

CONCLUSION

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From this study, it was concluded that:

- Seroprevalence of HCV infection among families of index cases was 15.9% versus 3.7% among families of controls.
- By using PCR prevalence of HCV infection among families of index cases was 8.6% versus 2.8% among families of controls.
- Prevalence increases with age significantly.
- Hospital admission, intravenous access, parenteral injection, blood transfusion, albumin transfusion, sutures, surgical procedures, endoscopy, urinary catheter, shaving at a barber and living with HCV infected persons are potential risk factors for HCV acquisition.
- Seroprevalence of HCV intrafamilial transmission in our study was 46.7% (35 positive families for intrafamilial co-infection for HCV infection out of total 75 positive index families), while by using PCR prevalence of HCV intrafamilial transmission was 31% (21 positive families for intrafamilial co-infection for HCV infection out of 75 total index positive families).
- Mother was more risky for intrafamilial co-infection to HCV infection than father or sibling (65 times versus 23 and 42 times respectively).
- Female index case was more risky for intrafamilial co-infection than male.
- There was a significant correlation between increasing age of index case and the co-infection rate.
- The sib-sib co-infection rate increased with increasing difference in age between infected siblings (higher if difference > 5 years).
- Sharing drink , sharing towels and sharing shaving instruments were independent predictors for HCV intrafamilial transmission.
- The phylogenetic analysis between the studied family members yielded no genetic concordance.

RECOMMENDATIONS

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From this study, we suggest various interventions, such as basic prevention procedures, infection control, screening programs, and raising public awareness to reduce the burden of the disease to further limit the spread of this infection.

- Ensuring infection control programs in all health care facilities.
- Efforts should be made to ensure blood donors continue to be screened for HCV.
- A policy requiring proper sterilization of medical and dental instruments
 - healthcare professionals should receive training on HCV, with specific instructions not to reuse syringes, as well as other techniques to reduce the risk of transmission.
- Screening in all pregnant women and to treat them accordingly. Infants born to HCV-positive mothers should also be screened and treated for HCV as soon as it presents.
- Screening of all children who have been subjected to risk factors of infection.
- Screening for all children at preparatory school for those with or without risk factors (as prevalence increases by age).
- Further research is needed to understand how intrafamilial transmission occurs with regard to spouses and children.
- recommendations for HCV infected individuals with regard to HCV transmission to other family members, not sharing shaving instruments ,not to drink together , not sharing towels or sharing food utensils.

REFERENCES

REFERENCES

- 1- Consensus Panel. National institutes of health consensus development conference statement: Management of hepatitis C:2002 June 10-12, 2002. *Hepatology* 2002; 36, S3-S20.
- 2- Geoffrey A, John S, Charles T, et al. Diagnosis and management of hepatitis C virus-infected children. *Pediatr Infect Dis J* 2011;30:983-5.
- 3- Alter MJ. Epidemiology of hepatitis C virus infection. *World J Gastroenterol* 2007;13:2436-41.
- 4- Frank C, Mohamed MK, Strickland GT, et al. The role of parenteral antischistosomal therapy in the spread of hepatitis C virus in Egypt. *Lancet* 2000;355:887-91.
- 5- Bakr I, Rekacewicz C, El Hosseiny M, et al. Higher clearance of hepatitis C virus infection in females compared with males. *Gut* 2006;55:1183-7.
- 6- Simmonds P, Bukh J, Combet C, et al. Consensus proposals for a unified system of nomenclature of hepatitis C virus genotype. *Hepatology* 2005; 42:962-73.
- 7- El-Raziky MS, El-Hawary M, Esmat G, et al. Prevalence and risk factors of asymptomatic hepatitis C virus infection in Egyptian children. *World J Gastroenterol* 2007; 13:1828-32.
- 8- John N. Pediatric hepatitis C. *Medscape Reference*. May 21,2012.
- 9- Murakami J, Okamoto M, Miyata H, et al. Evolution in the hypervariable region of hepatitis C virus in infants after vertical transmission. *Pediatr Res* 2000; 48:450-6.
- 10- Hoofnagle JH. Hepatitis C: the clinical spectrum of disease. *Hepatology* 2000; 26:15.
- 11- Thomson BJ, Finch RG. Hepatitis C virus infection. 1. Clinical microbiology and infection, 2005, 11:86-94.
- 12- Global distribution of hepatitis A, B and C. 2. *Weekly epidemiological record*, 2002, 77(6):41-8.
- 13- Medhat A et al. Hepatitis C in a community in Upper Egypt: risk factors for infection. *Amer J Trop Med Hyg* 2002, 66:633-8.
- 14- Hardeker W. Hepatitis C in childhood. *J Gastroenterol hepatol* 2002, 17:476-81.
- 15- Mamula P, Sreedharan R. Gastrointestinal tract infection. In: *Pediatric infectious diseases*, 1st ed. Oxford, Blackwell, 2005.
- 16- Jonas M. Children with hepatitis C. *Hepatology* 2002; 36:S173-8.
- 17- Mostafa K, Laurence S, Nabel N, et al. Transmission of hepatitis C virus between parents and children. *Am J Trop Med Hyg* 2006;75:16-20
- 18- Mohamed MK. Epidemiology of HCV infection in Egypt 2004. *Afro-arab Liver J* 2004;3:41-52.
- 19- Habib M, Mohamed MK, Abdel-Aziz F, et al. Hepatitis C virus infection in a community in the Nile Delta: risk factors for seropositivity. *Hepatology* 2001; 33: 248-253

- 20- Balbaa Sh. Prevalence of HCV in children attending outpatient clinic of El Shatby Hospital. M.D. Thesis. Alexandria University, Faculty of medicine, 2012:23-4.
- 21- Mohamed MK, Abdel-Hamid M, Mikhail NN, et al. Intrafamilial transmission of hepatitis C in Egypt. *Hepatology* 2005;42:683-7.
- 22- Lauer GM, Walker BD. Hepatitis C virus infection. *N Engl J Med* 2001;345:41-52.
- 23- Alter MJ. Epidemiology of viral hepatitis and HIV coinfection. *J Hepatol* 2006;44:S6-9.
- 24- Shepard CW, Finelli L, Alter MJ. Global epidemiology of hepatitis C virus infection. *Lancet Infect Dis* 2005;5:558-67.
- 25- Macedo de Oliveira A, White KL, Leschinsky DP, et al. An outbreak of hepatitis C virus infections among outpatients at a hematology/oncology clinic. *Ann Intern Med* 2005;142:898-902.
- 26- Williams IT, Perz JF, Bell BP. Viral hepatitis transmission in ambulatory health care settings. *Clin Infect Dis* 2004;38:1592-8.
- 27- Murphy EL, Bryzman SM, Glynn SA, et al. Risk factors for hepatitis C virus infection in United States blood donors. NHLBI Retrovirus Epidemiology Donor Study (REDS). *Hepatology* 2000;31:756-62.
- 28- Deterding K, Wiegand J, Gruner N, Wedemeyer H. Medical procedures as a risk factor for HCV infection in developed countries: do we neglect a significant problem in medical care? *J Hepatol* 2008;48:1019-20;author reply 1020-1.
- 29- Comstock RD, Mallonee S, Fox JL, et al. A large nosocomial outbreak of hepatitis C and hepatitis B among patients receiving pain remediation treatments. *Infect Control Hosp Epidemiol* 2004;25:576-83.
- 30- Krause G, Trepka MJ, Whisenhunt RS, et al. Nosocomial transmission of hepatitis C virus associated with the use of multidose saline vials. *Infect Control Hosp Epidemiol* 2003;24:122-7.
- 31- Lagging LM, Aneman C, Nenonen N, et al. Nosocomial transmission of HCV in cardiology ward during the window phase of infection: an epidemiological and molecular investigation. *Scand J Infect Dis* 2002;34:580-2.
- 32- Fornis X, Martinez-Bauer E, Feliu A, et al. Nosocomial transmission of HCV in the liver unit of a tertiary care center. *Hepatology* 2005;41:115-22.
- 33- Silini E, Locasciulli A, Santoleri L, et al. Hepatitis C virus infection in a hematology ward: evidence of nosocomial transmission and impact on hematological disease outcome. *Haematologica* 2002;87:1200-8.
- 34- Arafa N, Hoseiny ME, Rekacewicz C, et al. Changing pattern of hepatitis C virus spread in rural areas of Egypt. *J Hepatol* 2005;43:418-24.
- 35- Thorpe LE, Ouellet LJ, Hershov R, et al. Risk of hepatitis C virus infection among young adult injection drug users who share injection equipment. *Am J Epidemiol* 2002;155:645-53.

