

Prevalence of
Hepatitis B&C
in Pakistan



Pakistan Medical Research Council

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Foreword

Realizing the importance of hepatitis B and C in the country, Ministry of Health along with Standing Committee on Economic Affairs and Statistics assigned Pakistan Medical Research Council to do the survey for disease and thus assist the Ministry in calculating the disease quantum, identify the most probable route /source of disease transmission so that guidelines could be developed to prevent it.



I congratulate Pakistan Medical Research Council for conducting this first hepatitis B and C survey in the general population of Pakistan. The Statistics Division and Federal Bureau of Statistics assisted in drawing the scientific and representative sample size for the country. About 7000 houses in 350 Primary Sampling Units (PSU) all over Pakistan were surveyed comprising of about 49000 persons. Interviews were conducted and all available/consenting individuals were tested for hepatitis B and C.

The survey was done over almost a year where teams and its monitoring officers traveled the extremes of temperatures and places with restricted movements. The teams worked very hard and with full dedication. The compliance for testing from the population was excellent and no where the teams felt threatened or unwanted. The continuous supervision and regular supplies by the collaborating partners-Citilab was commendable and played a major role in timely completion of task.

The data shows 2.5% prevalence of hepatitis B and 5% of hepatitis C in general population. Within the provinces the hepatitis B was very high in Balochistan (4.3%) while it was 2.5% in Sindh, 2.4% in Punjab and 1.3% in NWFP. For HCV the disease was highest in Punjab (6.7%) followed by Sindh (5.0%), Balochistan (1.5%) and NWFP (1.1%).

The data shows that for hepatitis B prevention we need to enhance hepatitis B vaccination in the population. For HCV the major source of infection is syringe reuse for therapeutic injections by the health care providers. To prevent syringe reuse an easy way is to destroy syringe by cutting it. Moreover over 60% of the injections used by the health care providers are unnecessary. The higher is the injection use in a country the higher would be the blood born diseases. Therefore we also need to reduce our injection rate per person from the present 13 injections to 4-5 injections per person per annum.

Dr Huma Qureshi, Executive Director of PMRC and the PMRC research centres in different provinces were the work force behind all this effort and she has set a good example of coordination and collaboration.

Khushnood Akhtar Lashari
Secretary Health

Acknowledgments

Pakistan Medical Research Council would like to offer special thanks to Mr. Asad Elahi, Secretary Statistics for taking the initiative to invite PMRC to do this survey. The unconditional support of Mr. Khushnood Akhtar Lashari, the Secretary of Health, Ministry of Health in making this otherwise difficult task a walk over for us is greatly acknowledged.

The participation and support of senior staff of Federal Bureau of Statistics in taking out the sample size and timely provision of alternate PSUs in difficult areas of Sindh during floods and in trouble areas of Balochistan and NWFP and the support of their provincial coordinators and assistants in identification of areas and houses in extremely poor law and order situation areas of Balochistan and NWFP is appreciated with gratitude. Without their support this survey was impossible.

The active participation of staff and officers of the PMRC Research Centres in the survey and monitoring shows the will and eagerness of the researchers to undertake national studies with dedication and commitment. Thanks are due to all my team members from within PMRC and outside, whose tireless efforts made this impossible task possible. The tireless efforts of Mr. Mahmood Ahmed in organizing the visits to monitoring sites and bringing FBS teams in close collaboration with PMRC were a major contributor in completing the task. The data analysis was done with full dedication by Syed Ejaz Alam of PMRC, JPMC who has worked day and night on the data and brought out scientific and yet simple data which is easy to understand even by lay public.

Citilab wishes to thank Dr Muhammad Badar-e-Alam who provided insight into technical issues regarding collection, transportation and testing of blood samples. Thanks are also due to Dr Ashar Alamgir, Dr Zeeshan Ahmed and Dr Azfar for overseeing work of the teams and facilitating sample collection and to Dr. Kiran, Dr. Huma and Dr. Rakia in providing support in sample verification, labeling and data entry. Last but not least the efforts of Mr. Ghulam Fareed are appreciated with profound gratitude for providing support to our teams during sample collection by traveling all over the country to ensure right sample collection.

