

## 1. Introduction and Literatures Review:

### 1.1. Introduction:

Cancer is considered one of the major public health problem facing our world . Researchers have found that certain infections are associated with human cancers since about 1.2 million cases per year Infections involving viruses, bacteria and schistosomes have been linked to higher risks of malignancy(Pisani *et al .*, 1997).

Although viral infections have been strongly associated with cancers(Pujol and Devesa, 2005), bacterial associations also are significant. Important mechanisms by which bacterial agents may induce carcinogenesis include chronic infection, immune evasion and immune suppression ( Kuper *et al .*,2000) .

It has been shown that several bacteria can cause chronic infections or produce toxins that disturb the cell cycle resulting in altered cell growth (Kocazeybek *et al .*, 2003). The resulting damage to DNA is similar to that caused by carcinogenic apoptosis. Processes that encourage the loss of cellular control may be tumor initiators (directly causing mutations) or promoters (facilitating mutations) (Nougayrede *et al .*, 2003 ).

Tumorigenesis is initiated when cells are freed from growth restraints, later promotion results when the immune system is evaded favoring further mutations and increased loss of cell control. Subsequent invasion occurs if the tumor breaks down surrounding tissues. The worst outcome is metastasis which results when cells break away from the tumor and seed tumors at distant sites (Lax and Thomas , 2002 ).

The immune system is an important line of defense for tumor formation of malignancies that expresses unique antigens. Certain bacterial infections may evade the immune system or stimulate immune responses that contribute to carcinogenic changes through the stimulatory

and mutagenic effects of cytokines released by inflammatory cells (Schoppmann *et al.* , 2002). These include reactive oxygen species (ROS), interleukin-8 (IL-8), cyclooxygenase-2(COX-2) and nitric oxide (NO), (Biarc *et al.* , 2004),( Mannick *et al.* ,1996). Chronic stimulation of these substances along with environmental factors such as smoking, or a susceptible host appears to contribute significantly to carcinogenesis (Sheng *et al.* , 2001).

There are many studies were concerned with the isolation and identification of microbes associated with tumor cells of colon (Bentzien *et al.* ,2001), kidney (Yang *et al.* ,2005). In Iraq, a number of studies are conducted to isolate and identify the bacteria associated with tumor cells (Akif, 2003; AL-Husseiny, 2004).

Several researchers found that certain bacteria are associated with human cancers, but their role, however, is still unclear. Parsonnet (1995) found that certain bacteria are associated with carcinogenic factors, for instance, the heavy growth of *Bacteroides* spp. rather than the normal level in colon make the bacteria secreted certain material affecting the bile salts in present of another factors, the bile salts convert to secondary bile salts with carcinogenic affecting on living tissues. Wheras, Schadberg, (2000) stated that the presence of opportunistic bacteria as *Staphylococcus aureus* cause chronic infections in optimal condition, especially in immunocompromized patients.

### **1.1.1. Aim of the study**

This study was designed to isolate and identify of bacteria associated with tumor cells and their histopathological effects on transitional cells of urinary bladder. To perform this aim, the following objectives were performed:

1. Isolation and identification of bacteria associated with tumor cells of urinary bladder in comparison with bacteria isolated from UTIs.
2. Determination the sensitive and resistant isolates toward several antibiotics using disc diffusion test, in addition to the Minimal Inhibition Concentrations (MIC<sub>s</sub>) of bacterial isolates.
3. Determination of histopathological changes of tumor cells associated with bacterial isolates in comparison with normal cells using Eosin & Heamatoxyline staining.
4. Use of Immunehistochemistry technique (using cytokeratine 7) as tumor marker to confirm the diagnosis of urinary bladder cancer.