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SEXUAL TRANSMISSION OF HEPATITIS C: A REVIEW

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P.M. PANCHOLI

ABSTRACT

Objectives: To establish and understand the transmission of hepatitis C virus (HCV) and conclude on the possibility of sexual transmission as a route of transmission.

Data sources: Review of Literature via medline, the internet and articles in indexed journals.

Data selection: Published data from 1989 up to date found to have studied the sexual transmission of Hepatitis C Virus.

Data extraction: Abstracts of articles identified were assessed, read and analysed to determine possible relevance to the title.

Data synthesis: When relevance was established from the abstract the entire paper was then read and important points were included in the review.

Conclusion: The data acquired so far cannot convincingly conclude that hepatitis C is not transmitted sexually, as the possibilities do exist. There are a lot of factors that suggest that HCV is sexually transmitted. Present data clearly indicates that more research needs to be carried out on different aspects of HCV that may have lead to the discrepancies mentioned herewith. There may be a role played by various factors such as the age, sex, race, immune status, presence of co-existing HIV infection, and any other concurrent illnesses upon the sexual transmission of HCV.

INTRODUCTION

The identification of the hepatitis C virus (HCV) in the late 1980s was a substantial but minute step into the understanding of the virus. Hepatitis C is a leading cause of global health concern caused by HCV. Presently available data indicates that approximately 3% of the world's population is infected with HCV (170 million). HCV was identified recently (1989), and epidemiological data is incomplete. The precise magnitude of the problem and the relative contribution of the various routes of transmission have not been fully defined with population-based studies (1).

Table 1 shows the worldwide estimated prevalence of HCV.

HCV is a member of the family Flaviviridae (genus Hepacivirus), there are at least six clades or genotypes of HCV (1-6) and each may be further sub-divided into a large number of sub-clades or

subtypes (1a, 1b, 1c, etc). HCV is thought to have over 100 sub-types (2).

HCV is an enveloped, single-stranded, positive sense RNA virus 50 to 60 nanometres in diameter. The RNA genome is about 9.6 kilo bases in length. HCV replicates in the liver, and is detectable in serum during acute and chronic infection (3).

HCV is an important cause of viral hepatitis. Its long-term sequelae are liver cirrhosis, hepatic failure and hepatocellular carcinoma. Approximately 75-85% of those infected become chronic carriers and 10% progress to chronic liver disease. Extra hepatic associations with chronic HCV infection include, essential mixed cryoglobulinemia, membranoproliferative glomerulonephritis, porphyria cutanea tarda, keratoconjunctivitis sicca, lichen planus, autoimmune thyroiditis, mooren corneal ulcers, idiopathic pulmonary fibrosis and diabetes mellitus (7).

Table 1*Hepatitis C estimated prevalence and number infected by WHO Region*

WHO Region	Total Population (Millions)	Hepatitis C prevalence Rate%	Infected Population (Millions)	Number of countries by WHO Region where data are not available
Africa	602	5.3	31.9	12
America	785	1.7	13.1	7
Eastern Mediterranean	466	4.6	21.3	7
Europe	858	1.03	8.9	19
South-East Asia	1 500	2.15	32.3	3
Western Pacific	1 600	3.9	62.2	11
Total	5 811	3.1	169.7	57

Source: Weekly Epidemiological Record. No. 49, 10 December 1999, WHO

DISCUSSION

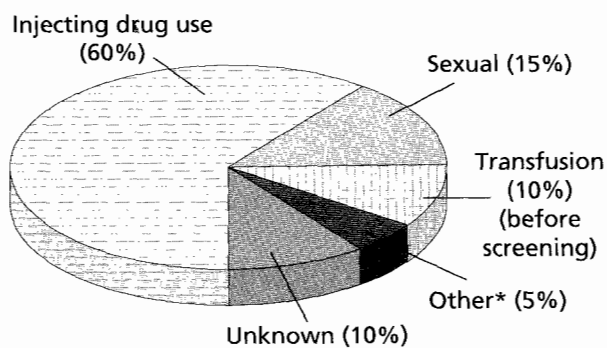
Hepatitis C virus is a blood-borne virus transmitted by percutaneous contact with infected blood.

There are many different modalities by which the spread of HCV may occur. These include; transfusion of blood and blood products such as albumin and cryoprecipitate, intravenous drug abuse (IVDA), haemodialysis, needle stick injuries in health care workers, high risk sexual practices (defined by anonymous sex, unprotected sex, anal intercourse, unfamiliar partners, sex while using drugs or sex for drugs or money), mother to child transmission, road traffic accidents, medical and dental procedures with poorly sterilised instruments, vaccinations, household contact, ear and body piercings, tattoos, acupuncture and rituals such as circumcision, scarification and bloodletting. In some cases no cause has been identified.

