Review Article

Review of Collaboration between Tribhuvan University Institute of Medicine in Nepal and National Center for Global Health and Medicine in Japan on Nosocomial Infection Control and Proposal for Improvement

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Introduction

In developing countries, where the incidence of infectious diseases is high and environmental conditions of healthcare facilities are poor, nosocomial infections may frequently occur.[1,2,3] Effective nosocomial infection control is crucial in the healthcare facilities of developing countries, but in actual fact, attention to it is still limited and control measures are not functioning well in many countries[4]. Furthermore, bacterial resistance to antibiotics is increasing worldwide and this fact is not a little affecting nosocomial infection. However studies about the actual situation of multi-drug resistant bacteria in developing countries along with measures to address such situation is still limited.[5]

Collaboration between Institute of Medicine, Tribhuvan University (IOM) in Kathmandu City, which is the core of medical services in Nepal and National Center for Global Health and Medicine (NCGM) in Japan has a long history, which dates back to the Medical Education Project by JICA. During the project period, various technical cooperation was implemented, however, technical guidance on nosocomial infection control was not included.

In view of the growing concern on nosocomial infection control and spread of antimicrobial resistant bacteria in recent years and based on the reliable relationship created through the project, IOM and NCGM decided a new collaboration focusing on research of nosocomial infection control including anti-microbial resistance (AMR). These collaborative activities were designed and conducted with the purpose to investigate the actual conditions of nosocomial infection control in Kathmandu City, Nepal as a basis for the possible contribution to its improvement.[6]

After reviewing the preceding researches and the technical cooperation, the following 4 researches were carried out in Nepal during January 2011- March 2016, followed by discussion and proposals for improvement. In this paper, we summarized these collaborative activities between the two institutions.

- Fact-finding survey of nosocomial infection control in hospitals in Kathmandu, Nepal- a basis for improvement
- Study on nosocomial bacterial pattern in Tribhuvan University Teaching Hospital
- Study on AMR in Nepal
- Study on medical personnel regarding nosocomial infection control (KAP survey)

Initiation of cooperation between IOM and NCGM

IOM was constructed by Japan's Grant Aid in 1980. Technical cooperation project by Japan International Cooperation Agency (JICA) had been implemented from 1980 to 1996 (Medical Education Project) with the purpose to establish medical education and strengthen the function of IOM including the Tribhuvan University Teaching Hospital (TUTH). NCGM dispatched chief advisors and experts to provide technical guidance. During the 16 years the project conducted various activities, aiming to achieve the purpose, to strengthen

hospital administration, education and training management, clinical medicine, basic science, nursing management, etc., however nosocomial infection control was not included. That was because in those days awareness on nosocomial infection control was still low not only in developing countries but also in developed countries.[7]

Nepal suffered political instability from 1996 to 2006 followed by a transition from the Kingdom of Nepal to the Federal Democratic Republic of Nepal in 2008. However, with the stabilizing of political conditions relationship between IOM and NCGM has recovered. In 2009, the Joint Symposium on Nosocomial Infection Control was held at IOM jointly organized by IOM and NCGM, resulting in recognition of the importance of nosocomial infection control and research collaboration.

Collaboration in research on nosocomial infection control and AMR

The following researches were carried out. Outlines are described briefly. For detailed information please refer to the publications indicated in each item.

1. Fact-finding survey of nosocomial infection control in hospitals in Kathmandu, Nepal- a basis for improvement:

This survey was carried out as a baseline study aiming to contribute to the improvement of nosocomial infection control at TUTH/IOM and consequently hospitals in Kathmandu City during 2011-2013. The primary purpose of this study was to evaluate nosocomial infection control conditions and to prepare the basic information needed to provide technical guidance. The actual condition of nosocomial infection control was examined at 17 leading hospitals in Kathmandu City with the method of questionnaire, site visits and key informant interviews. The obtained results were compared with the results of the past survey in 2003.[8]

The results showed gradual improvement in nosocomial infection control situation but further improvement is needed, particularly in practice in basic technics. Increase of antibiotics resistant bacteria was also suggested. Both the frequency of the meetings of nosocomial infection control committee and the frequency of ICT rounds by infection control teams increased. Also, some improvement in the monitoring of causative agents and in the information provision system for clinical settings were recognized. Issues to be addressed included improving the quality of the control system and training program, providing training to a wider range of staff members, improving waste disposal system, updating manuals, etc[9]. Among the targeted hospitals in this survey, TUTH showed comparatively good results. Bacteriological testing, guided by the JICA project, was functioning well and contributing to the surveillance of nosocomial infections. (Fig. 1,2,3,4)

These findings clearly reflected that there was a need of further improvement of nosocomial infection control with constant efforts focusing on training of medical staff to enhance basic fundamental techniques, enhancement of awareness, strengthening control system and preparation of necessary equipment.

