.
53. El-Ghazzawi E, Drew L, Hamdy L, El-Sherbini E, SadekSel-D, Saleh E. Intravenous drug addicts: A high risk group for infection with human immunodeficiency virus, hepatitis viruses, cytomegalo virus and bacterial infections in Alexandria Egypt. J Egypt Public Health Assoc. 1995; 70(1-2):127-50.
54. Elkareh S. HCV screening of donors in Governmental Blood Transfusion Centers at Menoufia Governorate (from Jan. 2008 to Oct. 2008).Vox Sang. 2009;13:89–90.
55. Abu-Raddad L, Akala FA, Semini I, Riedner G, Wilson D, Tawil O. Characterizing the HIV/AIDS epidemic in the Middle East and North Africa: Time for Strategic Action. Middle East and North Africa HIV/AIDS Epidemiology Synthesis Project. World Bank/UNAIDS/WHO Publication. Washington DC: The World Bank Press; 2010a.
56. Abu-Raddad LJ, Hilmi N, Mumtaz G, Benkirane M, Akala FA, Riedner G, et al. Epidemiology of HIV infection in the Middle East and North Africa. AIDS. 2010b;24(l2): S5-23.
57. Williams R. Global challenges in liver disease. Hepatology. 2006;44(521):26.

58. Medhat A, Shehata M, Magder LS, Mikhail N, Abdel-Baki L, Nafeh M, et al. Hepatitis C in a community in upper Egypt: Risk factors for infection. Am. J. Trop. Med. Hyg. 2002;66(5):633–638
59. El-Raziky MS, El-Hawary M, Esmat G, Abouzied AM, El-Koofy N, Mohsen N, et al. Prevalence and risk factors of asymptomatic hepatitis C virus infection in Egyptian children. World J Gastroenterol. 2007;28;13(12):1828-1832
60. Barakat SH, El-Bashir N. Hepatitis C virus infection among healthy Egyptian children: Prevalence and risk factors. J Viral Hepat. 2011;18(11):779-84.
61. Farghaly HS, Metwalley KA, Abd El-Hafeez HA. Hepatitis C virus infection in Egyptian children with type 1 diabetes mellitus: A single center study. Indian Journal of Endocrinology and Metabolim. 2014;18(2):197-201.
62. Irshad M, Peter S. Spectrum of viral hepatitis in thalassemic children receiving multiple blood transfusions. Indian J Gastroenterol. 2002;21:183-184.
63. Bortolotti F, Resti M, Giacchino R, Crivellaro C, Zancan L, Azzari C, et al. Changing epidemiologic pattern of chronic hepatitis C virus infection in Italian children. J Pediatr. 1998;133(3):378-381.
64. Agha S, Sherif LS, Allam MA, Fawzy M. Transplacental transmission of hepatitis C virus in HIV-negative mothers. Res Virol. 1998;149(4):229-234.
65. Kassem AS, El-Nawawy AA, Massoud MN, Abou El-Nazar SY, Sobhi EM. Prevalence of hepatitis C virus (HCV) infection and its vertical transmission in Egyptian pregnant women and their newborns. J Trop Pediatr. 2000;46(4):231-233.
66. Abdul Qawi K, Youssef A, Metwally MA, Ragih I, AbdulHamid M, Shaheen A. Prospective study of prevalence and risk factors for hepatitis C in pregnant Egyptian women and its transmission to their infants. Croat Med J. 2010;51(3):219-228.
67. Zahran KM, Badary MS, Agban MN, Abdel Aziz NH.Pattern of hepatitis virus infection among pregnant women and their newborns at the Women's Health Center of Assiut University, Upper Egypt. Int J Gynaecol Obstet. 2010;111(2):171-174.
68. Abo Elmagd EK, Abdel-Wahab KS, Alrasheedy ZE, Khalifa AS. An Egyptian study of mother to child transmission of hepatitis C virus. Int J Virology. 2011; 7(3):100-108.
69. Madwar MA, El-Gindy I, Fahmy HM, Shoeb NM, Massoud BA. Hepatitis C virus transmission in family members of Egyptian patients with HCV related chronic liver disease. J Egypt Public Health Assoc. 1999;74(3–4):313-332.
70. Shebl FM, El-Kamary SS, Saleh DA, Abdel-Hamid M, Mikhail N, Allam A, et al. Prospective cohort study of mother-to-infant infection and clearance of hepatitis C in rural Egyptian villages. J Med Virol. 2009; 81(6):1024-1031.
71. Mohamed MK, Magder LS, Abdel-Hamid M, El-Daly M, Mikhail NN, Abdel-Aziz F, Medhat A, Thiers V, Strickland GT. Transmission of hepatitis C virus between parents and children. Am J Trop Med Hyg. 2006;75(1):16-20
72. El-Nanawy AA, El Azzouni OF, Soliman AT, Amer AE, Demian RS, el-Sayed HM. Prevalence of hepatitis-C antibody seropositivity in healthy Egyptian children and four high risk groups. J Trop Pediatr. 1995;41(6):341–343.
73. Kandil ME, Rasheed MA, Saad NE. Hepatitis C and B viruses among some high risk groups of Egyptian children. J Med Sci. 2007;7(8):1259–1267.
74. Hammad AM, Zaghloul MH. Hepatitis G virus infection in Egyptian children with chronic renal failure (single centre study). Ann Clin Microbiol Antimicrob. 2009;8:36.
75. El-Karaksy H, Anwar GH, El-Raziky MS, El-Hawary M, Hashem M, El-Sayed R, et al. Anti-HCV prevalence among diabetic and non-diabetic Egyptian children. Curr Diabetes Rev. 2010;6(6):388–392.
76. El Gohary A, Hassan A, Nooman Z, Lavanchy D, Mayerat C, El Ayat A, et al. High prevalence of hepatitis C virus among urban and rural population groups in Egypt. Acta Trop. 1995;59(2):155–161.
77. Abdalla NM, Galal A, Fatouh AA, Eid K, Salama EEE, Gomma HE. Transfusion transmitted virus (TTV) infection in polytransfused Egyptian thalassemic children. J Med Sci. 2006;6(5):833–837.
78. Breban R, Doss W, Esmat G, Elsayed M, Hellard M, Ayscue P, et al. Towards realistic estimates of HCV incidence in Egypt. J Viral Hepat. 2013;20(4):294-6.
79. Castillo I, Pardo M, Bartolome J, Ortiz-Movilla N, Rodriguez-Inigo E, de Lucas S, et al. Occult hepatitis C virus infection in patients in whom the etiology of persistently abnormal results of liver-

