7.0 RECOMMENDATIONS AND FUTURE DIRECTIONS

The present study portrays a high prevalence of 69.50% MDR *P. aeruginosa* strains in the Shimla region of the Himachal Pradesh. The prevalence of multidrug resistant strains in a hospital setting is worrisome as there are very high chances of the spread of such strains in the hospitals as well as to the communities which could result in outbreaks. Although this is one time study carried out on isolates obtained during a period of two years, the constant surveillance and monitoring of the strains would be more meaningful that would help the clinicians to manage *P. aeruginosa* infections therapeutically as well as through suitable control strategies. Ours is possibly the first report regarding the prevalence of MBL’s and integrons in MDR *P. aeruginosa* strains in the state of Himachal Pradesh. Carbapenems are considered as the final course of has been observed in the state of Himachal Pradesh which will lead to the difficulty in treating the infections due to these organisms. The majority of the strains were susceptible to amikacin, cefepime, doripenem, levofloxacin, aztreonam, colistin, polymixin B and piperacillin/tazobactam. These observations suggest that these antibiotics can be useful to treat *P. aeruginosa* infections in this part. India is among the countries which have high rates of antibiotic consumption in both hospital and community settings. Therefore, drug resistance is a serious and difficult-to-manage public health hazard especially when it is established. Antibiotics are freely sold and for cost saving many patients are prematurely discharged from hospitals to complete their treatment at their residence. These practices would provide an undesired overpass between hospital and community for the dispersal of genes coding for multiple resistance to antibiotics. Previous studies indicate that resistance can arise within four to five years of usage (O’Brien, 2002 and Cobrella et al, 2000). In order to battle against MDR, research must also be carried out into new antimicrobials. Unless a new alternative is not found to antibiotic used currently and in the past, it is likely that resistance will arise to any new antibiotic that is introduced. Use of antibiotics must be minimised and regulated on a global scale. The emergence of resistance may also be delayed through combination therapy. As in our study, piperacillin alone was less effective than piperacillin/tazobactam combination. MBL production is a major clinical and public health problem as it has been increasingly reported and proves a
challenge to antimicrobial therapy. Other alternative therapy such as use of medicinal plant extracts can be tried to treat *P. aeruginosa* infections. In our laboratory, the antimicrobial activity of certain plant extracts such as leaf extracts of *Azadirachta indica* (Neem), *Trigonella foenum graecum* (Methi) (Batta et al, 2013) and ethanolic extracts of leaves of *Ocimum sanctum* (Tulsi) and *Murraya koenzi* (curry leaves) and *Camellia sinensis* (green tea) (Katoch et al, 2013) have been shown to be inhibitory to the *P. aeruginosa* isolates in vitro. Also the ethanolic extracts of cryptogams (*Adiantum raddianum, Polytrichum commune, Dryopteris filix mass* and *Marsilea minuta*) have also been shown to be inhibitory to this organism (Deepshikha et al, 2013).

Further, rapid detection of MBL producing Gram-negative bacilli is necessary in order to prevent carbapenemase resistant strains and to avert their spread. Continuous surveillance for MBL production is needed in both government aided and privately running hospitals. The molecular characterization can further be extended to MBL resistant genes other than VIM-2 and IMP-1. The full amplicons of these genes can give a better clue for phylogenetic relationship. Multilocus sequence typing (MLST) and pulse field gel electrophoresis (PFGE) could be the useful methods for studying the epidemiology of MBL-producing isolates on a global level as these methods could reveal the genetic relationship among the MBL producing isolates. A comprehensive MLST and PFGE database of MBL-producing isolates could be constructed from future studies. Because of limited number of MBLs in this study, it is not clear whether the favourable response was due to the prescribed course of medical treatment that included carbapenems. However, the majority of low MIC values of carbapenems might have been responsible for such results. Further clinical studies are needed to reveal the therapeutic role of carbapenems in MBL producing bacteria. These studies can and must be further extended to determine the multidrug resistance and MBL production in other bacteria such as *K. pneumoniae, A. baumannii, E. coli, S. marcens, S. aureus* etc which are among the leading organisms reported worldwide for the presence of MBLs and integrons.