- 36- Koester S, Glanz J, Baron A, et al. Drug sharing among heroin networks: implications for HIV and hepatitis B and C prevention. *AIDS Behav* 2005;9:27-39.
- 37- Hegan H, Thiede H, Weiss NS, Hopkins SG, Duchin JS, Alexander ER. Sharing of drug preparation equipment as a risk factor for hepatitis C. *Am J Public Health* 2001;91:42-6.
- 38- Alter MJ. Prevention of spread of hepatitis C. *Hepatology* 2002;36:S93-8.
- 39- Shapshak P, Somboonwit C, Drumright LN, et al. Molecular and contextual markers of hepatitis C virus and drug abuse. *Mol Diagn Ther* 2009;13:153-79.
- 40- Thompson ND, Perz JF, Moorman AC, Holmberg SD. Nonhospital health care-associated hepatitis B and C virus transmission: United States, 1998–2008. *Ann Intern Med.* 2009 Jan 6;150(1):33–9.
- 41- Piazza M, Borgia G, Picciotto L, et al. Detection of hepatitis C virus-RNA by polymerase chain reaction in dental surgeries. *J Med Virol* 2000;45:40-2.
- 42- Mohamed K, Magder S, Mikhail N, et al. Transmission of hepatitis C virus between parents and children. *Am J Trop Med Hyg* 2006;75:16-20.
- 43- Dusheiko GM, Smith M, Scheuer PJ, et al. Hepatitis C virus transmitted by human bite. *Lancet* 1990;336:503-4.
- 44- *Mastromatteo AM, Rapaccini GL, Pompili M, et al. Hepatitis C virus infection: other biological fluids than blood may be responsible for intrafamilial spread. Hepatogastroenterology* 2001;48: 193–196.
- 45- *Fabris P, Infantolino D, Biasin MR, et al. High prevalence of HCV-RNA in the saliva cell fraction of patients with chronic hepatitis C but no evidence of HCV transmission among sexual partners. Infection* 2000; 27: 86–91.
- 46- *Hermida M, Ferreira MC, Barral S, et al. Detection of HCV RNA in saliva of patients with hepatitis C virus infection by using a highly sensitive test. J Virol Methods* 2002;101: 29–35.
- 47- Laurent C, Henzel D, Mulanga-Kabeya C, et al. Seroepidemiological survey of hepatitis C virus among commercial sex workers and pregnant women in Kinshasa, Democratic Republic of Congo. *Int J Epidemiol* 2001;30:872-7.
- 48- Hepburn MJ, Lawitz EJ. Seroprevalence of hepatitis C and associated risk factors among an urban population in Haiti. *BMC Gastroenterol* 2004;4:31.
- 49- Memon MI, Memon MA. Hepatitis C: an epidemiological review. *J Viral Hepat* 2002;9:84-100.
- 50- Filippini P, Coppola N, Scolastico C, et al. Does HIV infection favor the sexual transmission of hepatitis C? *Sex Transm Dis* 2001;28:725-9.
- 51- Nyamathi A, Robbins WA, Fahey JL, et al. Presence and predictors of hepatitis C virus RNA in the semen of homeless men. *Biol Res Nurs* 2002;4:22-30.
- 52- Ferreira MC, Dios PD, Scully C. Transmission of hepatitis C virus by saliva? *Oral Diseases* 2005;11:230-5.
- 53- Cavaleiro NP. Sexual transmission of hepatitis C. Review. *Rev Inst Med*

- Trop Sao Paulo 2007;49:271-7.
- 54- Magder LS, Fix AD, Mikhaiil NN, et al. Estimation of the risk of transmission of hepatitis C between spouses in Egypt based on seroprevalence data. *Int J Epidemiol* 2005;34:160-5.
 - 55- Roberts EA, Yeung L. Maternal-infant transmission of hepatitis C virus infection. *Hepatology* 2002;36:S106-13.
 - 56- Esmat G, Hesham M, El-Raziky M, et al. Risk factors for hepatitis C virus acquisition and predictors of persistence among Egyptian children. *J Liv Internat* 2012;25:449-56.
 - 57- Larouche A, Daniel S, Soudeyns H. Pathogenesis of hepatitis C virus during pregnancy and childhood. *Viruses* 2012;4:3531-50.
 - 58- Mast EE, Hwang LY, Seto DS, et al. Risk factors for perinatal transmission of HCV and the natural history of HCV infection acquired in infancy. *J Infect Dis* 2005;192:1880-9.
 - 59- Tajiri H, Miyoshi Y, Funada S, et al. Prospective study of mother-to-infant transmission of hepatitis C virus. *Pediatr Infect Dis J* 2001; 20:10–4.
 - 60- Steininger C, Kundi M, Jatzko G, et al. Increased risk of mother-to-infant transmission of hepatitis C virus by intrapartum infantile exposure to maternal blood. *J Infect Dis* 2003;187:345–51
 - 61- Mok J, Pembrey L, P-A Tovo, Newell M-L. When does mother to child transmission of hepatitis C virus occur? *Arch Dis Child Fetal Neonatal Ed* 2005; 90:F156–F160.
 - 62- Meyer A. Transmission of Hepatitis C Virus From Infected Mother to Offspring During Subsequent Pregnancies. *J Ped Gastroenterol Nutr* 2000;30,491-3.
 - 63- Ruiz-Extremera A, Salmeron J, Torres C, et al. Follow-up of transmission of hepatitis C to babies of human immunodeficiency virus-negative women: the role of breast-feeding in transmission. *Pediatr Infect Dis J* 2000;19:511-516
 - 64- Conte D, Fraquelli M, Prati D, et al. Prevalence and clinical course of chronic hepatitis C virus (HCV) infection and rate of HCV vertical transmission in a cohort of 15,250 pregnant women. *Hepatology* 2000;31:751-755.
 - 65- Yeung L, King S, Roberts A. Mother-to-Infant Transmission of Hepatitis C Virus. *Hepatology* 2001;34:223-9.
 - 66- European Paediatric Hepatitis C Virus Network. Effects of mode of delivery and infant feeding on the risk of mother-to-child transmission of hepatitis C virus. *BJOG* 2001; 108 :371–7.
 - 67- European Paediatric Hepatitis C Virus Network. A significant sex—but not elective cesarean section —effect on mother-to-child transmission of hepatitis C virus infection. *J Infect Dis* 2005;192:1872–9
 - 68- Mack C, Gupta N, Leung D, et al. NASPGHAN practice guidelines: diagnosis and management of hepatitis C infection in infants, children, and

- adolescents. *J Ped Gastroenterol* 2012;54: 838–855
- 69- Leruez-Ville M, Kunstmann JM, De Almeida M, et al. Detection of hepatitis C virus in the semen of infected men. *Lancet* 2000;356:42-3.
- 70- Manavi M, Waatkins-Riedel T, Kucera E, et al. Evidence of hepatitis C virus in cervical smears. *J Infect* 2000;38:60-1.
- 71- Terrault NA. Sexual activity as a risk factor for hepatitis C. *Hepatology* 2002;36:S99-105.
- 72- Minola E, Baldo V, Baldovin T, et al. Intrafamilial transmission of hepatitis C virus infection. *Euro J Epid* 2006;21:293-7.
- 73- Inciardi JA, Surratt HL, Kurts SP. HIV, HBV, and HCV infections among drug-involved, inner-city, street sex workers in Miami, Florida. *AIDS Behav* 2006; 10(2):139–47.
- 74- Indolfi G, Bartolini E, Azzari C, et al. Intrafamilial transmission of hepatitis C virus: infection of the father predict the risk of perinatal transmission. *J Med Virol* 2008; 80(11):1907–11.
- 75- Pasha O, Luby S, Khan A, et al. Household members of hepatitis C virus-infected people in Hafizabad, Pakistan: infection by injections from health care providers. *Epidemiol Infect* 2000;123:515-8.
- 76- Ackerman Z, Ackerman E, Paltiel O. Intrafamilial transmission of hepatitis C virus: a systematic review. *J Viral Hepat* 2000;7:93-103.
- 77- Akhtar S, Moatter T. Intra-household clustering of hepatitis C virus infection in Karachi, Pakistan. *Trans R Soc Trop Med Hyg* 2004;98:535-9.
- 78- El-Raziky MS, El-Hawary M, El-Koofy N, et al. Hepatitis C virus infection in Egyptian children: single centre experience. *J Viral Hepat* 2004; 11: 471-476.
- 79- Ranjbar M, Golzardi Z, Sedigh L, et al. Intrafamilial seropositivity of hepatitis in patients with hepatitis B and C virus in hepatitis clinic in Hamadan, Iran. *Hepatology* 2012;11:32-6.
- 80- Jara P, Resti M, Hierro L, et al. Chronic hepatitis C virus infection in childhood, clinical patterns and evolution in 224 white children. *Inf Dis* 2003;36:275-80.
- 81- Kim YS, Chi HS, Ahn YO, et al. Lack of familial clustering of hepatitis C virus infection. *Int J Epide-miol* 1998;27: 525–529.
- 82- Kumar RM. Interspousal and intrafamilial transmission of hepatitis C virus: a myth or a concern. *Obstet Gynecol* 1998;91:426–431.
- 83- Napoli N, Fiore G, Vella F, et al. Prevalence of antibodies to hepatitis C virus among family members of patients with chronic hepatitis C. *Eur J Epidemiol* 1993:629–632.
- 84- Ruiz-Extremera A, Antonio Munoz-Gamez JA, Salmeron-Ruiz MA, et al. Genetic Variation in Interleukin 28B with respect to vertical transmission of hepatitis C virus and spontaneous clearance in HCV-infected children. *Hepatology* 2011;53:1830—8.
- 85- Freeman AJ, Dore GJ, Law MG, et al. Estimating progression to cirrhosis in