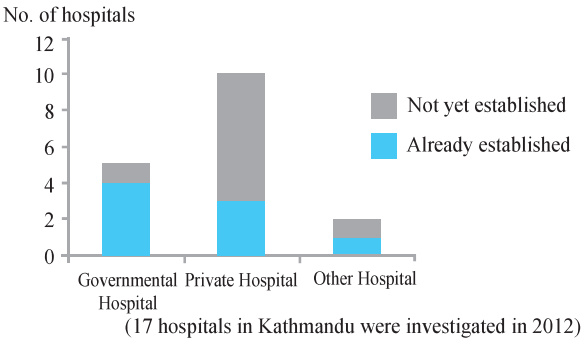

Figure 1: Hospitals with infection control committee.

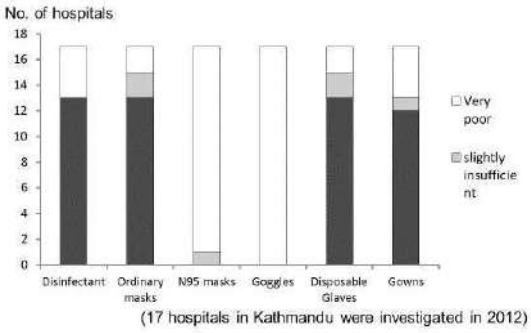

Figure 2: Hospitals satisfying standard requirement of personal protective equipment (PPE) and disinfectants.

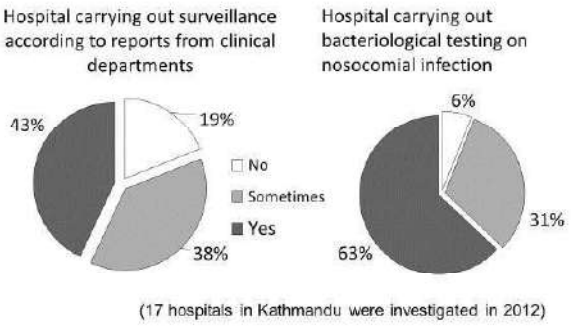

Figure 3: Surveillance situation

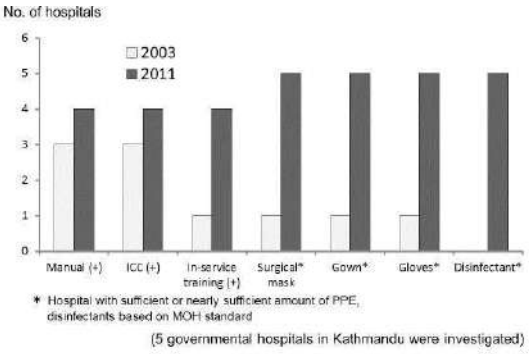

Figure 4 : Comparison of infection control situation between 2003 and 2011

2. Study on nosocomial bacterial pattern in Tribhuvan University Teaching Hospital:

This study was conducted with the aim to determine the bacteria causing nosocomial infections and their antibiotics resistant pattern. Total of 310 clinical specimens obtained from nosocomial infection cases were examined bacteriologically. Out of the 310 specimens (urine, sputum, pus, endotracheal secretion, blood) 333 bacteria were isolated. The most common isolates were *E. coli* followed by Acinetobacter species, *Klebsiella pneumoniae* and *Staphylococcus aureus*. The isolated bacteria showed high resistance to antibiotics. These findings suggested the necessity of constant monitoring of susceptibility of specific pathogens to commonly used anti-microbial agents along with preventive measures from dissemination of resistant strains.[10] (Table 1)

Table 1: Methicillin resistant *Staphylococcus aureus*

Specimens	Number of isolates	MRSA (%)
Urine	11	54.5
Sputum	15	66.7
Pus	15	66.7

41 clinical isolates were examined at TUTH

3. Study on AMR in Nepal

Emergence of multidrug-resistant pathogens has become one of the most serious problems in medical settings worldwide. There are serious concerns about dissemination of multi-drug-resistant nosocomial pathogens in Nepal. Firstly, we conducted studies on nosocomial respiratory infections and it suggested high frequency of multi-drug resistant bacteria.[11,12]

(Figure 5,6,7)

