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Name of the University, Hospital, Research Institute, Academy or Ministry

The Institute of Liver and Biliary Sciences

Name of the Division, Department, Unit, Section or Area

Hepatology

City New Delhi **Reference Number** IND-125

Title WHO Collaborating Centre on Viral Hepatitis and Liver Diseases

Report Year 12-2014 to 12-2015

1. Please briefly describe the progress made in the implementation of your agreed workplan as WHO collaborating centre during the past 12 months (or the reporting period listed above). Please report on how each workplan activity was implemented, if any outputs have been delivered, if any results have been achieved and if any difficulties have been encountered during this time. If an activity has previously been completed, has not started yet, or been placed on hold, please indicate this.

Activity 1

Title: Cohort Studies

Description: ILBS will undertake hospital based cohort studies of HBV and/or HCV positive individuals to evaluate acceptable (invasive versus non-invasive) and cost-effective modalities for assessment and progression of hepatic fibrosis.

The facility of advanced biochemical testing, Fibroscan and Hepatic Venous Pressure Gradient measurement (HVPG) are available in the institute.

In the ILBS, nearly 40,000 liver disease related new and follow-up patients were seen in the past one year. Nearly 1,100 liver biopsies were done on patients undergoing evaluation and treatment for liver diseases. Hence, these cohort studies could be implemented in the facility itself.

The institute has a well structured Institutional Review Board (IRB), registered with the National Registry at the Drug Controller General's Office. The study protocols would be initiated only after due submission and approval by the IRB. The study protocol will also be submitted to the ERC in line with WHO rules and regulations.

After designation in Dec 2014, ILBS arranged for infrastructure and staff required for the smooth functioning of WHOCC on Viral Hepatitis. The Centre was officially inaugurated and started on 5th May 2015 by Mr. Satyendra Jain, Health Minister, Govt of Delhi and Dr Nata Manabde, WR to India, WHO. We are herewith submitting the activities undertaken during the past 9 months.

Activities undertaken

The research proposal for a hospital based cohort study entitled “Cost effective non invasive diagnostic modalities and predictive model for development and progression of fibrosis among patients with Hepatitis B, Hepatitis C infection or non alcoholic fatty liver disease: A hospital based retrospective followed by prospective cohort study” has been developed and it was approved by the Institute’s Ethical Committee (IEC) on 9th Jan 2016 The study has also been registered at ClinicalTrials.gov with the Identifier number as: NCT02658786 and the work has started.

The available cases which underwent biopsy during 2000-2015 and are likely to be included in the study as retrospective cohort are approximately 2986 cases. This includes 1480 HBV, 600 HCV and 906 NAFLD cases.

The sample size calculated for the prospective cohort is 3000, which includes 1000 HBV, 1000 HCV and 1000 NAFLD cases.

Plan for 2016

- To continue enrolling the patients for prospective cohort
- To conduct a preliminary analysis for the data of retrospective cohort
- Seek financial support from WHO

Activity 2

Title: Training for clinicians in clinical management of viral hepatitis and its complications

Description: i. The team of expert hepatologists, clinical nutritionists and intervention radiologists at the ILBS would develop and/or improvise curricula for the clinical diagnosis and management of viral hepatitis, cirrhosis and liver cancer using current guidelines from Liver Associations, Global Advisory boards, WHO, and recent scientific evidences.

ii. The training program would be of two broad categories

a) Hepatitis Induction Program (HIP) - This will be a dedicated program for different level of health care workers (as mentioned below).

b) Hepatitis UpDate Program (HUP) - This will provide a continuous ongoing e-learning opportunity. The participants of the HIP will be entitled and encouraged to undertake the HUP- continuous self learning program. The scientific and policy related material for the HUP would be context dependent and will be constantly updated based on new data, evidence based analysis, and guidelines.

iii. The training curricula for the HIP will be ready for review within 9 months of designation of the CC. The quality and the usefulness of the contents will be assessed by a 3 tier peer review process before implementation; a) internal committee of experts, b) external reviewers, and , c) interaction and inputs from WHO officials.

iv) The HIP is aimed to deliver well organized and monitored training courses with defined outcomes, which will be termed as certificate courses. These will be available for different levels of health care workers and officials (as detailed below). ILBS being a Deemed-to-be- University for Liver and Biliary Sciences, the course material would be placed before the Academic Council of the University for consideration before certification.

v). WHO will arrange for clinicians and other operational staff from other countries to be sent to ILBS for training.

vi). The interactions with participants from different countries would help learn more about cost-effective screening and early detection strategies for liver diseases, cirrhosis and liver cancer.