- chronic hepatitis C virus infection. *Hepatology* 2001; 34(4 Part 1): 809–816.
- 86- Durmaz O. Hepatitis C infection in childhood. *Clinics and Research in Hepatology and Gastroenterology* 2012; 36, 294—296.
- 87- Nettleman M. Hepatitis C. *Medscape Reference* September 28,2012.
- 88- Gonzalez-Peralta RP, Langham MR Jr, Andres JM, et al. Hepato-cellular carcinoma in 2 young adolescents with chronic hepatitis C. *J Pediatr Gastroenterol Nutr* 2009;48:630–5.
- 89- Lok AS, Seeff LB, Morgan TR, et al. Incidence of hepatocellular carcinoma and associated risk factors in hepatitis C-related advanced liver disease. *Gastroenterology* 2009;136:138–48.
- 90- Madhoun MF, Fazili J, Bright BC, et al. Hepatitis C prevalence in patients with hepatocellular carcinoma without cirrhosis. *Am J Med Sci* 2010;339:169–73.
- 91- Forton DM, Thomas HC, Murphy CA, et al. Hepatitis C and cognitive impairment in a cohort of patients with mild liver disease. *Hepatology* 2002;35:433–9.
- 92- Voget M, Lang T, Frosner G, et al. Prevalence and clinical outcome of hepatitis C infection in children who underwent cardiac surgery before the implementation of blood-donor screening. *N Engl J Med* 2000;341:866-70.
- 93- Strickland DK, Riely CA, Patrick CC, et al. Hepatitis C infection among survivors of childhood cancer. *Blood* 2000;95:3065-70.
- 94- Visoná K, Baez F, Taylor L, et al. Impact of Hepatitis B and Hepatitis C Virus Infections in a Hematology-Oncology Unit at a Children’s Hospital in Nicaragua, 1997 to 1999. *Clinical and diagnostic laboratory immunology* 2002;9(3), 622–626
- 95- Bortolotti F, Verucchi G, Camma C, et al. Long-term course of chronic hepatitis C in children: from viral clearance to end-stage liver disease. *Gastroenterology* 2008;134:1900–7.
- 96- Hashem M, El-Karaksy H, Sobhy M, et al. Strong Hepatitis C Virus (HCV)–specific Cell-mediated Immune Responses in the Absence of Viremia or Antibodies Among Uninfected Siblings of HCV Chronically Infected Children. *J Inf Dis* 2011;203:854-61.
- 97- Delgado-Borrego A, Healey D, Negre B, et al. Influence of body mass index on outcome of pediatric chronic hepatitis C virus infection. *J Pediatr Gastroenterol Nutr* 2010;51:191–7.
- 98- Delgado-Borrego A, Jordan SH, Negre B, et al. Reduction of insulin resistance with effective clearance of hepatitis C infection: results from the HALT-C trial. *Clin Gastroenterol Hepatol* 2010;8:458–62.
- 99- Benhamou Y, Bochet M, DiMartino V, et al. Liver fibrosis progression in human immunodeficiency virus and hepatitis C virus coinfecting patients. *Hepatology* 2000;30:1054–1058
- 100- Alisi A, Comparcola D, Nobili V. Treatment of chronic hepatitis C in children: Is it necessary and, if so, in whom? *J Hepatology* 2010; 52:501-7.

- 101- Cesaro S, Bortolotti F, Petris MG, et al. An updated follow-up of chronic hepatitis C after three decades of observation in pediatric patients cured of malignancy. *Pediatr Blood Cancer* 2010;55:108–12.
- 102- Huang H, Shiffman ML, Cheung RC, et al. Identification of two gene variants associated with risk of advanced fibrosis in patients with chronic hepatitis C. *Gastroenterology* 2006;130:1679–87.
- 103- Mosbruger TL, Dugga P, Goedert JJ, et al. Large-scale candidate gene analysis of spontaneous clearance of hepatitis C virus. *J Infect Dis* 2010;201:1371–80 .
- 104- Bosi I, Ancora G, Mantovani W, et al. HLA DR13 and HCV vertical infection. *Pediatr Res* 2002;51:746–9.
- 105- Martinetti M, Pacati I, Cuccia M, et al. Hierarchy of baby-linked immunogenetic risk factors in the vertical transmission of hepatitis C virus. *Int J Immunopathol Pharmacol* 2006;19:369–78 .
- 106- Bevilacqua E, Fabris A, Floreano P, et al. Genetic factors in mother-to-child transmission of HCV infection. *Virology* 2009;390:64–70 .
- 107- Della Bella S, Riva A, Tanzi E, et al. Hepatitis C virus-specific reactivity of CD4B-lymphocytes in children born from HCV-infected women. *J Hepatol* 2005;43:394–402.
- 108- Yeung LT, To T, King SM, et al. Spontaneous clearance of childhood hepatitis C virus infection. *J Viral Hepatol* 2007;14:797–805.
- 109- Jhaveri R. Diagnosis and Management of Hepatitis C Virus–infected Children. *Pediatr Infect Dis J* 2011;30: 983–985.
- 110- Rerksuppaphol S, Hardikar W, Dore GJ. Long-term outcome of vertically acquired and post-transfusion hepatitis C infection in children. *J Gastroenterol Hepatol* 2004;19:1357–62.
- 111- Farci P, Quinti I, Farci S, et al. Evolution of hepatitis C viral quasispecies and hepatic injury in perinatally infected children followed prospectively. *PNAS* 2006 ; 103 : 8475–80.
- 112- Abdel-Hady M, Sira J, Brown R. M, et al. Chronic hepatitis C in children – review of natural history at a National Centre. *J Viral Hepatitis* 2011; 18: e535–40.
- 113- Iorio R, Giannattasio A, Sepe A, et al. Chronic hepatitis C in childhood: an 18-year experience. *Clin Infect Dis* 2005;41:1431–7.
- 114- NIH Consensus Statement on Management of Hepatitis C: 2002. *NIH Consensus State Sci Statements* 2002; 19:1–46.
- 115- Camarero C, Ramos N, Moreno A, et al. Hepatitis C virus infection acquired in childhood. *Eur J Pediatr* 2008;167:219–24.
- 116- Goodman ZD, Makhlof HR, Liu L, et al. Pathology of chronic hepatitis C in children: liver biopsy findings in the Peds-C Trial. *Hepatology* 2008;47:836–43 .
- 117- Gonzalez-Peralta RP, Kelly DA, Haber B, et al., International Pediatric Hepatitis C Therapy Group Interferon alfa-2b in combination with ribavirin

