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Policy Guidelines on HCV Testing

*Report of an Informal Consultation
New Delhi, 21–22 December 1999*

WHO Project: ICP RPS 001



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1. INTRODUCTION

An inter-country informal consultation was held in the South-East Asia Regional Office of WHO, New Delhi, on and 22 December 1999 to formulate policy guidelines on hepatitis C virus (HCV) screening in blood banks in South-East Asian countries. The meeting was attended by the participants from India, Indonesia, Myanmar and Nepal and was supported by staff from the Regional Office and WHO headquarters, as well as temporary advisers. Mr J.V.R. Prasada Rao was elected as the chairperson for the Consultation and Prof B.N. Tandon as the alternate chairperson. Dr Rajesh Bhatia was elected as the rapporteur. (The full list of participants and others is given in Annex 1.)

2. OBJECTIVES

The objectives of the consultation were to:

- (1) Review the magnitude of the burden of hepatitis C infection in SEAR countries;
- (2) Discuss the epidemiology of hepatitis C in the Region and the various strategies that could be adopted for its prevention and control;
- (3) Review the status of availability of different test kits for hepatitis C and their efficacy for reliable diagnosis vis-à-vis cost-effectiveness, and
- (4) Review and finalize the draft policy guidelines prepared by WHO on HCV testing at blood banks.

These objectives were discussed and achieved through the following thematic sessions (as per the programme given in 2):

- (1) Overview of the hepatitis C problem in SEAR countries and Country Reports;
- (2) Policies, procedures and pharmacopoeial regulations;
- (3) Issues for hepatitis C screening in SEAR countries, and
- (4) Possibility of HCV screening in SEAR countries.

3. INAUGURAL SESSION

Dr Uton Muchtar Rafei, WHO Regional Director, inaugurated the Consultation. He welcomed the participants and emphasized the need for ensuring the availability of safe blood. There was a large pool of hepatitis C virus (HCV) carriers throughout the world and it was urgently necessary to reduce this burden. Twenty-five million of these carriers were in SEAR countries with 12 million in India alone. Dr Uton stressed the need for formulating a cost-effective and practical strategy to combat this menace with emphasis on simple and easy-to-perform tasks that could significantly support disease control activities. He concluded by requesting the participants to formulate guidelines that were practical, acceptable and implementable in the developing countries of SEAR, where resources for the health sector were limited.

4. OVERVIEW OF HEPATITIS C PROBLEM IN COUNTRIES OF THE SOUTH-EAST ASIA REGION

4.1 Regional Overview

Dr Sudarshan Kumari, Regional Adviser, WHO/SEARO, presented the current knowledge about hepatitis C virus and the status of hepatitis C carriage in the Member Countries of SEAR based on published reports as well as estimates made by WHO. HCV was an RNA virus with six major genotypes and more than 130 subtypes. After its discovery in 1989, it had been found to be an important

cause of chronic liver diseases. Transfusion of unsafe blood, use of non-sterile syringes and equipment, injectable drug use, repeated haemodialysis and high-risk sexual activity were major known modes of transmission of HCV.

A global pool of an estimated 170 million carriers of HCV acted as a reservoir of this infection in the world. Whereas the USA and Western Europe had 4 and 5 million carriers respectively, nine countries of the SEA Region accounted for 25 million carriers -12 million of whom lived in India. According to WHO estimates, the following was the status of HCV carriers in the countries of this region.

Country	Carrier rate %	Carriers number in millions
Bangladesh	2.4	3.08
Bhutan	1.3	0.03
India	1.2	12.08
Indonesia	2.5	5.31
Maldives	1.8	0.005
Myanmar	3.9	1.92
Nepal	1.1	0.26
DPR Korea	1.6	0.38
Sri Lanka	1.4	0.26
Thailand	2.9	1.75
Total		25.075

Dr Sudarshan Kumari suggested that a strategy that ensured safe blood for transfusion and strict adherence to universal precautions in health settings might considerably reduce the burden of HCV in the future. To achieve this, mandatory screening of HCV in blood banks needed to be undertaken with extensive education for all categories of health care professionals.