Activities undertaken

- Training manuals, modules and SOPs for clinical diagnosis and management of viral hepatitis, cirrhosis and HCC are developed by WHO CC members and are under In-house validation and evaluation.
- An internal committee of experts has been constituted to review and validate the training material.
- Health Associate course module has been developed with the help of our nursing faculty and has been subjected to In-house validation and evaluation.

Plan for 2016

- To constitute an external experts group to validate the modules.
- To have inputs from WHO experts.
- To develop an online website for HUP, where all updates will be made available for viral hepatitis and liver diseases.
- To identify funding mechanisms for future training programs.

Activity 3

Title: Viral Hepatitis Diagnostic Laboratory Support Program

Description: 1. ILBS will help develop SOPs and provide support to existing national virology and immunology laboratories in the country/region with the capacity to diagnose, monitor and assess outcome of all types of viral hepatitis infections by providing guidance on quality assurance of viral hepatitis testing; serological, NAT based and molecular testing.

2. The training program would be of two levels

- a) For microbiologists, virologists, immunologists - short duration programs of 7-14 days
- b) For technicians - hands on training, wet-lab exposure, for 4-8 weeks on molecular diagnostics.

The ILBS laboratories are accredited by the National Accreditation Board for Laboratories (NABL) and follow the external quality control procedures.

Activities undertaken

- Training modules for lab diagnosis of viral hepatitis and bio-safety are developed by WHO CC members, one each for microbiologists and laboratory technicians.
- An internal committee of experts have been constituted to review and validate the modules.
- SOP's for each test and assay have been developed.
- Modules and SOPs are reviewed and finalized by the internal committee.
- An External Advisory Group has been constituted and its first meeting was held on 25th October 2015. The group includes Dr Ritu Chauhan, National Professional Officer Microbiologist from WHO, Prof. Pradeep Seth, Ex Head Department of Microbiology, AIIMS & President, Seth Research Foundation, Dr. Shashi Khare, National Center for Disease Control, and Prof. P Kar, Maulana Azad Medical College, New Delhi.
- Letters has been sent to all the members of External Advisory Group for 2nd Meeting to be held during the last week of February, 2016.

Plan for 2016

- Finalization of the 'Laboratory Technician Module' after an initial pilot training session, taking feed-back from the technical staff of the institute.
- To identify lab technicians (From various Microbiology/Virology Labs across Delhi/NCR) and to organize first training by the end of March, 2016 for pilot testing of modules and SOPs. The same would be given to the WHO for final evaluation and approval. Subsequently, the WHO would need to help for the selection and support of future trainees in the region.
- A letter has been sent to WHO Head Quarter, Geneva for providing a GeneXpert machine for point of care of Testing of viral loads for imparting training to various Laboratory technicians and Microbiologists on the same.
- WHO office could help to identify and support the participation of the technicians for the proposed workshops in 2016.

Activity 4

Title: Operational models for delivery of viral hepatitis treatment at lower income levels

Description: ILBS would do operational research to see how viral hepatitis treatment could be expanded to lower levels of healthcare within a healthcare delivery system and help prepare working modules likely to suit different geographical regions.

It could also help in evaluating bio-similars in different countries for their comparative antiviral efficacy so as to improve affordability and reach of antiviral drugs.

The institute has a well structured Institutional Review Board (IRB), registered with the National Registry at the Drug Controller General's Office. The study protocols would be initiated only after due submission and approval by the IRB. The study protocol will also be submitted to the ERC in line with WHO rules and regulations.

Activities undertaken

- A research proposal entitled "Operational research on community and facility based interventions to develop a working service delivery model for preventive, diagnostic and therapeutic services for viral hepatitis" has been developed. This study includes:-
 - A pilot study in Delhi, identifying two districts (test and control).
 - A pre-intervention baseline data (community based and facility based) will be collected from both districts.
 - All planned strategies will be implemented in the test district for a period of 6 months.
 - Post intervention results will provide the evidence for the planned strategies.
- We have collaborated with National Institute of Health and Family Welfare (NIHFW, New Delhi), during the development of research plan and will jointly conduct this study. An expert in operational research, Dr J P Shivdasani from NIHFW is a co-Investigator for this project.
- NIHFW has also allotted a thesis entitled "Study on awareness, health seeking behaviour, psychosocial and economic consequences among patients with chronic hepatitis B and C infection attending a tertiary care hospital in Delhi" to one of their PG student. The results of this study will provide patients perspective regarding service delivery for viral hepatitis.

Plan for 2016

To execute the study plan for operational research we will start the following activities:-

- To randomly select 2 districts from Delhi.
- To plot the existing health care delivery system in these districts and to collect the data on demography from each district
- To randomly select the existing facilities and communities
- To conduct in-depth interviews and focus group discussions in the community for baseline data
- To collect facility level data via record reviews, performance assessment, client perspectives and exit interviews
- To execute our interventional strategies (Community education, training of staff, making available the low cost diagnostics and treatment for viral hepatitis)
- Post interventional data will be collected after 6 months of intervention

After ethical approval we have to identify funding mechanisms for implementation of this study.