- for the treatment of chronic hepatitis C in children: efficacy, safety, and pharmacokinetics. *Hepatology* 2005;42:1010–8 .
- 118- Schwarz KB, Gonzalez-Peralta RP, Murray KF, et al. The combination of ribavirin and peginterferon is superior to peginterferon and placebo for children and adolescents with chronic hepatitis C. *Gastroenterology* 2011;140:450–8.
- 119- Wirth S, Ribes-Koninckx C, Calzado MA, et al. High sustained virologic response rates in children with chronic hepatitis C receiving peginterferon alfa-2b plus ribavirin. *J Hepatol* 2010;52:501–7.
- 120- Bekisz J, Schmeisser H, Hernandez J, et al. Human interferons alpha, beta and omega. *Growth Factors* 2004;22:243–51 .
- 121- Stefan W. Current treatment options and response rates in children with chronic hepatitis C. *World J Gastroenterol* 2012; 18(2): 99-104.
- 122- Bostan N, Mahmood T. An overview about hepatitis C: a devastating virus. *Crit Rev Microbiol* 2010;36:91–133.
- 123- World Health Organisation. Hepatitis C: global prevalence. *Weekly Epidemiological Record* 1999; 74: 421-428.
- 124- Global surveillance and control of hepatitis C. Report of a WHO Consultation organized in collaboration with the Viral Hepatitis Prevention Board, Antwerp, Belgium. *J Viral Hepat* 1999; 6: 35-47.
- 125- Madhava V, Burgess C, Drucker E. Epidemiology of chronic hepatitis C virus infection in sub-Saharan Africa. *Lancet Infect Dis* 2002; 2: 293-302.
- 126- Eassa S, Eissa M, Sharaf SM, et al. Prevalence of Hepatitis C Virus Infection and Evaluation of a Health Education Program in El-Ghar Village in Zagazig, Egypt. *J Egypt Public Health Assoc* 2007;82:379–404.
- 127- Said ZN, El-Sayed MH, El-Bishbishi IA, et al. High prevalence of occult hepatitis B in hepatitis C infected Egyptian children with haematological disorders and malignancies. *Liver Int.* 2009; 29(4): 518–24. [PubMed: 19192168].
- 128- 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.
- 129- Aziz F, Habib M, Mohamed MK, et al. Hepatitis C virus (HCV) infection in a community in the Nile Delta: population description and HCV prevalence. *Hepatology.* 2000; 32:111–115.
- 130- Nafeh MA, Medhat A, Shehata M, et al. Hepatitis C in a community in Upper Egypt: I. Crosssectional survey: *Am J Trop Med Hygiene.* 2000; 63:236–41.
- 131- Lee M, Yang I, Yuan Y, et al. Epidemiology and natural history of hepatitis C virus infection *World J Gastroenterol* 2014 July 28; 20(28): 9270-9280.
- 132- Khattab MA, Eslam M, Sharwae MA, et al. Seroprevalence of hepatitis C and B among blood donors in Egypt: Minya Governorate, 2000–2008. *Am J Infect Control* 2010, 38(8):640–641.

- 133- Strickland GT, Elhefni H, Salman T, et al. Role of hepatitis C infection in chronic liver disease in Egypt. *Am J Trop Med Hyg* 2002, 67(4):436–442.
- 134- Demian AD: Prevalence of anaesthetic co-morbid factors among urological patients in a tertiary referral centre in Egypt. *Egyptian J Anaesth* 2004, 20(3):325–330.
- 135- Darwish MA, Faris R, Darwish N, et al. Hepatitis C and cirrhotic liver disease in the Nile delta of Egypt: A community-based study. *Am J Trop Med Hyg* 2001, 64(3–4):147–153.
- 136- Pereir L, Martelli C, Moreira R, et al. Prevalence and risk factors of Hepatitis C virus infection in Brazil, 2005 through 2009: a crosssectional study. *BMC Infectious Diseases* 2013, 13:60
- 137- Awadalla H, Ragab M, Nassar N, et al. Risk factors of hepatitis C infection among egyptian blood donors. *Cent Eur J Public Health* 2011; 19 (4): 217–221.
- 138- Alter MJ, Kruszon-Moran D, Nainan OV, et al. The prevalence of hepatitis C virus infection in the United States, 1988 through 1994. *N Engl J Med* 1999; 341: 556-562.
- 139- Armstrong GL, Wasley A, Simard EP, et al. The prevalence of hepatitis C virus infection in the United States, 1999 through 2002. *Ann Intern Med* 2006; 144: 705-714.
- 140- Hutchinson SJ, Goldberg DJ, King M, et al. Hepatitis C virus among childbearing women in Scotland: prevalence, deprivation, and diagnosis. *Gut* 2004; 53: 593-598.
- 141- Sosa-Jurado F, Hernández-Galindo V, Meléndez-Mena D, et al. Detection of hepatitis C virus RNA in saliva of patients with active infection not associated with periodontal or liver disease severity. *BMC Infectious Diseases* 2014, 14:72.
- 142- Kalil KA, Farghally HS, Hassanein KM, et al. Hepatitis C virus infection among paediatric patients attending University of Assiut Hospital, Egypt. *J Eastern Mediterranean health* 2010, 16(4):356–361.
- 143- El-Medany OM, El-Din Abdel Wahab KS, Abu Shady EA, et al. Chronic liver disease and hepatitis C virus in Egyptian patients. *Hepatogastroenterology* 1999, 46(27):1895–1903.
- 144- Sun CA, Chen HC, Lu CF, et al. Transmission of hepatitis C virus in Taiwan: prevalence and risk factors based on a nationwide survey. *J Med Virol* 1999; 59: 290-296
- 145- Kane A, Lloyd J, Zaffran M, et al. Transmission of hepatitis B, hepatitis C and human immunodeficiency viruses through unsafe injections in the developing world:model-based regional estimates. *Bull World Health Organ* 1999; 77: 801-807
- 146- Stark K, Poggensee G, Höhne M, et al. Seroepidemiology of TT virus, GBC-C/HGV, and hepatitis viruses B, C, and E among women in a rural area of Tanzania. *J Med Virol* 2000; 62: 524-530
- 147- Chowdhury A, Santra A, Chaudhuri S, et al. Hepatitis C virus infection in the

- general population: a community- based study in West Bengal, India. *Hepatology* 2003; 37: 802-9.
- 148- Doerrbecker J, Friesland M, Ciesek S, et al. Inactivation and survival of hepatitis C virus on inanimate surfaces. *JID* 2011;204:1830-8.
- 149- Rich JD, Taylor LE. The beginning of a new era in understanding hepatitis C virus prevention. *J Infect Dis* 2010;202:981-3.
- 150- Alter HJ, Houghton M. Clinical Medical Research Award. Hepatitis C virus and eliminating post-transfusion hepatitis. *Nat Med* 2000; 6: 1082-6.
- 151- Shan H, Wang JX, Ren FR, et al. Blood banking in China. *Lancet* 2002; 360: 1770-5.
- 152- Tagny CT, Mbanya D, Tapko JB, et al. Blood safety in Sub-Saharan Africa: a multi-factorial problem. *Transfusion* 2008; 48: 1256-61.
- 153- Jafri W, Jafri N, Yakoob J, et al. Hepatitis B and C: prevalence and risk factors associated with seropositivity among children in Karachi, Pakistan. *BMC Infect Dis.* 2006; 23(6):101.
- 154- Waheed Y, Shafi T, Safi SZ, et al. Hepatitis C virus in Pakistan: a systematic review of prevalence, genotypes and risk factors *World. J Gastroenterol.* 2009; 15:5647–53.
- 155- Rosa R, Martinelli A, Passos A. Risk factors for hepatitis C virus transmission in the municipality of Catanduva, State of São Paulo: a case-control study. *Rev Soc Bras Med Trop* 2014;47(3):295-301.
- 156- Mohamoud Y, Mumtaz G, Riome S, et al. The epidemiology of hepatitis C virus in Egypt: a systematic review and data synthesis. *BMC Infectious Diseases* 2013, 13:288.
- 157- Esmat G, Hashem M, El-Raziky M, et al. Risk factors for hepatitis C virus acquisition and predictors of persistence among Egyptian children. *Liver Int* 2012 ; 32(3): 449–56.
- 158- Saleh DA, Shebl F, Abdel-Hamid 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):921–8.
- 159- El-Sadawy M, Ragab H, El-Toukhy H, et al. Hepatitis C virus infection at Sharkia Governorate, Egypt: seroprevalence and associated risk factors. *J Egypt Soc Parasitol* 2004, 34(1):367–84.
- 160- Suzuki T, Omata K, Satoh T, et al. Quantitative detection of hepatitis C virus (HCV) RNA in saliva and gingival crevicular fluid of HCV-infected patients. *J Clin Microbiol* 2005, 43(9):4413–7.
- 161- Shafique M, Ahmad N, Awan FR, et al. Investigating the concurrent presence of HCV in serum, oral fluid and urine samples from chronic HCV patients in Faisalabad, Pakistan. *Arch Virol* 2009, 154(9):1523–7.
- 162- Wang CC, Morishima C, Chung M, et al. High serum hepatitis C virus (HCV) RNA load predicts the presence of HCV RNA in saliva from individuals with chronic and acute HCV infection. *J Infect Dis* 2006, 193(5):672–6.

