Hospital infection (HI) is a public health problem mainly because they increases morbidity and mortality of hospitalized patients, time of hospital stay and cost of treatment (Jarvis 1987). The most infection are treated on an empirical basis clinical experience has indicated the presence of numerous cases resistant to conventional chemotherapy, microbial resistance rates to commonly prescribed antibiotics have increased recently. Resistance to commonly prescribed antibiotics is an expanding global problem and has been observed in developed and developing countries (Finch R.G., 1998; Farrar E.W., 1985; Rahal K, Wang F, et al., 1997; Tennor FC., Hughes J.M, 1996).

The current era of rapid development in antimicrobial chemotherapy began in 1935, with the discovery of the sulfonamides by Domark in 1940. Chain and Florey demonstrated that penicillin, which had been observed in 1929 by Fleming, could be made into an effective chemotherapeutic substance, during the next 25 years, chemotherapeutic research largely centered around antimicrobial substances of microbial origin called antibiotics.
Despite the wide spread availability of antibiotics, infections caused by antibiotics resistant bacteria are a growing concern in hospital, the hospital environment may play a significant role in the transmission of micro organism (Al Barrak A, McLeod J., 1998).

The history of the antibiotic era shows that wide spread use of new antibiotics foster emergence of resistant clinical isolates, after possessing novel antimicrobial resistance mechanism the discovery and synthesis of antimicrobial agents are extremely valuable for human being in the treatment of infectious diseases, many infectious diseases once considered incurable because curable due to antimicrobial agents antibiotics. Such as Penicillin, Streptomycin, Erythromycin etc., however, the emergence and spread of drug resistance in bacteria, and its associates with serious infectious diseases have recently increased (Jones R.N., 2001) thus it is becoming difficult to treat infectious diseases caused by drug resistant bacteria. (Mitscher L.A., Pillai S.P., (1999). An extremely serious problems with drug resistant bacteria in the emergence and spread of multi drug resistant bacteria as implied by the terms “multi drug resistant” many antimicrobial agents are not effective against multi drug resistant and hence it is very difficult to treat infection due to such multi drug-resistant bacteria there are many genes for drug resistance in bacterial genomes and in extra chromosomal DNA, which are responsible for different mechanism of drug resistance such as drugs efflux, pumps, enzymes that inactivates drugs and alterations in targets of the drugs (Potman M., Van Veen H.W., Konings W.W., 2000). It has been shown that antibiotic therapy can select for antibiotic
resistant strain in the fecal flora (Datta N., M.C., Faiers, et al., 1971; Gruneberg R.N., J.M. Smellie et al., 1973; Harfley C.C., and M.H., Richmand 1975) and that R-Plasmid medicated antibiotic resistance can spread in a population subjected to heavy antibiotics therapy (Levy S.B., G.B. Fitz Gerald and A.B. Macone 1976) and in hospitalized patients. (O’Brien T.B., D.G., Ross et al., 1980) In the entero bacteria isolated from hospitalized patients, multi drug resistance due to transferable extra chromosomal circular DNA has been shown to be a common character (O’Brien T.B., D.G. Ross et al., 1980; Harkness J.C., F.M. Andurson and W. Datta 1975; Prikazsky V., L. Koskova et al., 1978).

Hospitals and particularly intensive care units are an important breeding ground for the development and spread of antibiotic resistant bacteria. An antibiotic resistance gene may transpose from one plasmid to another, may transfer on a plasmid from one bacterial cell to another or may remain in a bacterial cell which leaves one person and colonize another (Falkon S., 1975) they shown the dissemination of a single plasmid into multiple strains and species of Enterobacteria isolated from many patients in one hospital this is the consequence of exposing to heavy antibiotics use a high density patient population in fragment contact with health care staff and the attendant risk of cross infection (Flaherty J-P., Weinstern R.A., 1996; Gold H.S., Moellering R.C., 1996). Antibiotic resistance increases the morbidity and mortality associated with infection and contributes substantially to rising cost of care resulting from prolonged hospital stay and the need for more expensive drugs (Flaherty J-P., Weinsteni R.A., 1996; Gold H.S., Moellering R.C., 1996; Cohem.
Half of all hospitalized patients received antibiotics, are estimated that 25 to 50% of all antibiotics prescriptions are inappropriate as a result of incorrect choice in drug dose, or duration (Pestotnik, SL, Classen De., et al., 1996; Alvarezherma F., 1996; Kunin, CM., 1990;)

Overuse of antimicrobial agents and poor compliance with infection—control measures have been identified as the major reason for increasing trends in antimicrobial resistance. The mechanism of action of most antimicrobial drugs is not completely understood. However, it is convenient to present the mechanism of action under four headings.

Inhibition of cell wall synthesis. Alteration of cell membrane permeability or antibiotics of active transport across cell membranes. Inhibition of protein synthesis (i.e., inhibition of translation and transcription of genetic materials) Inhibition of nucleic acid synthesis.

CHROMOSOMAL RESISTANCE: This develops as a result of spontaneous mutation in a locus that controls susceptibility to a given antimicrobial drug. The presence of the antimicrobial drugs serves as a selecting mechanism to suppress susceptible organism and favor the growth of drug-resistant mutants. Spontaneous mutation occurs with a frequency of $10^7$ to $10^{12}$ and this is an frequent cause of the emergence of clinical drug resistance in a given patient.
EXTRA CHROMOSOMAL RESISTANCE

Bacteria often contain extra chromosomal genetic elements called "Plasmid". R-factors are a class of plasmids that carry genes for resistance to one and often several antimicrobial drugs. Plasmid genes for antimicrobial resistance often control the formation of enzymes capable of destroying the antimicrobial drugs. These plasmids determine resistance to penicillins and cephalosporin's by carrying genes for the formation of β-Lactamases.

Genetic material and plasmids can be transferred by the following mechanisms.

Transduction: - Plasmid DNA is enclosed in a bacterial virus and transferred by the virus to another bacterium of the same species.

Transformation: - Naked DNA passes from one cell of a species to another cell, these altering its genotype this can occur through laboratory manipulation.

Conjugation: - A Unilateral transfer of genetic material between bacteria of the same or different genera occurs during a mating (conjugations) process, this is mediated by a fertility (F) factor that results in the extension of sex pili from the donor (F+) cell to the recipient plasmid or other DNA is transferred through these protein tubules from the donor to the recipient cell. A series of closely linked genes, each determining resistance to one drug, may thus be transferred from a resistant to a susceptible bacterium this is the commonest method by which multi drug resistance spreads among different genera of gram-negative bacteria. Transfer of resistance plasmids also occurs among some gram-positive cocci.
**Transposition:** - A transfer of short DNA sequences (Transposons, Transposable Elements) occurs between one plasmid and another between a plasmid and a portion of the bacterial chromosome within a bacterial cell.

- An extensive knowledge of molecular mechanism underlying bacterial drug resistance, especially multi drug resistance is required to control multi drug resistant bacteria and to treat patient infected with multi-drug resistant bacteria successfully. Hence the present topic leading to the award of P.hD., programme has been proposed aiming at the following objectives.

- To isolate the different types of bacteria from hospitalized patient.

- Identification of bacteria by bio-chemical reaction.

- To determine the antibiotic sensitivity (disc – diffusion) pattern and (dilution) method

- To Isolate and purify the multi-drug resistant bacteria by using special medias.

- To isolate and characterize the extra chromosomal DNA from multi drug resistant bacteria.

- To compare extra chromosomal DNA between gram positive and gram negative organism.

- To study the nature of extra chromosomal DNA by conjugation method.

- To study the stability and characterization of extra chromosomal DNA by transformation method.