CDC data suggests that 60% of HCV has been acquired by IVDA, 15% by sexual transmission, 10% by unscreened transfusions, 10% is unknown and 5% by other minor causes.

Figure 1 shows the relative proportions of the different sources of acquiring HCV infection.

Whether HCV can be sexually transmitted is controversial. There have been studies both in favour and against the issue. HCV has been identified

Figure 1*Sources of infection for persons with hepatitis C*

* Haemodialysis; health-care work; perinatal

Source: http://www.cdc.gov/ncidod/disease/hepatitis/c/plan/HCV_infection.htm

in semen and cervicovaginal secretions in low concentrations (8-10). This can support the theory of sexual transmission but does not in itself necessarily prove that infection may occur via a sexual route. A number of studies have suggested that sexual transmission of HCV does not occur.

The risk of sexual transmission of HCV infection was evaluated among 895 monogamous heterosexual partners of HCV chronically infected individuals in a long-term prospective study. This provided a

follow-up period of 8,060 person per year. Three HCV infections were observed during follow-up corresponding to an incidence rate of 0.37 per 1,000 person per year. However, the infecting HCV genotype in one spouse (2a) was different from that of the partner (1b), which clearly excluded sexual transmission. The remaining two couples had concordant genotypes, but sequence analysis of the NS5b region of the HCV genome, showed that the corresponding partners carried different viral isolates, which excluded the possibility of intra-spousal transmission of HCV. This led to the conclusion, that the risk of sexual transmission of HCV within heterosexual monogamous couples is extremely low or even null (6). This study however excluded some of the patients whose partners were already infected with HCV at the start of the trial. It could be argued that HCV transmission may already have occurred in these individuals. Another point to note is that even though partners had different sequence analysis of the NS5b region rates this could be attributed to random mutations within the virus. Similarly a study by Lee *et al* in a non-endemic area looked at 50 sexual partners mainly of patients with haemophilia and HCV (median length of sexual relationship was 13 years) and found a zero percent rate of HCV in the partners (5). A study in Germany of 86 women, who were chronically infected by contaminated anti-D immunoglobulin showed that the rate of HCV in sexual partners was zero percent (4).

Canadian researchers studied the prevalence and incidence of hepatitis C virus (HCV) infection in the ongoing Omega Cohort Study of men who have sex with men (MSM). One thousand and eighty five consenting men attending a follow-up visit were tested for HCV. If the test results were positive for HCV, they were compared with test results from previous serum samples collected from the time of entry into the original cohort study to determine the time of infection. It was found that prevalence of HCV at entry was strongly associated with IVDA and it was hence concluded that sexual transmission of HCV among MSM appears to be rare (11). The study had an excessive number of MSM who were intravenous drug abusers compared to those who did not use intravenous drugs. This may explain the findings in this study.

Although the above studies suggest that sexual transmission of HCV does not occur, there has been evidence to support the fact that sexual transmission

does occur but nevertheless it is not the main method of transmission. The CDC states that "Sexual exposures account for about 15% of cases of hepatitis C. Although the risk for transmitting HCV infection through sexual intercourse is low, sex is a common behaviour in the general population, a substantial proportion of the adult population has had unprotected sex with multiple partners, and there are a large number of persons with HCV infection. While other types of exposures are more likely to transmit HCV (e.g., transfusion from an infected donor), they account for a smaller proportion of infections because of the relatively small proportion of the population in whom these exposures have occurred." (Refer to Figure 1).

Mendes-Correa *et al* (2) conducted a study to look for risk factors associated with HCV infection among patients with HIV. Independent risk factors for transmission were; intravenous drug use and use of inhaled illicit drugs. However, a history of an intravenous drug user as a sexual partner or one who had received blood transfusions or a sexual partner with a past history of hepatic disease were also independent factors. This study suggested that although blood transmission of HCV may be the primary route of transmission, sexual transmission also occurs (12).

In an Italian study involving heterosexual partners of HCV infected patients, a total of 899 at-risk partners of HCV-infected patients were enrolled in a single-blind randomised controlled trial and assigned to receive 4 ml of intramuscular immune serum globulin (ISG) every two months from unselected donors (450 partners) or placebo (499 partners). Seven partners developed acute HCV infection (increased aminotransferase levels and appearance of HCV-RNA): six of the placebo group and only one of the ISG-treated. The risk of infection was significantly higher in controls versus treated individuals. Six couples had genotype 1b (85%), and one couple had genotype 1a; HCV sequence homology strongly supported sexual transmission. This demonstrated that HCV infection can be sexually transmitted and that giving immune serum globulin to partners of infected patients can reduce the rate of sexual transmission of HCV (13).