- 163- Lins L, Almeida H, Vitvisk L, et al. Detection of hepatitis C virus RNA in saliva is not related to oral health status or viral load. *J Med Virol* 2005, 77(2):216–220.
- 164- Enomoto A, Yoshino S, Hasegawa H, et al. Phylogenetic investigation for the risk of hepatitis C virus transmission to surgical and dental patients. *J Viral Hepat* 2001; 8: 148–153.
- 165- Saleha D, Sheblb F, El-Kamary S, et al. Incidence and risk factors for community-acquired hepatitis C infection from birth to 5 years of age in rural Egyptian children. *Trans R Soc Trop Med Hyg* 2010; 104(5): 357–63.
- 166- Arrieta JJ, Rodriguez-Inigo E, Ortiz-Movilla N, et al. In situ detection of hepatitis C virus RNA in salivary glands. *Am J Pathol* 2001, 158(1):259–64.
- 167- Vera-Otarola J, Barria MI, Leon U, et al. Hepatitis C virus quasispecies in plasma and peripheral blood mononuclear cells of treatment naive chronically infected patients. *J Viral Hepat* 2009, 16(9):633–43.
- 168- Toussirof E, Le Huede G, Mougin C, et al. Presence of hepatitis C virus RNA in the salivary glands of patients with Sjogren's syndrome and hepatitis C virus infection. *J Rheumatol* 2002,29(11):2382–5.
- 169- Kamili S, Krawczynski K, Maccaustland K, et al. Infectivity of hepatitis C virus in plasma after drying and storing at room temperature. *Infect Control Hosp Epidemiol* 2007; 28:519-24.
- 170- Amodio E, Di Benedetto MA, Gennaro L, et al. Knowledge, attitudes and risk of HIV, HBV, and HCV infections in hairdressers of Palermo city (South Italy). *European J Public Health* 2009; 20:433-7.
- 171- Deneluz AC, Oliveira S, Focaccia R. Survey of hepatitis B and C infection control: procedures at manicure and pedicure facilities in São Paulo, Brazil. *Braz J Infect Dis* 2010; 14: 502-7.
- 172- Stroffolini T, Lorenzoni U, Menniti-Ippolito F, et al. Hepatitis C virus infection in spouses: sexual transmission or common exposure to the same risk factors? *Am J Gastroenterol* 2001; 96:3138- 41.
- 173- Keiserman DR, Both CT, Mattos AA, et al. Intrafamilial transmission of hepatitis C virus in patients with hepatitis C and human immunodeficiency virus coinfection. *Am J Gastroenterol* 2003; 98:878- 83.
- 174- Shin HR, Kim JY, Ohno T, et al. Prevalence and risk factors of hepatitis C virus infection among Koreans in rural area of Korea. *Hepatol Res* 2000; 17: 185-96.
- 175- Post JJ, Dolan KA, Whybin LR, et al. Acute hepatitis C virus infection in an Australian prison inmate: tattooing as a possible transmission route. *Med J Australia* 2001; 174:183-4.
- 176- Nishioka AS, Gyorkos TW, Joseph L, et al. Tattooing and transfusion-transmitted diseases in Brazil: a hospital-based cross-sectional matched study. *European J Epidemiol* 2003; 18:441-9.
- 177- Ernst E, Sherman KJ. Is acupuncture a risk factor for hepatitis? Systematic review of epidemiological studies. *J Gastroenterol Hepatol* 2003; 18:1231-6.

- 178- Reynolds L, Mckee M. Possible risks of transmission of bloodborne infection via acupuncture needles in Guizhou Province, Southwest China. *J Altern Complement Med* 2008; 14:1281-5.
- 179- Pérez CM, Suárez E, Torres EA, et al. Seroprevalence of hepatitis C virus and associated risk behaviours: a population-based study in San Juan, Puerto Rico. *Int J Epidemiol* 2005; 34: 593-9.
- 180- Hagan H, McGough JP, Thiede H, et al. Syringe exchange and risk of infection with hepatitis B and C viruses. *Am J Epidemiol* 1999; 149: 203-13.
- 181- Kassem AS, El-Nawawy AA, Massoud MN, et al. Prevalence of hepatitis C virus (HCV) infection and its vertical transmission in Egyptian pregnant women and their newborns. *J Trop Pediatr* 2000, 46(4):231–3.
- 182- Zahran KM, Badary MS, Agban MN, et al. 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):171–4.
- 183- Abo Elmagd EK, Abdel-Wahab KS, Alrasheedy ZE, et al. An Egyptian study of mother to child transmission of hepatitis C virus. *Int J Virology* 2011, 7(3):100–8.
- 184- Shebl FM, El-Kamary SS, Saleh DA, 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):1024–31.
- 185- Grazia Tosone, Alberto Enrico Maraolo, Silvia Mascolo, et al. Vertical hepatitis C virus transmission: Main questions and answers. *World J Hepatol* 2014; 6(8): 538-48.
- 186- Reker C, Islam K.M. Risk factors associated with high prevalence rates of hepatitis C infection in Egypt. *Internat J Inf Dis* (2014);25:104–6.
- 187- Clarke A, Kulasegaram R. Hepatitis C transmission – where are we now? *Int J STD AIDS* 2006;17:74-80; quiz 80.
- 188- Santantonio T, Medda E, Ferrari C, et al. Risk factors and outcome among a large patient cohort with community-acquired acute hepatitis C in Italy. *Clin Infect Dis* 2006;43:1154-9.
- 189- Vivas-Arceo C, Benavides SA, De Jesus TJ, et al. Hepatitis C virus: prevalence and routes of infection among blood donors of West Mexico. *Hepatol Res* 2003, 25(2):115–23.
- 190- Alvarez-Munoz MT, Vences-Aviles MA, Damacio L, et al. Hepatitis C virus RNA (HCV-RNA) in blood donors and family members seropositive for anti-HCV antibodies. *Arch Med Res* 2001, 32(5):442–5.
- 191- Akhtar S, Moatter T. Multilevel modeling of intra household spread of hepatitis C virus infection, Karachi, Pakistan. *Am J Trop Med Hyg* 2007; 76: 446-9 .
- 192- McMahon JM, Pouget ER, Tortu S. Individual and couplelevel risk factors for hepatitis C infection among heterosexual drug users: a multilevel dyadic analysis. *J Infect Dis* 2007; 195: 1572-81.