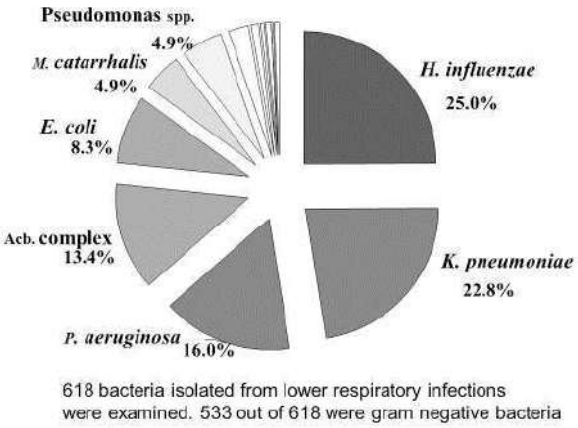

Figure 5: Distribution of gram-negative bacterial isolates (n=533)

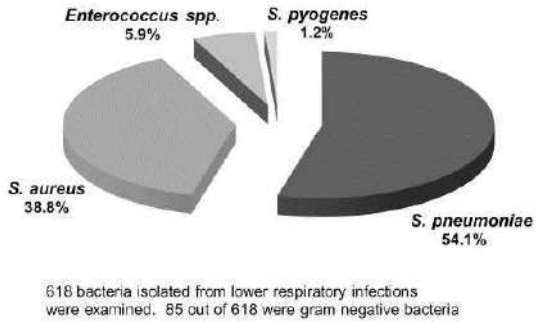

Figure 6: Distribution of gram positive bacterial isolates (n=85)

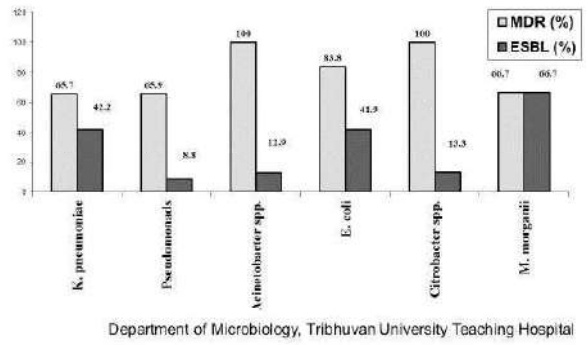

Figure 7: Multi drug resistance (MDR) vs. Extended Spectrum Beta Lactamase (ESBL) producing bacteria.

Then we conducted a study on drug resistant pathogens isolated from inpatients in TUTH. During the period April 2012- November 2014, a total of 308 gram-negative bacteria were isolated from nocomomial infection cases including *Acinetobactor baumanii, Escherichia coli*, *Klebsiella pneumoniae*, *Pseudomonas aeruginosa, Providencia rettgeri*, *Serratia marescens* and *Stenotrophomonas maltophilila*. These isolates and some other isolates were analyzed bacteriologically and genetically, and the following precious findings were obtained. These findings were reported in international journals along with at assembly of medical societies.

1) The new variant of New Delhi methalo-β-lactamase producers were identified from *Escherichia coli* and named NDM-8 and NDM-12 respectively (the first case in the world).[13,14]

2) "AAC (6')-Iak" gene in *Strenotrophomonas martophilia* was identified (the first case in Nepal).[15]

3) *Providencia rettgeri* producing NDM-1 Metallo-β-Lactamase and ArmA 16S rRNA Methylase was detected (the second case in the world).[16]

4) The new variant of New Delhi methalo-β-lactamase producers were identified from *Escherichia coli* in 2015 and named NDM-13.[17]

5) Multiple drug resistant bacteria with strong resistance to Carbapenem and Amynoglycoside were isolated. [18,19]

6) AAC (6')-Ial gene was identified for the first time in *Serratia marcescens*.[20]

Particularly it is outstanding that 3 new strains of New Delhi metalo-βlactamase producer (NDM) were discovered among the nosocomial infection cases and named NDM-8, 12, and 13.[13,14,17]

These findings suggested a significant increase in drug resistance of gram negative bacilli, which are facilitating nosocomial infections, in medical settings in Nepal. (Table 2)