4.2 Country Reports

(1) *Nepal*

Various community based studies have shown the prevalence of anti-HCV antibody in 0.4% of soldiers as well as healthy people of four districts in Nepal; 1.1% in hospital staff and 1.5% in relatives of patients with chronic liver disease. None of the HCW (student nurses) or pregnant women was found to be a carrier of HCV. Among the blood donors 0.4% were reactive for anti-HCV antibody in 1994 and 1.8% in 1996. All blood banks in Nepal are under the control of the Red Cross and the testing of blood for anti-HCV is mandatory.

Almost three-fourths of the injectable drug addicts tested in Nepal are carriers of HCV. An estimated 40,000 youth in the age group of 18-25 are considered to be injectable drug users and most of them are anti-HCV positive.

Social customs such as using the same razor for shaving the head among various subpopulations are widely prevalent and conducive for the spread of HCV.

(2) *Myanmar*

During 1997-98, out of 1018 blood donors, 103(10.1%) were found to be reactive for anti-HCV antibody. However, a study conducted among the normal population (n=161) and patients with chronic liver diseases (n=210) during 1998-99 revealed the presence of HCV-RNA in 1.9% and 24.3% individuals respectively.

(3) *India*

Review of various published data from India suggests a carrier rate for HCV in the general population represented by voluntary blood donors and pregnant women ranging between 0.09 and 2.5%. In studies where strict donor selection criteria were adopted, the carrier rates were extremely low.

Initial results obtained from studies being performed in communities also indicate a much less carrier rate than the estimated one. The mandatory testing of blood from voluntary blood donors for HCV is planned to start from June 2000 in all 1455 licensed blood banks of the country.

HCV is also responsible for considerable morbidity and mortality in chronic liver diseases in India. In sporadic acute viral hepatitis cases, HCV positivity has ranged between 0.2 and 17.6% while the rates in fulminant hepatic failure and subacute hepatic failure range from 6.2 to 45%. HCV has been incriminated as the cause of liver cirrhosis in 3.3% to 31.5% cases and that of hepatocellular carcinoma in 15.1 to 42% cases.

(4) *Bangladesh*

While reports on hepatitis A and B are available from Bangladesh, those on hepatitis C are extremely limited. In a limited study 2.4% HCV positivity in professional blood donors and 0% of voluntary blood donors has been demonstrated; 45.3% of the primary hepatocellular carcinoma cases were also found to be positive for HCV antibodies.

(5) *Bhutan*

Studies on hepatitis C are limited in Bhutan as well, except for the report by WHO in its Weekly Epidemiological record (1997) and a WHO SEARO publication, SEA/HS/209 (Health Situation in the South-East Asia Region, 1994-1997). The HCV prevalence in the general population of Bhutan according to these reports is 1.30%.

(6) *Indonesia*

An estimated 45,000 cases of liver cirrhosis and 18,000 cases of hepatocellular carcinoma are detected every year in Indonesia. Reports based on surveys in the general population and voluntary blood donors in the provinces project HCV carrier status ranging from 2.1 to 3.9%. The range of HCV positivity in blood donors is

between 0.5 and 3.4%; 0.8% of medical students carry HCV. Among the cases with hepatocellular carcinoma, 47.3% were reactive for anti-HCV antibody and so were 8% of patients on maintenance haemodialysis. Household contacts, sharing private items (such as tooth brushes) and extramarital sexual activity have been identified as probable risk factors in the development of HCV infection.

(7) *Maldives*

HCV studies from Maldives are once again scanty and the available data through a WHO SEARO report (1999) project HCV positivity in the general population of Maldives as 1.8%. No report is available on HCV-related liver diseases or about its involvement in the high-risk groups.

(8) *Democratic People's Republic of Korea*

HCV prevalence in the general population of DPRK has been reported to be 1.6%; 53.1% in chronic hepatitis, 30.5% in patients with cirrhosis of liver, and around 30% in hepatocellular carcinoma cases.