Executive Summary

The first prevalence report on Hepatitis B and C in Pakistan

Meta analyses of over 300 papers published on hepatitis in Pakistan from 1980-2004 were analyzed to get cumulative figures for the disease. Over 95% of these studies were hospital or clinic based, therefore carried a biased figure. These figures were 3-4% for hepatitis B (HBV) and 4-6% for hepatitis C (HCV) making an overall aggregate of 7-10%. Reflecting these figures on 160 million population it was estimated that about 16 million cases are exposed to these 2 viruses. As these were hospital based studies, therefore, there was a strong need to do the actual prevalence study and find out the disease burden.

This is the first survey on the prevalence of hepatitis B and C in Pakistan conducted from July 2007 to May 2008. The survey was done in collaboration with Ministry of Health, Statistics Division, Federal Bureau of Statistics (FBS) and Pakistan Medical Research Council (PMRC).

The contract was outsourced to Citilab, a private laboratory. The formulation of field teams, their training, transport and logistic arrangements in the fields were the responsibility of the contract laboratory. The teams collected baseline household and personal information performed blood tests at the site and gave reports to those who were tested. The extra blood was frozen for further use.

PMRC did the overall monitoring of the project in collaboration with the Executive District Officers (EDO), Nazims or seniors of the community.

A sample size of 7000 houses in 350 primary sampling units (PSUs) all over Pakistan was calculated by FBS. Each PSU had 20 houses; with an average family size of 6.7 persons per house, about 47000 persons were expected to be checked.

Whole blood devices were used and their sensitivity and specificity was checked against ELISA using serial dilutions. Only devices having an over 98% sensitivity and specificity were used.

A total of 47043 persons were screened. Overall prevalence of hepatitis B (HBsAg) was 2.5% and hepatitis C (HCV) was 4.9%. Overall HBeAg positivity was 14.4% with 17% in Balochistan, 15.3% in Sindh, 14.1% in Punjab and 8.4% in NWFP. For HCV the prevalence within provinces showed 5% in Sindh, 6.7% in Punjab, 1.1% in NWFP and 1.5% in Balochistan. For HBV the figures were 2.5% in Sindh, 2.4% in Punjab, 1.3% in NWFP and 4.3% in Balochistan.

The sample size was more targeted towards getting the country and provincial prevalence, therefore although all districts were checked but their figures can not be used as the real prevalence in each district. Prevalence of HCV and HBV in different districts is given below. In Sindh the HBV figures were high in Khairpur (6.3%), Ghotki (5.9%), Larkana (4.3%), Noshero Feroze (4%). For HCV very high figures were seen in Ghotki (12.7%), Sanghar (7.8%), Dadu (7.2%), Hyderabad (5.7%), Thatta (5.4%), Shikarpur and Jacobabad 5.3% each.

In Punjab high figures for HBV were seen in Dera Ghazi Khan (5.7%), Islamabad (5.6%), Rahim Yar Khan (4.7%) and Jhang (4.1%). The figures for HCV were very

high in Vehari (13.1%), Hafizabad (12.9%), Pakpattan, (10.6%) and Bahawalnagar (10.1%).

In NWFP high HBV prevalence was seen in Upper Dir (5%), Lower Dir (3.2%) and Bannu (2.7%) and high HCV was seen in Hango (6.4%), Swat (3%) and Battagram (2.7%).

In Balochistan high figures for HBV were seen all over the province with very high prevalence in Musakhel (14.7%), Loralai (7.4%) and Sibi (7.3%). High HCV figures were seen in Musakhel (5.3%), Jafarabad (5.2%) and Barkhan (3.8%).