Table 2: Discovery of NDM variants in the world

NDM variants	Organism and country	Reference
NDM-1	*E. coli and K. pnewnoniae* (Sweden)	Yong D. et. al., 2009
NDM-2	*Acinetobactor baumanii* (Egypt)	Kaase M. et. al., 2011
NDM-3	*E. coli* (Australia)	Rogers B.A. et. al., 2013
NDM-4	*E. coli* (India)	Nordmann P. et. al., 2012
NDM-5	*E. coli* (United Kingdom)	Hornsey M. et. al., 2011
NDM-6	*E. coli* (New Zealand)	Williamson D.A. et. al., 2012
NDM-7	*E. coli* (Canada)	Accession no. JX262694
NDM-8*	***E. coli* (Nepal)**	**Tada T. et. al., 2013***
NDM-9	*K. Pnewnoniae* (China)	Accession no. KC999080
NDM-10	*K. Pnewnoniae* (India)	Accession no. KF361506
NDM-11	Assigned (not known)	www.lahey.org/ studies
NDM-12*	***E. coli* (Nepal)**	**Tada T. et. al., 2014***
NDM-13*	***E. coli* (Nepal)**	**Shrestha B., Tada T. et. al., 2015***

4. Study on Medical Personnel regarding Nosocomial Infection Control (KAP survey):

This study was carried out with the aim to assess the level of awareness and actual practice of "hand-washing",

which is a basic prevention method of nosocomial infection control among medical personnel, and then use the obtained results for improvement. Total of 163 medical personnel (doctors, nurses and laboratory technicians) at Tribhuvan University Teaching Hospital (TUTH) were subjects of this study. A questionnaire, direct observation at important departments, and discussions were used. The following results were obtained

Table 3: Knowledge on hand hygiene among hospital staff: Answer to the question "What is the purpose of hand Washing?"

Respondents (Professions)	To prevent infection from Pt. to pt. (%)	To be clean (%)	For self-protection (%)	Both to prevent infection & self-protection (%)
Doctors=27	7 (25.2)	0	0	20 (74.1)
Nurse=86	54 (62.8)	1 (1.2)	14 (16.3)	17 (19.7)
Ward attendants=32	8 (25.0)	21 (65.6)	2 (6.3)	1 (8.1)
Laboratory technicians =18	6 (33.3)	2 (11.1)	1 (5.6)	9 (50)
Total=163	75 (46.0)	24 (14.7)	17 (10.4)	47 (28.9)

- *Knowledge*: 74.1% of doctors had an accurate knowledge of hand-washing (significance, timing, methods and effects), while only 19.7% of nurses and 50.0% of laboratory technicians had such knowledge.
- *Attitude*: 83.3% of laboratory technicians, 59.3% of nurses and 29.6% of doctors considered that they had an accurate knowledge. Regarding motive of hand-washing, fear for infections during medical practices accounted for a relatively high proportion (55.5% in doctors). Reasons given for not practicing hand-washing as instructed were: “I was busy” (46.0%), “I thought it wasn’t necessary because I wore gloves” (33.1%), “Something urgent came up” (11.7%). 38.7% answered that hand-washing is important. Poor levels of hand-washing practice among newly hired personnel and the importance of education for newly hired staff members were indicated.
- *Practice*: The following results were obtained regarding the degree of hand-washing in actual practice: “Prior to contact with patients” (55.8%), “After contact with patients” (97.5%), and “At the end of work" (96.1%). Practice levels were higher in nurses than in doctors. Drying and wiping methods were: hand dryer (52.7%), shared-use towels (22.7%), personal towel or handkerchief (12.3%), and natural drying (3.7%).

The study indicated that doctors at TUTH have a relatively good knowledge regarding hand-washing, but do not follow it in actual practice. A large number of nurses and laboratory technicians lack knowledge, and have a low degree of hand-washing in actual practice prior to contact with patients. It is important to provide improved training for medical staff regarding nosocomial infection control and prevention, which are mainly based on standard precautions. [21] (Table 3)

Training for newly recruited nurses in nosocomial infection control

Following the proposal of the nursing department of TUTH/IOM a training program for newly recruited nurses was improved and intensified training course on nosocomial infection control for newly recruited nurse was conducted in 2015. In advance of organizing the training course, NCGM provided training equipment such as a computer and a projector.

Joint Conferences

The Joint Conferences on Infectious Diseases with Growing Concern in Recent Years in Nepal were organized in January 2013 and December 2014 in collaboration between IOM and NCGM. At these conferences collaborative researches and activities including nosocomial infection control and AMR were presented followed by active discussion aiming for improvement.

Discussion

The results of the fact-finding study revealed the actual situation of nosocomial infection control and existing

problems in Nepal. The awareness on nosocomial infection control among medical staff in Kathmandu City, Nepal is increasing in recent years and the major hospitals are making efforts to improve the nosocomial infection control, however, the situation is still poor, requiring more efforts.