- 193- El-Zayadi A, Khalifa AA, El-Misiery A, et al. Evaluation of risk factors for intrafamilial transmission of HCV infection in Egypt. *J Egypt Public Health Assoc* 1997; 72(1–2):33–51.
- 194- Plancoulaine S, Mohamed MK, Arafa N, et al. Dissection of familial correlations in hepatitis C virus seroprevalence suggests intrafamilial viral transmission and genetic predisposition to infection. *Gut* 2008;57:1268-74.
- 195- Doss W, Mohamed MK, Esmat G, et al. Modes of transmission. Egyptian national Control strategy for viral hepatitis 2008-2012. Ministry of health and population, National committee for the control of viral hepatitis. Egypt ,2012: 3.
- 196- Toda T, Mitsui T, Tsukamoto Y, et al. Molecular analysis of transmission of hepatitis C virus in a nurse who acquired acute hepatitis C after caring for a viremic patient with epistaxis. *J Med Virol* 2009; 81:1363-70.
- 197- Hosoglu S, Celen MK, Akalin S, et al. Transmission of hepatitis C by blood splash into conjunctiva in a nurse. *Am J Infec Control* 2003; 31:502-4.
- 198- Centers for Disease Control and Prevention (CDC). Update US Public Health Service guideline for the management of occupational exposures to HBV, HCV, and HIV and recommendations for post exposure prophylaxis. RR11. *MMWR* 2001; 50:1-54.
- 199- Ciesek S, Friesland M, Steinmann J, et al. How stable is the HCV? Environmental stability of HCV and its susceptibility to chemical biocides. *J Infect Dis* 2010;201:1859-66.
- 200- Lock G, Dirscherl M, Obermeier F, et al. Hepatitis C – contamination of toothbrushes: myth or reality? *J Viral Hepatol* 2006;13:571-3.
- 201- Hahn JA, Page-Shafer K, Lume PJ, et al. hepatitis C virus seroconversion among young injection drug users: relationships and risks. *J Infect Dis* 2002;186:1558-64.
- 202- Jimenez AP, Eldin N, El-Daly M, et al. HCV iatrogenic and intrafamilial transmission in Greater cairo, Egypt. *Gut* 2010;59:1554-60.
- 203- Mostafa A, Taylor S, El-Daly M, et al. Is the hepatitis C virus epidemic over in Egypt? Incidence and risk factors of new hepatitis C virus infections. *Liver Int* 2010;30:560-6.
- 204- Yee LJ. Host genetic determinants in hepatitis C virus infection. *Genes Immun* 2004;5:237-45.
- 205- Morice Y, Roulot D, Grando V, et al.. Phylogenetic analyses confirm the high prevalence of hepatitis C virus (HCV) type 4 in the Seine-Saint-Denis district (France) and indicate seven different HCV-4 subtypes linked to two different epidemiological patterns. *J Gen Virology* 2001; 82: 1001–12.

APPENDICES

Appendix A

The questionnaire

i- Health care related risk factors:

- 1- Name
- 2- Age
- 3- Sex
- 4- Residence
- 5- Telephone
- 6- Occupation
- 7- Social standard
- 8- History of previous hospital admission (including NICU), site
- 9- History I.V. access
- 10- History of parenteral injection (site, route)
- 11- History of blood transfusion
- 12- Circumcision
- 13- History of any sutures (site, place)
- 14- History of surgical procedures (place)
- 15- History of endoscopy or urinary catheter
- 16- History of dental procedures
- 17- History of abscess drainage
- 18- Ear piercing
- 19- Folk medicine
- 20- Tattooing
- 21- History of parenteral antibillharizial treatment (tartar)
- 22- Manicure, pedicure
- 23- Shaving at a barber
- 24- Living with HCV infected patient and for how long
- 25- Family history of chronic liver disease, hemodialysis patient or on repeated blood transfusion

ii- Intra-familial high risk behaviors

I- Contact risk factors

- 1- Time contact by hours
- 2- Sleeping pattern

II- Eating habits risk factors

- 1- Eating together
- 2- Sharing spoons
- 3- Drinking together

III- Risky behaviors for HCV co-infection

- 1- Sharing towels

- 2- Sharing personal tools (combs, hairbrushes, toothbrushes, soap, shared cottons)
- 3- Sharing sharp instruments (scissors, pedicure tools)
- 4- Sharing shaving instruments

IV- Direct exposure

- 1- Accidental exposure to the blood or any secretions to the skin or to the eye
- 2- History of getting bitten by infected persons

Appendix B

Modified social score for family social leveling

(Modified after Fahmy& El Sherbini 1983)

I & II education and work of father and mother

• Read and write or illiterate	Not working	1
• Read and write or illiterate	working	2
• Literate certificate	Not working	3
• Literate certificate	working	4
• Primary education	Not working	5
• Primary education	working	6
• Preparatory education	Not working	7
• Preparatory education	working	8
• Secondary education	Not working	9
• Secondary education	working	10
• University education	Not working	11
• University education	working	12

12 for father and 12 for mother = 24 points

III Percapita income / month

• 1000	8	Enough and saving
• 500 – < 1000	6	Enough only
• 250 - <500	4	Not enough and loan
• <250	4	Not enough, loan andnot repaid

IV Family size

• 3 or 4	8
• 5	6
• 6	4
• +7	0

V Crowding index

- < persons per room 3
- 2 2
- 4 1
- +5 0

VI Sanitation

- Water 1
- Sewage 1
- refuse 1

Total = 24 +8 +8 +3 +3 =46

38-46

34.5-<38

23-<34.5

<23

High social level

High middle social level

Low middle social level

low social level

PROTOCOL

**STUDY OF INTRAFAMILIAL TRANSMISSION OF
HEPATITIS C VIRUS AMONG FAMILY MEMBERS OF
CHILDREN WITH CHRONIC HEPATITIS C VIRUS
INFECTION**

دراسة لانتشار الإصابة بالتهاب الكبدى الفيروسى سى بين افراد عائلات الأطفال
المصابين بالتهاب الكبدى الفيروسى سى المزمن

Protocol of a thesis submitted
to the Faculty of Medicine
University of Alexandria
In partial fulfillment of the
requirements of the degree of
Master of Pediatrics

خطة بحث مقدمة
لكلية الطب
جامعة الإسكندرية
إيفاءً جزئياً
لشروط الحصول على درجة
الماجستير فى طب الأطفال

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INTRODUCTION

Hepatitis C virus (HCV) is an enveloped virus that, at present, chronically infects about 130 million people worldwide.⁽¹⁾ One hallmark of HCV is its high degree of sequence variability, which likely contributes to its ability to establish chronic infections. Different patient isolates are grouped into 6 genotypes and more than 100 subtypes within the genus Hepacivirinae of the family Flaviviridae.⁽²⁾ HCV genotypes are numbered from 1-6, genotype 1(subtypes 1a and 1b) is by far the most prevalent genotype worldwide.⁽³⁾ Persons newly infected with HCV typically are either asymptomatic or have a mild clinical illness. HCV RNA can be detected in blood within 1–3 weeks after exposure. The average time from exposure to antibody to HCV (anti-HCV) seroconversion is 8–9 weeks, and anti-HCV can be detected in >97% of persons by 6 months after exposure. Chronic HCV infection develops in 70%–85% of HCV-infected persons; 60%–70% of chronically infected persons develop evidence of active liver disease. Most infected persons remain unaware of their infection because they are not clinically ill. However, infected persons serve as a source of transmission to others and are at risk for CLD and other HCV-related chronic diseases for decades after infection.⁽⁴⁾ Persistent infection with variable degree of liver damage often progressing in severity over the course of decades. Hepatitis C virus poses an important risk of liver fibrosis which is usually initiated in the portal area. Accordingly, a large number of patients are at risk of severe sequelae including life-threatening conditions like cirrhosis and hepatocellular carcinoma.⁽⁵⁾

The best available treatment, a combination of polyethylene glycol (PEG)-conjugated interferon alpha and ribavirin, is not effective in every patient and can be associated with severe adverse effects. ⁽⁶⁾ A prophylactic vaccine isn't so far available.

Egypt has the highest prevalence of HCV infection of any country in the world, with an estimated 8 million infected inhabitants in 1999. ⁽⁷⁾ In rural areas, HCV prevalence ranges from 10% in children to 45% in adults. The origins of this HCV epidemic have been attributed to the parenteral treatment of schistosomiasis by antimony salts between 1960 and 1982. ⁽⁷⁾ In developing countries, blood transfusions and unsafe injections used during treatments are thought to be the major routes of transmission. ⁽⁸⁻¹¹⁾ However, recent studies in highly endemic areas have shown that a substantial proportion of HCV infections, particularly in children, cannot be accounted for by iatrogenic factors, strongly suggesting the involvement of other modes of transmission. ⁽¹²⁾ Perinatal mother-to-child HCV transmission remains limited, accounting for less than 5% of pediatric cases. ⁽¹³⁾ While sexual transmission of HCV has been suggested, ^(11, 14, 15) it is much less efficient for HCV than for other sexually transmitted viruses. ⁽¹¹⁾ Finally several studies have reported that HCV infection may cluster in families or households, based on the higher prevalence of HCV infection among family members of infected cases (mainly patients with chronic liver diseases, hemophilia, or on haemodialysis) than in controls. ⁽¹⁶⁻¹⁸⁾ As anti-HCV seropositivity might be 5- to 10- fold higher in individuals living with an HCV-positive patient compared to general population. Possible explanations are familial sharing of genes predisposing to HCV infection, ⁽¹⁹⁾ familial sharing of at risk behaviors exposing to HCV infection, and intrafamilial transmission,

possibly sexual or domestic (ie, unapparent parenteral transmission through sharing of nail trimmers or other grooming items such as razors or toothbrushes.⁽²⁰⁾

In our study, we search for the possibility of intrafamilial transmission of HCV infection. We will also investigate the familial resemblance in chronic HCV infection by using phylogenetic study (study of gene sequences of HCV).