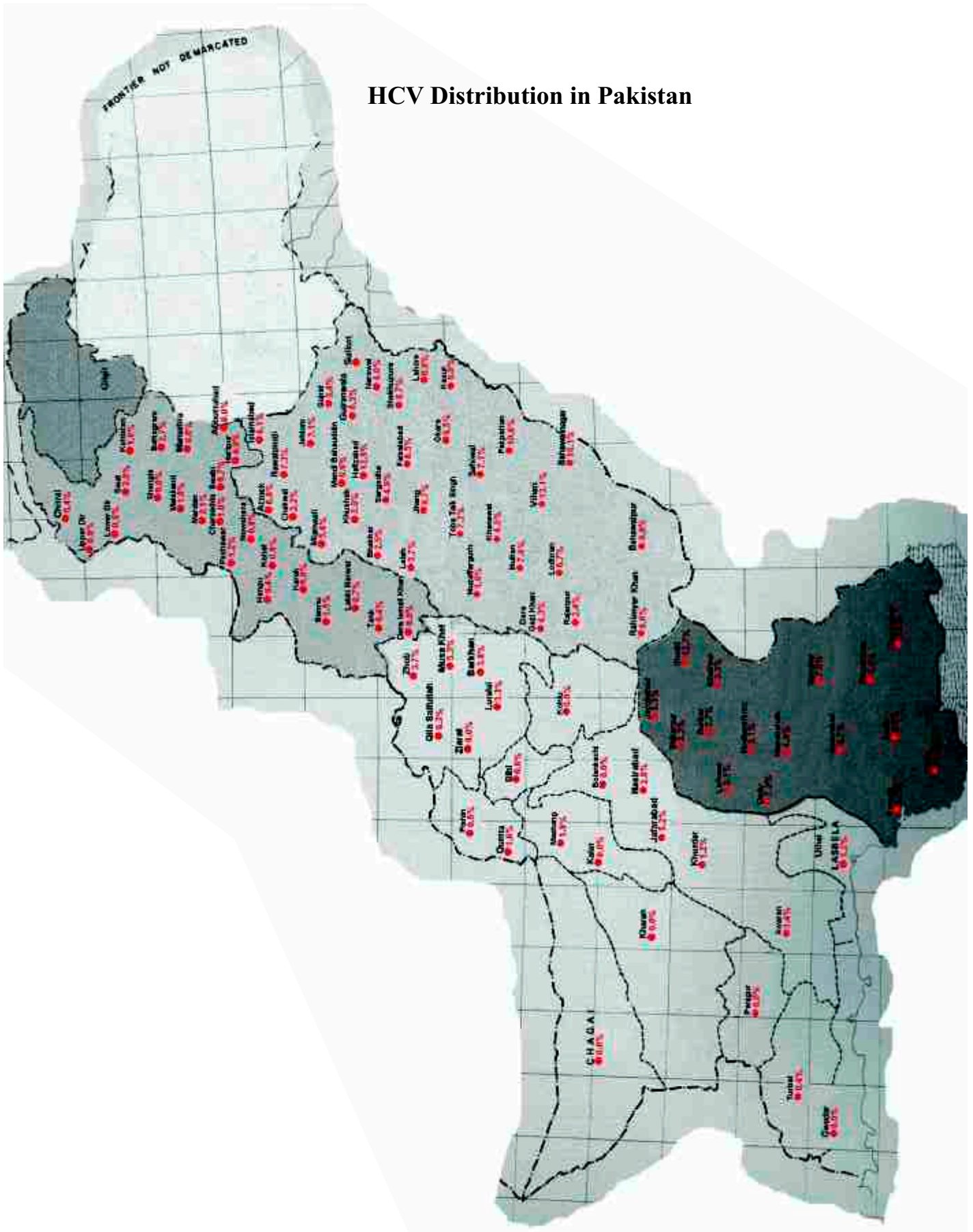
Gender showed slight preponderance of males for HBV all over Pakistan but no difference was seen in HCV. HBV distribution in Balochistan showed 5.2% disease prevalence in males and 3.4% in females. High HBV prevalence among females in Balochistan indicates a large reservoir of disease resulting in either horizontal or possibly vertical transmission.

With the advancement of age the HCV exposure seems to be increasing showing old exposure plus addition of new cases. The HBV exposure in younger population is low suggesting protection through vaccination.

Therapeutic injection use due to various ailments was high and showed strong positivity to HCV prevalence. About 30% of the screened population was taking more than 5 injections per person per year. With the increasing numbers of injections per person per year the exposure rate also increased. The positivity of HCV was twice more in those where a syringe was reused.

To control the disease in Pakistan, one has to increase the hepatitis B vaccination in newborns and high risk groups. For HCV the use of therapeutic injections has to be curtailed to a minimum of 3-4 injections per person per year with stronger injection safety measures.

HCV Distribution in Pakistan



Background

The Standing Committee on Economic Affairs and Statistics had asked the Statistics Division to do a survey on the prevalence of hepatitis, HIV/AIDS and hypertension, as these cases were on a rise. First consultative meeting on this issue was held between Mr. Asad Elahi, Secretary Statistics, Dr Huma Qureshi, Executive Director, Pakistan Medical Research Council, Dr Mubashir Ahmad Khan, Principal Research Officer, Pakistan Medical Research Council, Dr Sania Nishtar, President Hearfile and a representative from National Program on HIV/AIDS.

