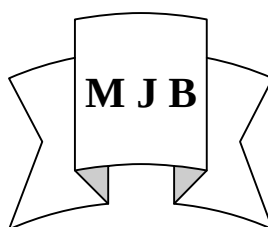


Epidemiological Study of malignant tumors of urinary bladder in Babylon City

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**Abstract:-**

this study was prepared to study malignant tumors of urinary bladder in Babylon City in term of histopathological aspect.

Eighty one case of histologically proven primary urinary bladder tumor were collected during the period from 2005-2007, the results were as follow:

1. 71/81 case were transitional cell carcinoma, 8/81 case were squamous cell carcinoma, 1/81 was adenocarcinoma and 1/81 was undifferentiated carcinoma.
2. Male three times affected more than female.
3. Age distribution of bladder carcinoma was 25-80 year.
4. Regarding transitional cell carcinoma, most of the cases were from grade II (50/71) (70.45%).
5. Muscle invasion was present in 27.1% of the cases as follow:
 - A. muscle invasion was present in 18.3% of cases of transitional cell carcinoma .
 - B. muscle invasion was present in 100% of cases of squamous cell carcinoma.

Objective: the aim of the study is to know the most common and important tumors of urinary bladder in Babylon city and to identify its histological features.

Keyword:-

Tcc: Transitional cell carcinoma

Scc: Squamous cell carcinoma

خلاصة البحث باللغة العربية :-

تم إجراء هذا البحث لغرض عمل دراسة إحصائية لأورام المثانة في محافظة بابل ومعرفة أكثر أنواعها شيوعاً . وكانت النتائج كالآتي :-

1. تم جمع 81 حالة لسرطان المثانة خلال الفترة 2005-2007 وكان عدد حالات سرطان المثانة الأطلائي الانتقالي 71 حالة وعدد حالات سرطان المثانة الأطلائي الحرشي 8 حالات وحالة واحدة لكل من سرطان المثانة الغدي وسرطان المثانة الغير متميز .
2. كانت نسبة إصابة الذكور هي ثلاثة أضعاف إصابة الإناث .
3. كان معدل العمر للإصابة بسرطان المثانة هو من 25 – 80 سنة .
4. بالنسبة لسرطان المثانة الأطلائي الانتقالي فإن أكثر الحالات كانت من المرتبة الثانية بنسبة 70,4 % .
5. كانت نسبة اختراق الورم لجدار المثانة العضلي هي 27.1 % من مجموع الحالات وهي كالآتي :-
 - أ- نسبة اختراق ورم المثانة الأطلائي الانتقالي لجدار المثانة العضلي هي 18.3 % .

ب- نسبة اختراق ورم المثانة أطلائي الحشفي لجدران المثانة العضلي هي 100% .

Introduction:-

Urothelial carcinoma are 3-4 times more common in male than female, the peak age of incidence is at 50-80 years. The most important risk factors are cigarette smoking, occupational exposure to aryl amines, chronic cyclophosphamide exposure, chronic inflammation such as chronic schistosomiasis heamatobium infection, stag horn calculus, recurrent infections, bladder extrophy (1)

The major prognostic factors depend on histological type of tumor ,degree of differentiation' of tumor (grade),depth of muscular invasion(stage),age of patient and mode of therapy.

Cellular CLASSIFICATION:

More than 90% of carcinoma bladder are transitional cell carcinoma (Tcc), about 6-8% are squamous cell carcinoma (Scc) & 2% are adeno carcinoma..(2)

A-Transitional cell carcinoma (urothelial Carcinoma):

Several grading system have been proposed for grading of Tcc. These are primarily based on cytological appearance of tumor rather than its architecture or invasiveness. The first widely used grading system in which the Tcc divided into four grades as follows (3).

Grade I: microscopically, it is composed of regular frond like papillae composed of a central fibro vascular core that is covered by a few layers of uniform transitional cells, mitosis are rare or absent.

Grade II: these characterized by more solid appearance and firmer consistency, microscopically, the papillary configuration persists, but there is more crowding and layering of cells, enlargement and hyperchromasia of nuclei, and more than an occasional mitotic figures.

Grade III: papillary areas may still be present but are irregularly distributed, the

cell masses in small groups and mitotic figures are easily found.