AIM OF THE WORK

The aim of this work is to assess possibility of HCV intrafamilial transmission, and its contribution to the overall HCV risk of transmission among children attending the outpatient clinic of Alexandria University Children's Hospital.

SUBJECTS

The study will be conducted on family members of 50 children with chronic HCV infection “persistently positive HCV PCR for at least 6 months” (cases). The study will also include family members of 50 randomly selected children with negative anti-HCV antibody (controls) from those attending the outpatient clinic of Alexandria University Children's Hospital.

Exclusion criteria:

* Concomitant HBV infection or any other chronic liver diseases.

METHODS

All children and their families will be subjected to the following:

1. Thorough history taking through a special questionnaire. The questionnaire will emphasize the following:

- The residence of the patient whether urban or rural and the socioeconomic class.

- The risk factors for HCV infection including;

- * Intravenous access (history of blood or blood product transfusion, IV catheters and previous intravenous injections).

- * Surgical procedures (circumcision, sutures, abscess drainage, surgical biopsy, caesarean section, dental maneuvers, episiotomy, sclerotherapy of varicose veins and endoscopy).

- * Folk medicine practice, tattooing, shaving at barber, pedicure, manicure, needle pricks including ear piercing.

- * Household practice (living with a household with HCV infection).

_ Family history of chronic liver disease, repeated blood transfusions for any of family members, hemodialysis patients or drug addicts within the family.

- Domestic high risk behaviors as; sharing of nail trimmers or other grooming items such as razors or toothbrushes and being bitten by HCV infected patients.

- If there is more than one member in the family positive for HCV PCR; how long being staying together in the same house.

2. Full clinical examination stressing on the condition of liver and spleen and whether there is jaundice or ascites.

3. All studied children and their family members will be screened for anti-HCV antibodies using ELISA test and all positive cases will be confirmed by using HCV PCR.

4. In case of more than one family members are positive by HCV PCR, they will be subjected to phylogenetic analyses (study of gene sequences of isolated viruses from different hosts).

5. A written consent will be obtained from all studied persons.

6. All positive cases will be followed in the hepatology outpatient clinic for further assessment.

RESULTS

The results obtained will be tabulated and analyzed with the use of appropriate statistical methods.

DISCUSSION

The results will be discussed in view of achievement of the aim, and will be compared with those of published similar studies.

REFERENCES

1. Alter MJ. Epidemiology of hepatitis C virus infection. *World J Gastroenterol* 2007; 13:2436-41.
2. Simmonds P, Bukh J, Combet C. Consensus proposals for a unified system of nomenclature of hepatitis C virus genotypes. *Hepatology* 2005; 42:962-73.
3. Anonymous. EASL clinical practice guidelines: Management of HCV infection. *J hepatol* 2011; 55:245-64.
4. Centres for disease control and prevention. Treatment guidelines of HCV 2010. www.cdc.gov/std/treatment/2010/hepc.htm. Jan 2011.
5. Doerrbecker J, Friesland M, Ciesek S. Inactivation and survival of HCV on inanimate surfaces. Hannover, Germany. *J Infect Dis* 2011; 204:1830-8.
6. Manns MP, Wedemeyer H, Cornberg M. Treating viral hepatitis C: efficacy, side effects, and complications. *Gut* 2006; 55:1350-9.
7. Frank C, Mohamed MK, Strickland GT. The role of antischistosomal therapy in the spread of hepatitis C virus in Egypt. *Lancet* 2000; 355:887-91.
8. Lauer GM, Walker BD. Hepatitis C virus infection. *N Engl J Med* 2001; 345:41-52.
9. Thomson BJ, Finch RG. Hepatitis C virus infection. *Clin Microbial Infect* 2005; 11:86-94.
10. Alter MJ. Epidemiology of viral hepatitis and HIV co-infection. *J*

Hepatology 2006; 44 S: 6-9.

11. Shepard CW, Finelli L, Alter MJ. Global epidemiology of hepatitis C virus infection. *Lancet Infect Dis* 2005; 5:558-67.
12. Arafa N, Hoseiny ME, Rekacewicz J. Changing pattern of hepatitis C virus spread in rural areas of Egypt. *J Hepatol* 2005; 43:418-24.
13. Roberts EA, Yeung L. Maternal-infant transmission of hepatitis C virus infection. *Hepatology* 2002; 36 S: 106-13.
14. Laurent C, Henzel D, Mulanga-Kabeya C. Seroepidemiological survey of hepatitis C virus among commercial sex workers and pregnant women in Kinshasa, Democratic Republic of Congo. *Int J Epidemiol* 2001; 30:872-7.
15. Hepburn MJ, Lawitz EJ. Seroprevalence of Hepatitis C and associated risk factors among an urban population in Haiti. *BMC Gastroenterol* 2004; 4:31.
16. Ackerman Z, Ackerman E, Paltiel O. Intrafamilial transmission of hepatitis C virus: a systematic review. *J Viral Hepat* 2000; 7:93-103.
17. Akhtar S, Moatter T. Intra-household clustering of hepatitis C virus in Karachi, Pakistan. *Trans R Soc Trop Med Hyg* 2004; 98:535-9.
18. Mohamed MK, Abdel-Hamid M, Mikhail NN. Intrafamilial transmission of hepatitis C virus in Egypt. *Hepatology* 2005; 42:683-7.
19. Jimenez A, Sharaf Eldin N, Rimlinger F. HCV iatrogenic and intrafamilial transmission in Greater Cairo, Egypt. *Gut* 2010; 59:1554-60.

20. Hermida M, Ferreiro MC, Barral S. Detection of HCV RNA in saliva of patients with hepatitis C virus infection by using a highly sensitive test. J Virol Methods 2002; 101:29-35.

الملخص العربي

الملخص العربي

الالتهاب الكبدي الفيروسي سي يصيب حوالي ٣% من سكان العالم. معدل انتشار الفيروس في الدول المتقدمة اقتصادياً قليل يصل إلى ١-٢% من السكان البالغين بينما يصل إلى ٥-١٠% من سكان الدول الأقل تقدماً. سجلت مصر أعلى معدلات لانتشار الفيروس لتصل إلى ١٥-٢٠%. في دراسة سابقة تم إجرائها على الأطفال كان معدل الأنتشار ٥,٨%.

اهم الطرق المعروفة في انتقال العدوى:

- نقل الدم او مشتقاته.
- زرع الاعضاء.
- علاج البلهاريسيا الحقني.
- الشك بالبر المصابة عن طريق الخطأ.
- دخول المستشفى.
- التدخل الجراحي او علاج الاسنان.
- من الام لطفلها.
- بين افراد الاسرة.
- استخدام ادوات المريض الخاصة مثل شفرات الحلاقة او غيرها من ادوات الحلاقة.
- استخدام ادوات الاكل و الشرب الخاصة بالمريض.

لقد تناولنا في هذا البحث دراسة مختلف عوامل الخطورة المسببة للالتهاب الكبدي الفيروسي سي بين الاطفال وبحثنا انتقال الفيروس بين العائلات و مدى اسهام هذا العامل في معدل الازدياد في الاصابة بالفيروس.

تم تطبيق البحث على افراد عائلات ٧٥ طفلاً مصاباً بفيروس الالتهاب الكبدي المزمن (يتطاب بقاء تحليل الحمض النووي للفيروس ايجابي على الاقل ٦ شهور) اعمارهم تتراوح بين ٢-١٨ سنة، ٤٦ ولد و ٢٩ بنت. الحالات تم جمعها من عيادة الكبد الخارجية بمستشفى الشاطبي الجامعي بالاسكندرية. ايضاً شمل البحث افراد عائلات ١٠٦ طفلاً تم اختيارهم بطريقة عشوائية ممن يباشرون علاجهم بالعيادات الخارجية لمستشفى الاطفال الجامعي بالشاطبي.