(9) *Sri Lanka*

From the limited literature available, HCV in the general population of Sri Lanka is reported to be 1.4% (WHO, SEARO), while no report is available on its role in acute and chronic liver diseases besides the high-risk groups.

(10) *Thailand*

The general population has HCV infection ranging between 0.5 and 5.6% (mean + SD : 2.94 + 2.15) with commercial sex workers having a higher risk of acquiring HCV infection (9.5%). In the liver diseases group, 23.0% of CLD patients and 8.4-17.0% of HCC cases were (mean +SD 12.23 + 4.37) due to HCV. The problem of

HCV is implicated in 20% of haemodialysis cases, 23.8% of thalassaemics and 95.3% of injectable drug users.

5. ECONOMIC LOSS DUE TO HEPATITIS C AND COST-EFFECTIVENESS OF PREVENTIVE MEASURES

The review of the status of hepatitis C in SEAR countries and the variety of the resultant chronic liver diseases in the most productive age group clearly indicate the tremendous adverse effect of these diseases on the quality of life as well as the economic loss to the individual, the family and the community at large. Published studies are available indicating the cost-effectiveness of existing preventive measures, especially screening of blood for HCV antibody in bringing down the burden of HCV.

6. POLICIES, PROCEDURES AND PHARMACOPOEIAL REGULATIONS

The procurement of serological kits for the screening of HCV varies from country to country within the Region. Guidelines for the import of the kits as well as the licensing of indigenously produced kits have been developed by the National Regulatory Authority of India. The imported kits can be critical and non-critical. The former include sero-diagnostic kits for hepatitis B surface antigen, HIV-1 and HIV-2, blood grouping sera and hepatitis C kits. Every consignment of these kits has to undergo evaluation in designated laboratories before its import is permitted. The kits should also meet the criteria of being produced under acceptable GMP and being permitted for free sale within the country of origin. The National Regulatory Authority circulates a list of evaluated kits for procurement by various agencies. Kits required for use in national programmes can be purchased after these have been approved by WHO or the National Control Authority.

7. KITS AVAILABLE FOR DETECTION OF ANTI-HCV ANTIBODY

The only tests currently approved by the US Food and Drug Administration (FDA) for the diagnosis of HCV infection are those that measure anti-HCV. PCR technology for the detection of HCV-RNA is available albeit in a limited number of institutions. Routine use of this methodology in all the blood banks is currently not feasible in the countries of this region.

There has been considerable improvement in the efficacy of EIA-based sero-diagnostic kits for HCV in the recent past. Third-generation kits are easily available and have demonstrable advantages over previous-generation kits in terms of sensitivity and specificity. Cut-off criteria for minimum sensitivity and specificity of various kits need to be developed for HCV. Since blood banks shall be using a screening test, the kits must have a demonstrably very high sensitivity (approaching almost 100%) so that no infected blood is allowed to be transfused and at the same time should also have reasonable specificity so that wastage of precious blood can be prevented.

A study conducted by WHO on the efficacy of various rapid kits for the detection of anti-HCV antibody has shown their sensitivity to vary from 98 to 100% and specificity from 92 to 100%, indicating thereby their utility in those blood banks where EIA-based tests cannot be performed for some reason.

8. QUALITY ASSURANCE PROCEDURES

8.1 Test Kit Evaluation and Approval at National Level

Test kits for utilization as screening kits need to be assessed by a competent and accredited laboratory. The assessments should focus on the operational characteristics of these assays such as ease of performance and their sensitivity and specificity on a small panel of well-characterized sera of diverse geographical origin,

and indicate their suitability for use in a small blood-collection centre.

8.2 National External Quality Assessment Scheme

The objective of the National External Quality Assessment Scheme (NEQAS) is to assess the quality of laboratory performance on a national basis and to provide assurance to consumers that laboratory results are reliable. All laboratories carrying out tests for the screening of blood for anti-HCV antibody should participate in NEQAS, including regional and district hospitals and blood transfusion centres. Considerable human and financial resources are required in order to set up a successful external quality assessment scheme.