During this meeting and further many meetings it was decided that HIV/AIDS screening is done on voluntary basis and the program was already collecting data using this approach therefore there was no need to do survey on this sensitive issue and people will not volunteer to be checked using blood screening on the spot. For hypertension there was already enough data available to calculate the disease burden, therefore again no requirement was felt to do a survey on urgent basis.

As hepatitis was on a rise and there were no prevalence data available therefore it was decided to carry out a prevalence study on hepatitis B and C in the whole country with the help of Federal Bureau of Statistics who shall take out the sample size and mobilize its teams to coordinate with PMRC and the survey teams in identifying the house, the head of the household and information on number of family members.

Introduction

Hepatitis B and C viruses spread through blood and body secretions. These viruses have infected mankind for centuries but hepatitis B virus was discovered in 1970s and hepatitis C in 1990s.

Both viruses have an acute illness where patients have acute jaundice and very high serum ALT (a part of liver function tests). In majority (90%) of adults, acute hepatitis B resolves within 2-3 months with full recovery. The scenario is different in new born and up to 5 years of age where full recovery is seen only in 10% while 90% develop chronic liver disease. In acute hepatitis C full recovery occurs in only 20-30% of cases while 70-80% require treatment for clearance of disease as they may go on to develop chronic liver disease.

If the mother is HBsAg positive and is also positive for HBeAg (a marker for infectivity) than there is a 90% chance that she will transmit the disease to her newborn. If the mother is HBsAg positive and not HBeAg positive, than the probability goes down to 20-30%.

It is therefore mandatory to check pregnant mothers for these 2 viruses. For the former scenario the newborn has to receive 2 immunizations within 24 hours of birth, the hyper immune globulin at one site and the hepatitis B vaccine at another site. For the latter group only hepatitis B vaccine is recommended.

Exposure of the virus in the neonatal period

Due to poorly developed immune system the body is unable to produce antibodies against the virus, so the virus stays within the body; without producing any damage to the liver. These cases have the HBsAg in the blood for life but their liver function tests remain normal all through life and all markers that show viral activation are absent in these cases. Exposure to the virus between 2-5 years of life is dangerous because the body's immune system is partially developed. The body produces inadequate antibodies against this virus; which are not adequate enough to throw the virus out nor are low enough to not to produce a reaction. This low-grade reaction produces chronic liver disease in these children, which persists for life.

Majority of adult hepatitis B cases that we see are children and neonates who have been exposed to this virus in early life and have carried the virus due to reasons mentioned above.

Once a person has 2 positive reports of HBsAg 6 months apart, than there is almost a 100% chance that this individual will carry the virus for life and will always be found positive on tests whenever tested. Natural seroconversion over years occurs in 5-20% cases in each country depending upon the genes and genotypes of HBV.

Once exposed to hepatitis B virus, antibodies develop naturally in over 90% adults within 6 months of exposure. Vaccination also produces antibodies in over 90% of the

cases. Antibodies (Anti HBs) once produced either following natural recovery or following vaccination persist for life, though their levels may go down with time. Any exposure to the virus any time after production of antibodies will automatically enhance antibody production during that period to protect the individual. Booster dose is therefore not required as a routine in most cases.

Majority of the cases with hepatitis C virus get infected without any history of jaundice or liver disease. During acute infection, which is noticed in 20% cases, the individual has jaundice and raised ALT. Anti HCV becomes positive after 6 months of exposure so this test should not be used for the diagnosis of acute hepatitis. On the contrary if this test is found positive in an otherwise acute case than the diagnosis of acute hepatitis C should be excluded.

The acute infection clears in 20-30% cases while in the rest it persists as chronic hepatitis C. It is a very slowly progressing disease and in about 25% cases over 10 years it progresses to chronic liver disease and over another decade in 25% it goes to advanced disease.

Anti HCV is a marker of exposure and it will remain positive for life, its presence does not confirm disease. PCR defines active disease.

Subjects and Methods

Sample Size

Universe: The universe consists of all urban and rural areas of the four provinces of Pakistan defined as such by 1998 Population Census excluding FATA, Military restricted areas of NWFP. Thus population of excluded areas constituted about 3% of the total population.