- ١- تم أخذ التاريخ المرضي للاطفال و عائلاتهم عن طريق استبيان و قد اشتمل الاستبيان على ما يلي:
 - العمر، والنوع، ومحل الإقامة (سواء ريف او حضر)، والعمل، والمستوى الاجتماعي و الاقتصادي الذي يتم حسابه وفقاً لطريقة الحساب المعدلة للمستوى الاجتماعي للأسرة.
 - عوامل الخطر بالنسبة لعدوى للالتهاب الكبدي الفيروسي سي و تشمل:
 - الطريق الوريدي (نقل الدم و مشتقاته مشتقاً نقل الالبومين، وجود قسطرة وريدية، وجود حقن وريدي سابق) و مكان كلاً منهم.
 - تاريخ مرضي للحجز بمستشفى و مكانها.
 - تاريخ مرضي لاجراءات جراحية (ختان، خياطة جراحية، فتح خراج، عينة جراحية، الاجراءات الجراحية للاسنان، العلاج التليفي للدوالي، و عمل منظار) و مكان كلاً منهم.
 - ممارسات الطب الشعبي، وجود وشم، حلاقة لدى حلاق عمومي، المانيكير، الباديكير، الحقن عن طريق الجلد، و ثقب الاذن.
 - اصابة احد افراد الاسرة بالالتهاب الكبدي الفيروسي سي.
 - وجود تاريخ مرضي في الاسرة بمرض كبدي مزمن، نقل الدم بصفة مستمرة، الغسيل الكلوي الدموي، او ادمان المخدرات.
 - وجود بعض الممارسات الاسرية:

- عدد الساعات المنقضية مع الفرد المصاب.
- هل افراد الاسرة ينامون او ياكلون معاً ام لا.
- بعض الممارسات المنزلية التي يمكنها نقل الفيروس مثل: وجود مهذب اظافر مشترك، المشاركة فى شفرات الحلاقة بين افراد الاسرة، المشاركة فى ادوات المائدة كالكوب او الملعقة، المشاركة فى الفوط الخاصة، المشاركة فى الادوات الخاصة كالمشط، الصابون، فرش الشعر، فرش الاسنان، او القطن، التعرض للدم بالطريقة الخطأ او اى من افرازات الشخص المصاب، او العض بواسطة الشخص المصاب.

- ٢- الفحص الكامل للشخص مؤكداً على حالة الكبدو الطحال و هل توجد صفرا ام لا.
- ٣- كل الاطفال و عائلاتهم خضعوا لتحليل مضادات الفيروس سى باستخدام الاليزا. تم عمل تحليل الحمض النووى للفيروس سى للاشخاص الايجابيين لتحليل مضادات الفيروس سى.
- ٤- فى حال وجود اكثر من فرد بالاسرة ايجابى لتحليل الحمض النووى للفيروس سى تم عمل تحليل جينى للفيروس لكلاً منهما.

يوضح البحث ما يلى:

- المعدل المصلى لانتشار الاصابة بالالتهاب الكبدى الوبائى بين عائلات الاطفال المصابة ١٥،٩%، و ٨،٦% باستخدام تحليل الحمض النووى للفيروس سى .
- المعدل المصلى لانتشار الاصابة بالالتهاب الكبدى الوبائى بين عائلات الاطفال الغير مصابة ٣،٧%، و ٢،٨% باستخدام تحليل الحمض النووى للفيروس سى .
- يزداد الانتشار مع زيادة العمر، مع كل عام زيادة فى عمر المريض تزداد العرصة للاصابة بعدوى الالتهاب الكبدى الفيروسي سى بنسبة ١،٣ مرة.
- المرضى اللذين دخلوا المستشفيات كانوا ٦ مرات اكثر عرضة للاصابة بعدوى الالتهاب الكبدى الفيروسي سى عن المرضى اللذين لم يدخلوا المستشفيات.
- المرضى اللذين تعرضوا لقسطرة وريدية كانوا ١٠ مرات اكثر عرضة للاصابة بعدوى الالتهاب الكبدى الفيروسي سى عن المرضى اللذين لم يتعرضوا لقسطرة وريدية.
- المرضى اللذين تعرضوا لحقن وريدى كانوا ١٠ مرات اكثر عرضة للاصابة بعدوى الالتهاب الكبدى الفيروسي سى عن المرضى اللذين لم يتعرضوا للحقن الوريدى.
- المرضى اللذين تعرضوا لنقل الدم كانوا ٥ مرات اكثر عرضة للاصابة بعدوى الالتهاب الكبدى الفيروسي سى عن المرضى اللذين لم يتعرضوا لنقل الدم.
- المرضى اللذين تعرضوا لنقل الالبومين كانوا ١٦ مرة اكثر عرضة للاصابة بعدوى الالتهاب الكبدى الفيروسي سى عن المرضى اللذين لم يتعرضوا لنقل الالبومين.
- المرضى اللذين تعرضوا لخيطة جراحية كانوا ٤ مرات اكثر عرضة للاصابة بعدوى الالتهاب الكبدى الفيروسي سى عن المرضى اللذين لم يتعرضوا لخيطة جراحية.
- المرضى اللذين تعرضوا لعمليات جراحية او عينات استكشافية كانوا ٢ مرة اكثر عرضة للاصابة بعدوى الالتهاب الكبدى الفيروسي سى عن المرضى اللذين لم يتعرضوا لعمليات جراحية او عينات استكشافية. عموماً المرضى اللذين تعرضوا لاي اجراء تدخلى كانوا ٩ مرات اكثر عرضة للاصابة بعدوى الالتهاب الكبدى الفيروسي سى عن المرضى اللذين لم يتعرضوا لاجراء تدخلى.
- المرضى اللذين تعرضوا لمنظار او لتركيب قسطرة بولية كانوا ٥ مرات اكثر عرضة للاصابة بعدوى الالتهاب الكبدى الفيروسي سى عن المرضى اللذين لم يتعرضوا لمنظار او لتركيب قسطرة بولية.
- المرضى اللذين يحلقون عند حلاق عمومى كانوا ٢ مرة اكثر عرضة للاصابة بعدوى الالتهاب الكبدى الفيروسي سى عن المرضى اللذين لا يحلقون عند حلاق عمومى.
- المرضى اللذين يعيشون مع شخص مصاب بالالتهاب الكبدى الفيروسي سى كانوا ٥ مرات اكثر عرضة للاصابة بعدوى الالتهاب الكبدى الفيروسي سى عن المرضى اللذين لا يعيشون مع شخص مصاب.

- المعدل المصلى لانتشار الاصابة بالالتهاب الكبدى الفيروسى سى داخل اسر العائلات المصابة تصل الى ٦٠،٧%، و الى ٣١% باستخدام تحليل الحمض النووى للفيروس.
- الام اكثر عرضة من الاب او الاخ لانتقال الاصابة من و الى الطفل.سواء باستخدام الاليزا أو باستخدام تحليل الحمض النووى للفيروس.
- الام ٦٥ مرة لانتقال الاصابة من و الى الطفل بينما الاب ٢٣ مرة لانتقال الاصابة من و الى الطفل ، و الاخ ٤٢ مرة لانتقال الاصابة من و الى الطفل مقارنة بالاسر السلبية لانتقال الفيروس داخلها.
- الاناث كانوا اكثر عرضة من الذكور لانتشار الاصابة منهم او اليهم.
- مع زيادة عمر الطفل المصاب يزداد معدل انتشار الفيروس بين افراد عائلات الأطفال المصابة.
- مع زيادة فرق العمر بين الاطفال المصابة يزداد معدل انتشار الفيروس بين افراد عائلات الأطفال المصابة (خاصة اذا كان الفرق اكثر من ٥ سنوات).
- المشاركة فى الشرب، استخدام الفوط الشخصية ، وادوات الحلاقة مع الاطفال المصابة تعتبر عوامل مستقلة لانتقال الالتهاب الكبدى للفيروسى سى داخل العائلات.
- الاطفال الذين يشاركون الشرب مع الطفل المصاب ٤ مرات عرضة للاصابة بالالتهاب الكبدى الفيروسى سى عن الاطفال اللذين لا يشاركون.
- الاطفال الذين يشاركون استخدام الفوط الشخصية مع الطفل المصاب ١٤ مرة عرضة للاصابة بالالتهاب الكبدى الفيروسى سى عن الاطفال اللذين لا يشاركون.
- الاطفال الذين يشاركون استخدام ادوات الحلاقة مع الطفل المصاب ٤ مرات عرضة للاصابة بالالتهاب الكبدى الفيروسى سى عن الاطفال اللذين لا يشاركون.
- تم عمل تحليل جينى للفيروس للأفراد المصابة فى عائلتين والذى تبين انهما غير متطابقين جينياً فى كلاً من العائلتين.