9. POLICY GUIDELINES ON HCV SCREENING IN BLOOD BANKS

Draft policy guidelines on HCV screening in blood banks in countries of the S.E. Asia Region encompassing various issues which need to be addressed were presented and discussed thoroughly. The finalized guidelines will be published soon by WHO/SEARO for distribution to various countries.

10. CONCLUSIONS

Hepatitis C has already emerged as a major public health problem in the countries of WHO's South-East Asia Region with far-reaching implications because of the chronicity of the infection that leads to chronic liver disease, cirrhosis of liver and primary hepatocellular carcinoma. The disease burden is enormous though difficult to quantify in terms of economic loss. Many broad facets of the epidemiology of the disease have been established across the world. This has facilitated the development of control strategies. Member Countries of SEAR need to take up the issue of

preventing the spread of hepatitis C virus on a priority basis since treatment of chronic carriers is both difficult and expensive with low success rates. To cut short the transmission of HCV, screening of blood with reliable kits of acceptable sensitivity and specificity as well as vigorous implementation of universal precautions need to be accorded top priority.

Extensive deliberations by the participants resulted in the consensus that HCV testing must be made mandatory in all the blood banks of the countries.

The participants made the following recommendations:

11. RECOMMENDATIONS

11.1 To Member Countries

(1) *Epidemiology*

(a) Available data from SEAR countries indicate hepatitis C to be a major problem with unsafe blood as the most important mode of transmission. The data need further refinement for the precise quantification of disease burden, better elucidation of disease epidemiology, especially the geographical mapping, and the age-sex stratification of the carriers. An effective surveillance system needs to be launched by the Member Countries. Multi-centric community-based studies may also be undertaken to ascertain the prevalence of hepatitis C carriers in the countries.

(2) *Prevention of transmission of HCV from blood, blood components, organs, tissues and semen*

(a) Rigid criteria for the selection of voluntary donors must be developed and strictly implemented so as to eliminate potentially infected sources of unsafe blood.

- (b) Testing for anti-HCV antibody must be made mandatory in all the blood banks as early as possible to reduce the burden of HCV and cut short one of the important modes of transmission of this infection.
- (c) Testing for anti-HCV antibody should be part of the integrated blood safety procedures along with testing for HIV, hepatitis B surface antigen, antitreponemal antibody and malarial parasite.
- (d) Existing WHO guidelines on safety in the preparation of plasma products inclusive for hepatitis C should be scrupulously followed.
- (e) All donors of organs/tissues/semen should be tested for HCV antibody and those that are reactive for HCV should not be utilized for transplantation.
- (f) A system of sentinel surveillance to monitor post-transfusion infection due to HCV should be developed.

(3) *Prevention of HCV transmission from high-risk procedures/practices*

- (a) Universal precautions for infection control must be integrated in the routine working of all health care workers and those who are pursuing research in university and R&D settings in order to avoid occupational and nosocomial transmission of HCV besides HIV and hepatitis B virus.
- (b) Use of disposable/sterile syringes and instruments, safe injection practices, proper sterilization techniques, avoiding reuse and sharing of contaminated equipment and supplies both in the field and in health care institutions must be strictly adhered to.
- (c) Comprehensive health education messages for the prevention of blood borne infections, especially hepatitis B and C viruses, must be included in ongoing IEC campaigns against HIV.

(4) Screening for Hepatitis C

- (a) For mandatory HCV screening in blood banks, at least third-generation anti-HCV EIA test with kits of a quality approved by the national control authority should be used.
- (b) The procedures adopted for HIV kits may be adapted to purchase kits for hepatitis C as well as hepatitis B surface antigen to ensure the quality of the kits and, their uniformity, as well as to bring down the cost.
- (c) In emergency situations where EIA test is not possible, a rapid test with specifications approved by the National Control Authority should be used.
- (d) Evaluation of the kits should be undertaken by accredited national/regional laboratories to assess the quality of the HCV kits before these are purchased.
- (e) The quality assurance programme for the evaluation of the kits should be strengthened.
- (f) Designated laboratories may undertake molecular biological studies to correlate findings based on serological studies as well as for the confirmation of representative HCV-reactive sera.