function tests is unknown. Journal of Infectious Diseases. 2004;189(1):7-14.
80. Saad Y, Zakaria S, Ramzy I, El Raziky M, Shaker O, Elakel W, Said M, Noseir M, El-Daly M, Abdel Hamid M, Esmat G. Prevalence of occult hepatitis C in Egyptian patients with non alcoholic fatty liver disease. Open Journal of Internal Medicine. 2011;1(2):ID:7699,4.
81. Welker MW, Zeuzem S. Occult hepatitis C: How convincing are the current data? Hepatology. 2009;49(2):665–675.
82. Saad Y, Zakaria S, Ramzy I, El Raziky M, Shaker O, Elakel W, et al. Prevalence of occult hepatitis C in Egyptian patients with non-alcoholic fatty liver disease. Open Journal of Internal Medicine. 2011;1(2):33-37.
83. Youssef SS, Nasr AS, El Zanaty T, El Rawi RS, Mattar MM. Prevalence of occult hepatitis C virus in Egyptian patients with chronic lymphoproliferative disorders. Hepatitis Research and Treatment. 2012; 2012:Article ID 429784:6.
84. Gad YZ, Mouas N, Abdel-Aziz A, Abousmra N, Elhadidy M. Distinct immunoregulatory cytokine pattern in Egyptian patients with occult Hepatitis C infection and unexplained persistently elevated liver transaminases. Asian Journal of Transfusion Science. 2012;6(1): 24-28.
85. Amin RS, Abd Elaziz MM, El Iawindi M. Evaluation of an Isolation Program of Hepatitis C Virus Infected Hemodialysis Patients in Some Hemodialysis Centers in Egypt. ISRN Nephrology. 2013;(2013) :Article ID 395467:5.

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