Sampling Frame: Federal Bureau of Statistics has developed its own sampling frame for urban area. Each city/town has been divided into a number of enumeration blocks (E.B). Each enumeration block consists of 200 to 250 households on the average with well-defined boundaries and maps. The lists of enumeration blocks updated in 2004 and the lists of villages/mouzas/dehs published/prepared by Population Census Organization were used as sampling frame. Enumeration blocks and villages were considered as Primary Sampling Units (PSUs) from urban and rural domain respectively.

Stratification Plan

a) Urban Domain

- i. **Large Sized Cities:** Each of Karachi, Lahore, Gujranwala, Faisalabad, Rawalpindi, Multan, Hyderabad, Sukkur, Sargodha, Bahawalpur, Sialkot, Peshawar, Quetta and Islamabad have been considered as large sized city. Each of these cities constitutes a separate stratum which has been further sub-stratified according to low, middle, high income groups based on the information collected in respect of each enumeration block at the time of demarcation/updating of urban area sampling frame.
- ii. **Remaining Urban Areas:** After excluding the population of large sized cities from the population of respective administrative division of a province, the remaining cities/towns have been grouped together to form a stratum called other urban areas. Thus each division in remaining urban areas in the four provinces constitutes a stratum.

b) Rural Domain

In rural domain, each district in the Punjab, Sindh and NWFP provinces has been considered as independent and explicit stratum whereas in Balochistan province each administrative division constitutes a stratum.

Sample Size and it's Allocation

Considering the variability for the characteristics for which estimates are to be prepared, population distribution and field resources available, a sample size of about 7000 sample households (SSUs) have been considered appropriate to provide reliable

estimates of key variables at National and Provincial level with desired reliability constraints.

The entire sample households (SSUs) have been drawn from 350 Primary Sampling Units (PSUs) out of which 138 are urban and 212 are rural. As urban population is more heterogeneous therefore, higher proportion of sample size has been assigned to urban domain. Similarly NWFP and Balochistan being the smaller provinces and to get reliable estimates for these provinces higher proportion of sample has also been fixed to these provinces. After fixing the sample size at provincial level, further distribution of sample PSUs and SSUs to different strata in rural and urban domains in each province has been made proportionately, keeping in view the minimum requirement of each stratum.

The distribution of sample PSUs and SSUs in the urban and rural domain of the four provinces is shown in **Table 1**.

Table-1: PSUs and SSUs in the urban and rural domain of the four provinces

| Province | Sample PSUs | | | Sample SSUs | | |
|--------------|-------------|------------|------------|-------------|-------------|-------------|
| | Total | Urban | Rural | Total | Urban | Rural |
| Punjab | 175 | 68 | 107 | 3500 | 1360 | 2140 |
| Sindh | 78 | 38 | 40 | 1560 | 760 | 800 |
| NWFP | 55 | 17 | 38 | 1100 | 340 | 760 |
| Balochistan | 42 | 15 | 27 | 840 | 300 | 540 |
| Total | 350 | 138 | 212 | 7000 | 2760 | 4240 |

Sample Design

A stratified two-stage sample design was adopted for the survey.

Sample Selection Procedure

- a) **Selection of Primary Sampling Units (PSUs):** Enumeration blocks in urban domain and villages/mouzas/dehs in rural domain were taken as primary sampling units (PSUs). In the urban domain, sample PSUs from each ultimate stratum/sub-stratum have been selected with probability proportional to size (PPS) method of sampling scheme. In urban domain, the number of households in enumeration block as per last updated list during 2004 and population of villages/mouzas/dehs according to population census 1998 have been considered as measure of size.
- b) **Selection of Secondary Sampling Units (SSUs):** Households within sample PSUs have been taken as secondary sampling units (SSUs). A specified number of households i.e. 20 from each urban and rural sample PSU have been selected with equal probability using systematic sampling technique with a random start.

With each house having an average family size of 6.7 persons, in Punjab 3500 houses comprising of 23450 persons, in Sindh 1560 houses with 10452 persons, in NWFP 1100 houses with 7370 persons and in Balochistan 840 houses with 5628 persons were to be checked.

STAFF OF FBS



Contracting Firm

Using standard protocol of tender and selection of the best firm, Citilab of Rawalpindi/ Islamabad won the contract. The laboratory has 6 qualified postgraduate doctors looking after each section of the laboratory with over a dozen qualified technicians and many qualified phlebotomists and other support staff. A major part of the basement of the laboratory was converted and reallocated to the hepatitis survey with special fridges and freezers and centrifuge machines to cater the blood separation and storage. A 2 day's training workshop of the laboratory personnel was done by Executive Director, PMRC/ Project Director at different occasions to train the trainers.