A study in the United States of America showed that sexually active non-IVDA, non-transfused women, engaging in high-risk sexual behaviour (as defined earlier) were shown to be 14.2 times

more likely to have HCV infection than women not engaging in high risk sexual activities (14). A number of other studies have shown that there is an increased risk of acquiring HCV with increasing number of sexual partners and STIs (15,16-18).

Several studies have observed increased prevalence rates of HCV in MSM compared with the rest of the general population but this could not always be clearly attributed to sexual transmission (15,19-23). Buchbinber *et al* studied 6704 MSM and found an increased transmission of HCV among MSM. This was linked with unsafe sexual practices amongst MSM (e.g. receptive anal intercourse and fisting), history of herpes simplex and HIV (19).

A study in San Francisco showed no increase in HCV prevalence or incidence in MSM with recent high-risk sexual behaviour or new herpes simplex infections or new HIV infections but did find higher rates in people over 50 years and those with chronic HIV (24). This study established that co-infection with HIV may have an important role to play in the sexual transmission of HCV. In Uruguay a study of male transvestite commercial sex workers found a HCV transmission rate of 6.5% and associations with HIV infection, non-injecting drug use and sex with foreigners; this lead to the conclusion that sexual transmission was a secondary factor in HCV acquisition among those co-infected with HIV (20).

As observed in the past with other diseases, asymptomatic sexually transmitted diseases may play a role. Asymptomatic trichomoniasis has been shown to facilitate transmission of HIV (25) and there is a theoretical possibility that trichomoniasis or other sexually transmitted infections (STI's) may act as a co-factor in the sexual transmission of HCV as well.

On analysis of the above data there are many discrepancies which could have occurred for various reasons. The specificities and sensitivities of different tests used in different studies may be varied this may also have lead to false positives and negatives in different studies. It could also be that the older tests were less sensitive and specific when compared to the newer ones. The varied methodologies and statistical analysis methods used in these different studies may also be responsible for conflicting results. The study design and the initial questionnaires should be planned in such a way

that they account for other modes of transmission that may occur in couples, such as sharing of toothbrushes and razors. There may also be different stages of infection in the human body and the virus may only be infective in certain stages. Transmission rates may be different for transmission from males to females and vice-versa.

Some studies have reported (26,27) the spontaneous loss of hepatitis C virus (HCV) antibodies in HCV-exposed persons and further studies are required to quantify this rate of loss of HCV anti-bodies. This may also be an important point to note when analysing discrepancies reported with the transmission routes of HCV. In some cases no probable cause has been identified leading to transmission of HCV in certain individuals. More probing may reveal new, interesting theories related to the transmission of HCV.

CONCLUSION

The data acquired so far cannot convincingly conclude that hepatitis C is not transmitted sexually, as the possibilities do exist. There are a lot of factors that suggest that HCV is sexually transmitted; It has been detected in seminal and vaginal fluid, it has a high prevalence in a sexually active group, it occurs more frequently in those at risk of acquiring sexually transmitted diseases such as commercial sex workers and MSM. HCV has been associated with other STI's such as HIV. Partners of those with STI's are at risk. HCV also has risk factors similar to other STI's such as unprotective sexual intercourse and multiple sexual partners.

Present data clearly indicates that more research needs to be carried out on different aspects of HCV that may have lead to the discrepancies mentioned herewith. There may be a role played by various factors such as the age, sex, race, immune status, presence of co-existing HIV infection, and any other concurrent illnesses. The amount of viral inoculum during sexual intercourse which itself is dependant on other factors such as the type of sexual encounter/s and presence of any other sexually transmissible infections amongst others may also have a role to play. It could also be that different subtypes of the virus maybe transmitted by different modes.

Important questions remain concerning the transmission and public health control of this

infection. With continued collaboration and cooperation within the scientific community we may one day be able to answer these questions.

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ANNOUNCEMENT



KENYA ASSOCIATION OF DERMATOLOGISTS

Dermatology Symposium Celebrating 20th Anniversary of Inception of KAD

Date : Saturday 10th November 2007

Venue : Lecture Theatre, Aga Khan University Hospital

Time : 8.00 am – 5.00 pm

Theme : Dermatology In General Medicine

Registration : Free

For any enquiries contact: Dr. E.N. Kamuri, KNH, Doctors' Plaza, No. 23
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All Are Welcome