(5) Training and Quality Assurance

- (a) Training of laboratory functionaries in blood banks should precede the implementation of the national policy for mandatory testing for HCV. The training should be comprehensive from the blood banks' mandatory points of view and not in isolation for HCV testing alone. Issues such as biosafety should be given adequate importance. In countries with a large number of blood banks, the quality of training and curriculum and should be uniform and should be developed after assessing the training needs of the users. The training can be expedited by organizing it at various locations with one national institution coordinating the activity

- (b) An External Quality Assessment Scheme (EQAS) should be in place to ensure quality of results by the blood banks. The staff of blood banks should also be trained in, and encouraged to undertake, internal audit.

(6) National Control Authority

- (a) Functionaries of the national control authority should be trained in various regulatory aspects of blood banking to ensure effective supervision of blood banks in their domain.
- (b) The national control authority should also ensure procurement of quality kits and coordinate blood safety as a whole with suitable components of training and quality assurance programmes.
- (c) National/regional laboratories should be identified for supporting national control laboratories and undertaking EQAS.

11.2 To WHO

- (1) WHO/SEARO should provide all technical back-up for the implementation of activities related to hepatitis C testing.
- (2) WHO should provide technical support in training national trainers as well as national regulatory authority professionals for the effective implementation of the national policy of ensuring safe blood supply.
- (3) WHO should assist Member Countries in initiating national external quality assessment schemes (NEQAS) for the testing of blood for transmissible agents. It should also assist national laboratories in participating in international external quality assessment schemes (IEQAS).
- (4) WHO should support countries in the evaluation of kits, choice of kit reagents and supply of standard strains.

Annex 1

LIST OF PARTICIPANTS

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Annex 2

AGENDA

Tuesday, 21 December 1999

09.00-09.30 Registration

09.30-10.00 Opening Ceremony and Regional Director's Address

Session I ***Overview of Hepatitis C problem in SEAR Countries***
(Chaired by Mr J.V.R. Prasada Rao)

10.30-11.00 Hepatitis C – An overview Dr Sudarshan Kumari

11.00-11.30 North India Dr B.N. Tandon

11.30-12.00 Western India Dr Vidya Arankalle

12.00-12.30 South India Dr S.P. Thyagarajan

Session II ***Overview of Hepatitis C problem in SEAR Countries***

13.30-14.00 Indonesia Dr Suwandhi Widjaja

14.00-14.30 Myanmar Dr Ye Myint

14.30-15.00 Nepal Dr Anil Kumar Mishra

Session III ***Policies, Procedures & Pharmacopial Regulations***

15.30-16.00 Role and obligations of NACO Mr J.V.R. Prasada Rao
in Blood Safety in India

16.00-16.30 Drug Regulations,
evaluation procedures &
monitoring Strategies for blood
screening Kits Dr Ashwini Kumar

Wednesday, 22 December 1999

Session IV *Issues of Hepatitis C – Screening in SEAR Countries*

(Chaired by: Dr B.N. Tandon)

09.00- 09.30	Serological v/s Molecular methods in HCV diagnosis – current status	Dr. S.P. Thyagarajan
09.30-10.00	Global evaluation of HCV testing Kits	Dr Gaby Vercauteren
10.00-10.30	HCV Test Kits and their evaluation	Dr Vidya Arankalle
11.00-11.30	HCV Test Kits evaluation – NIB experience	Dr Rajesh Bhatia
11.30-12.00	Economic feasibility of Mandatory HCV Screening in SEAR countries	Dr S.P. Thyagarajan

Session V *Feasibility of HCV Screening in SEAR Countries*

12.00-12.45	Brainstorming session (All participants)	
13.30-15.30	“Finalization of Policy Guidelines for HCV Screening in SEAR –Topic to be introduced by Dr S.P. Thyagarajan	
16.00-16.30	Conclusions and recommendations	
16.30-16.45	Closing remarks	