As the results of our studies, in medical settings in Nepal, a significant growth in drug resistance of gram negative bacilli was clearly observed. Particularly it is noteworthy that multiple drug resistant bacteria with strong resistance to Carbapenem and Amynoglycoside were isolated and new strains of New Delhi metalobeta lactamase producing bacteria were identified. Besides, another studies revealed widespread of ESBL-producing *E. coli* [22] and Rotavirus in hospitals.[23] These results revealed the spread of multi-drug resistant bacteria in medical settings in Nepal. Measures must be urgently taken to address this situation. To implement measures effectively, active intervention not only by medical facilities but also by governmental agencies, furthermore inter-sectoral collaboration, is needed.[24]

The spread of drug resistant bacteria in medical settings is one of the emerging health priority issues and suspected to be one of the leading causes of nosocomial infections.[25,26] As the cause of the increasing resistance, the following factors are suspected: abuse of antibiotics, inadequate information on bacterial resistance to antibiotics, inappropriate feedback of the information on bacterial resistance to clinical practice, inappropriate stewardship of antibiotics, increasing population movement across the border, antibiotics abuse in domestic animals, lack of inter-sectoral collaboration among relevant institutions, poor health knowledge of local residents, etc.

Hand washing is the most fundamental technic for nosocomial infection control. The results of the KAP survey indicated that the degree of hand washing prior to patient contact was low. Doctors at TUTH have a relatively good knowledge regarding hand washing, but do not follow it in actual practice. The greatest motivation for hand washing was fear of contracting diseases, whilst lack of hand washing products such as soap, water as well as forgetfulness were major constraints to hand washing. It is recommended that hospital should provide education for the staff on the importance of hand washing and prepare facilities for hand washing along with soap and disinfectants.

During the SARS outbreak in 2013 many Asian countries were affected and nosocomial infections frequently occurred, causing a lot of casualties. It is true that this outbreak demonstrated the importance of nososomial infection control and promoted the awareness on it.[27,28] Nepal fortunately did not experience a large outbreak of nosocomial infection as did in many Asian countries. In Nepal in recent years there is a growing concern to improve nosocomial infection control but awareness on nosocomial infection control is still low and opportunities to take technical guidance is limited.

In view of these circumstances, emphasis must be placed on observance of basic techniques (standard precautions) such as hand washing and the wearing of masks. The enlightenment activities, such as distribution of manuals and teaching materials and the organizing of training courses for the medical staff, are very useful and effective for the improvement of nosocomial infection control. Training course for newly recruited nurses should be continued and expanded across the country. Moreover, detailed status of nosocomial infection and causative agents should be strictly monitored, and antibiotics must be correctly used.[29,30]

One of the authors had conducted technical cooperation and researches in nosocomial infection control in Vietnam. The Ministry of Health in Vietnam has attached high importance to nosocomial infection control since 2000 and JICA projects supported to enhance it. As a result, nosocomial infection control has been strengthened and constant efforts to upgrade the skills and knowledge of medical staff has been continued by medical staff. In addition, experiencing the SARS outbreak and its containment awareness on nosocomial infection among medical staff increased. Strengthening nosocomial infection control was useful to enhance the quality of medical care.[31,32]

Nosocomial infection control is a crucial factor to provide high-quality medical care. In addition effective nosocomial infection control will reduce hospitalization and unnecessary costs for hospitals.[33,34] The findings we have obtained would be useful evidence in starting to establish effective control systems and measures. Importance should be placed, in particular, on the training of medical staff to enhance fundamental skills and to establish a proper control system. The constant effort and preparedness will contribute to enhance the quality of medical care and make it possible to apply stringent nosocomial infection control promptly when emerging infectious diseases occur. To implement

nosocomial infection control effectively, active intervention not only by medical facilities but also by governmental organizations, furthermore inter-sectoral collaboration, is needed.

Proposal

The authors stress the following importance:

1) It is warranted to improve nosocomial infection control in hospitals.

2) At hospital levels, it is important to enhance the awareness of medical staff provide training, establish appropriate control system on nosocomial infection control along with improvement of stewardship of antibiotics.

3) Multi-drug resistant bacteria are spreading in medical settings, requiring urgent measures.

4) To address the above issues not only efforts of hospitals but also strong leadership of government is needed.

5) It is necessary to monitor nosocomial infection control situation at all levels of healthcare facilities.

6) National Level Infection Control Committee should be formed.

Conflict of interest: None declared.

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