2. Please briefly describe your collaboration with WHO in regards to the activities of the WHO collaborating centre during the past 12 months (e.g. means of communication, frequency of contact, visits to or from WHO). Please feel free to mention any difficulties encountered (if any) and to provide suggestions for increased or improved communication (if applicable).

A total of ten (10) meetings were held between WHO officials and WHO CC, ILBS members either at WHOCC or at WHO country office. Minutes of meetings were developed and shared on regular basis through e-mail. The purpose of meetings was to discuss the progress done and to plan out the strategies to successfully undertake the activities planned under WHOCC.

During these meetings Dr Nicole Seguy, Dr Bharat Rewari, and Dr Sukarma Tanwar constantly provided technical support to WHOCC. Dr Razia Pendse and Dr Ritu Chauhan also facilitated us in few meetings. We constantly had telephonic discussions with WHO team at WHO Country office to India regarding different activities.

On 28th July 2015, WHOCC, ILBS in collaboration with WHO has organized 2nd National Consultative Meeting on Hepatitis C. The theme of meeting was "Can we eliminate Hepatitis C from India by 2020?" The report on this meeting was drafted and is ready to be released soon.

ILBS as WHOCC, is also identified by Ministry of Health and Family Welfare (MOHFW), Government of India, as an apex training institute for the upcoming National Program for Prevention and Control of Viral Hepatitis. We also participated in a small expert group meeting held on 30th November, 2015 at National AIDS Control Organization (NACO) under the chairmanship of AS&DG NACO. Agenda for the meeting was to plan and discuss a possible phased roll out of treatment plan for hepatitis C involving NACO, NCDC and WHOCC, ILBS.

On 4th of December, 2015, ILBS organized 18th Hepatitis Day in collaboration with Government of Delhi. ILBS involved 30 schools organizing poster competition and spreading awareness among teachers and students. ILBS also developed posters and banners and displayed at 200 Delhi Metro Stations disseminating awareness all over Delhi.

WHOCC, ILBS has also organized a two day workshop on "Hepatitis C in Asia" during an International Single Topic Conference on Hepatitis C. This conference was organized by Asia Pacific Association for the study of the Liver (APASL) on 18-20th Dec 2015.

It would however have been more productive if some initiatives are also taken by the WHO HQs and the Regional Office to engage and utilize the technical expertise of the WHOCC in the field of hepatitis and liver diseases. Guidance and more frequent interactions would help better outcomes in 2016.

3. Please briefly describe any interactions or collaborations with other WHO collaborating centres in the context of the implementation of the above activities (if any). If you are part of a network of WHO collaborating centres, please also mention the name of the network, and describe any involvement in the network during the last 12 months.

Dr Ekta Gupta, Additional Professor, Virology and an active member of WHOCC represented the Institute in a Regional workshop on strategic information of HIV, Hepatitis and STI held at Bangkok, Thailand, during 12th – 14th October 2015 as a visiting faculty from WHOCC.

During the two day workshop on "Hepatitis C in Asia" organized at an International Single Topic Conference on Hepatitis C during 18th -20th Dec 2015, WHO CC invited Dr John Ward, Director, Division of Viral Hepatitis, CDC Atlanta, USA as a guest speaker. We requested him to guide us for different activities and to be a member of our external advisory group to validate our training material. Dr. Razia Pendse, Regional advisor, HIV/AIDS and STI, Department of Communicable Diseases, was also actively involved and delivered a talk during this workshop.

We are planning to collaborate with WHOCC at CDC Atlanta to further substantiate our work on Viral Hepatitis. It is requested that if the HQs could help in the networking and connectivity.

We are not a part of any WHO CC Network, as we have not found any available network on viral hepatitis or liver diseases. Please suggest us if we can be a part of any such network or we need to create one.

4. Please briefly describe any type of technical, programmatic, advisory or other support received from WHO during the past 12 months for the implementation of the agreed activities listed above (if any).

No financial support from WHO has so far been received. During the teleconference, Dr Hande had indicated that the WHO HQ would help in identifying some funding source for the projects under different TORs. We do expect financial support from WHO in 2016.

Dr Razia Pendse from WHO-SEAR office and Dr Nicole Seguy, Dr Bharat Rewari, and Dr Sukarma Tanwar from WHO Country office of India are constantly providing technical and advisory support for different activities.

Dr Ritu Chauhan from WHO is a member to our external advisory group for developing and validating training modules on "Screening and Diagnosis of Viral Hepatitis" for microbiologists and Lab Technicians.