

6. Conclusion

The prevalence of ESBLs and increasing number of resistance mechanism in this geographical part of the world has been proved that irrational use of expanded spectrum cephalosporins possibly act as a contributor for antibiotic resistance. The frequencies of infections caused by gram negative pathogens are increasing at an alarming rate and pose to be a serious clinical threat. There are various mechanisms which are involved in genetic adaptation to antibiotics which can be considered as genotypic marker to minimize expansion of resistance. In the present study, widespread dissemination of multiple ESBLs possibly depend on the combination of diverse aspect including efficient capture and transfer of *bla*_{ESBLs} by mobile genetic elements, high stability, and selective pressure generated by huge use of expanded spectrum cephalosporins in clinical setting. Also, it has been found that expanded spectrum cephalosporins can increase the production of β -lactamases among gram negative rods and is a key progressions for broaden of resistance in this study area.

In the current scenario, presence of different ESBL producing phenotypes, resistant to multiple group of cephalosporins, their increasing number of enzymes and resistance mechanisms contributing to a superior analysis of definite plasmids; their genetic surroundings may be proposed as an efficient tool to initiate intervention strategies for preventing or slow down their spread in the hospital and community environment. Dissemination of resistance determinants via conjugative transfer of plasmids is of chief concern as the therapeutic alternatives are strictly restricted due to an increasing risk of their selection within susceptible host leading into treatment failure.

The present investigation has the following highlights and comments;

- The prevalence rate of ESBL producers among hospital and community isolates was 54.29%, which is very high and it needs the urgent measures to slow down the spread of these ESBLs.

- About 13% of the ESBL producers showed MIC towards oxyimino-cephalosporins below the break point level which is indication of the false susceptibility and is quite alarming as it may lead in to the treatment failure, thus routine screening of ESBLs is recommended in diagnostic microbiology laboratory in this part of the world.
- To the best of our knowledge presence of SHV-148 in clinical isolates was the second report from the world and presence of VEB-1, PER-1, GES-5, OXA-10, OXA-2 were the first report from this geographical part of the country. Thus it underscores the necessity of molecular epidemiological investigation in this region.
- There were significant number of isolates (n=126) harbouring multiple β -lactamase genes which is quite alarming in terms of their genetic trafficking in the hospital setting and management of hospital infection.
- Most of the isolates were harbouring integron which played an important role in the capture and persistence of ESBL genes which are broadly disseminated among diverse host range. Presence of diverse genetic context of ESBL types and plasmid Inc groups in a single centre study is unique and reflects diverse origin, acquisition and mobilization of the *bla*_{ESBL} in this tertiary referral hospital.
- Presence of diverse genetic array in *E. coli* isolates carrying CTX-M-15 gene points to an evolutionary process which likely promotes the maintenance of this ESBL gene in this hospital environment and is the efficient tools for mobilization and expression of β -lactamase genes.
- In this study, the vertical transmission dynamics of the resistant genes in terms of high stability could underscore the importance of their maintenance and bacterial survivability in the environment with antibiotic pressure, and even in the condition when this pressure is withdrawn.

- Elevated transcription level of different *bla*_{ESBLs} under different expanded spectrum cephalosporins showed role of ESBL genes in host adaptation against specific antibiotic stress.
- Imipenem and tigecycline came up with good activity (89.16% and 84.44% respectively) and which could be considered as therapeutic alternatives.

As from the last one decade there is no new β -lactam antibiotics and inhibitors came in this country and nor in pipeline in near future. So, the current study emphasizes the judicious use of β -lactam antibiotics so as to formulate the suitable infection control procedures; as well as there is urgent need for exploration of newer β -lactam antibiotics and inhibitors to decrease the morbidity and mortality rate in this geographical part of the world. It also emphasizes to develop the simple and rapid diagnostic tools which identify the origin, acquisition and resistance mechanisms to avoid the treatment failure in near future. Thus, there is urgent need of monitoring of these gram negative hospitals acquired pathogens and their molecular as well as genetic investigation possibly will help in resistance surveillance as well as in formulating the proper antibiotic policy in clinical setting.