CITILAB ISLAMABAD





Testing/Evaluation of Rapid Test Devices

As all tests were to be done in the field and reports given to the people there and then therefore it was mandatory that rapid whole blood device should be procured for the survey. There are variable qualities of rapid devices available in the country whose results vary from best to none. Therefore to tackle this issue first of all WHO approved rapid devices were searched and where WHO/EU certified devices were not available then other parameters like their use in international studies and their comparative test figures available on net were retrieved and compared.

Based on the above strategy the “**Determine**” by **Abbott** was approved for hepatitis B. This test is WHO approved with over 95% sensitivity and specificity, while for hepatitis C no device was WHO approved therefore the reliable companies were requested to supply 100 devices each for local testing on known ELISA positive and negative samples of hepatitis C cases at the department of blood bank and transfusion services of Jinnah Postgraduate Medical Centre, Karachi. Fresh samples of known positive and negative cases were supplied by the Specialized Centre for Gastroenterology and Hepatology of Pakistan Medical Research Council. Tests were done with serial dilutions for each sample. “Advanced quality” rapid test for HCV was finally selected and used.

Survey Forms

During the survey 5 forms were to be filled which comprised of a consent form, a household form, an individual form, a report and a referral form for those found positive for the disease. All these were translated into Urdu language to help interviewer in posing the right question to get the right answer. A reverse translation from Urdu to English was also done to check if the translated questions had the same message.

Pilot Testing

All these forms were tested in a pilot study on 10 houses in different vicinities of Islamabad and Rawalpindi. Few questions in the individual form and the household form were rephrased to get desired information. These forms were then retested and when found correct were finalized.

Training of the Trainers

In the training all participants were appraised about the current situation of hepatitis B and C in the country and how the transmission occurs and how disease spreads.

TRAINING AND PRE TESTING







Six forms/brochures were made which included:

1. Information brochure
2. Consent form
3. House hold information form
4. Individual form
5. Report form
6. Referral form

Trainers were trained on the **information brochure**, which was given to the head of the family to make him aware about the disease and its modes of spread and consequences. It also gave them information that the Ministry of Health, Government of Pakistan was extending help to get right figures about disease prevalence.

The **Consent form** was to be signed by the head of the household or a senior member of the family and either signature or a thumb impression was taken in front of 2 members of the house and the team leader.

The **house hold information form** contained information on water and sanitation facilities, number of household members in the house, their relation to the head of the household. Information was also collected on the age, gender, education and employment status of the family members. This information was gathered to know about number of members present in the house, because all members of the family were to be checked for the disease irrespective of the age and gender.

A separate **individual form** was filled for each member of the house to get first hand information about their present and past infection with hepatitis and the possible risk factors for its transmission. Special questions were posed for sharing the toothbrushes and the razors and the use of injections for common ailments and whether a new syringe is used or a re used syringe is used. Individual form of each person was filled irrespective of whether he/she was present at that time or not to know the family size and their health status and the health seeking behavior.

PROFORMA FILLING









A **report** was given to all persons who gave blood for testing. All reports of the whole house hold members were handed over to the head of household or a senior person of the head of the family.

Referral form was filled for all those cases that were found positive. They were referred to the nearest functioning site of the Prime Minister's Program on the control of hepatitis for confirmation of disease by ELISA and treatment if required.

REPORT DELIVERY



Training of Phlebotomists

All technicians were trained on taking out the blood sample from the vein and through the prick in case of infants and newborns. Though all laboratory technicians were already trained to collect blood but to maintain standardization a uniform training was done for all technicians. All technicians were made to run at least 2-3 hepatitis B and C rapid tests using whole blood as almost all of them were trained on performing the rapid test with serum and not whole blood. Special training was done on marking the names of the individuals on the devices and on the storage gel tubes where the PSU code was written along with house number and the person number and name. The tested rapid blood kit/devices once checked were pasted on the individual report forms to keep a record. The reports were also written on the back side of each individual form in pre assigned box, so that if the devices are lost the written report remains.

Blood was collected in gel tubes for further testing and serum separated and stored.

FIXING OF DEVICES ON PROFORMA