Grade IV: papillary areas are scanty or absent, cellular atypia and pleomorphism are so marked that transitional cell nature of the tumor may be obscure, mitotic figure are frequent & a typical .the tumor are usually widely invasive.

Other classification according to world health organization international society of urological pathology (WHO/ ISUP)(4,5) is to divide the neoplastic lesion into flat and papillary and separate evaluation of papillary neoplasm for grades (based on architecture and cytology), the types of papillary neoplasm recognized in this classification are the following:-

-papilloma

-papillary neoplasm with low malignant potential

-low grade papillary carcinoma

-high grade papillary carcinoma

It is obvious that satisfactory classification of this tumor has not yet reached, it is believed that the original grading system is easy to be applied in practice and it is used in our study.

The grading of Tcc is of great prognostic value, thus the tumor at lower end of spectrum has low incidence of recurrence and negligible incidence of in situ and invasive carcinoma (6,7)

Stromal invasion by transitional cell carcinoma proceeded by two stage, invasion of lamina propria and invasion of muscular layer, the pathological staging is better prognostic indicator than histological grade.(8)

B-Squamous cell carcinoma:

Pure squamous cell carcinoma account for up to 10% of carcinoma of bladder, but in countries endemic for schistosomiasis, this rate is much higher.

Pre-existing squamous metaplasia with long standing chronic inflammation is typically give rise to tumor.

Histologically, some are well differentiated exhibit obvious squamous differentiation with keratinization, others are poorly differentiated.

Although clinical behavior is similar to Tcc, the prognosis is worse as the patients usually presented in advanced stage, and about 95% show muscle invasion at time of diagnosis.(1)

C-Adeno carcinoma:

This is very rare & form less than 2 % of tumors, they may arise in areas of glandular metaplasia, adeno carcinoma of bladder produce abundant mucin & tumor surface may be gelatinous.

The histological features are similar to colonic carcinoma and range from well differentiated glands forming neoplasm to poorly differentiated signet ring carcinoma.(1)

D-Un differentiated carcinoma:

These are tumors in which the neoplastic cells show neither transitional nor squamous or glandular differentiation , the cells range from large polygonal pleomorphic cells, to small cells to spindle sarcomatoid cells(1).

Material & Methods:

Between 2005-2007, eighty one case with histologically proven primary bladder cancer were collected from teaching hospital in Hilla city for 3 years duration.

-The tumors are assessed cystoscopically as there is bladder mass and surgical biopsy taken by cystoscope by Trans urethral resection.

-The biopsy is formalin fixed, paraffin embedded and stained by Heamatoxilin and Eosin and studied histopathologically

-Clinical staging was done for all cases and the tumors were categorized and graded histologically .

-We use chi-square test (χ^2) to analysis our data.

Results:-

Eighty one patient with histologically proven carcinoma of urinary bladder were studied. The patients range in age from 25-80 year (mean 52.5 year) and there were 60 male and 21 female, male : female ratio was 3:1 (male is significantly affected more than female ($p<0.01$)).

The frequency of Tcc were 71 case (87.6 %), 53 of them were male and 13 were female, male : female ratio was 3:1 (male is significantly affected more than female ($p<0.01$), the mean age of Tcc was 52.5 year.

Th frequency of Scc were 8 case (9.8%), 5 of them were male and 3 of them were female, male : female ratio was 5:3 (there is no significant difference between male and female ($p>0.05$), the mean age of Scc was 57.5year.

The frequency of adeno carcinoma was 1 (1.2 %) and of undifferentiated carcinoma was 1 (1.2%).

Inconcern to Tcc, the frequency of grade I, II, III & IV were 8(11.2%),50 (70.4 %), 11 (15.4 %) and 2 (2.8 %) respectively (there is significant difference between grades of Tcc ($p<0.01$)).

In concern to Scc, the frequency of well differentiated Scc was 3(37.5%) and of moderate differentiated Scc was 5(62.5%) and of poorly differentiated Scc was zero.

Muscle invasion is present in 22 case(27.1%) (13 Tcc,8Scc and 1 adenocarcinoma).

Acomparison was made between patients with Tcc and Scc in table number 2,in this series,the mean age of patients with Tcc is 52.5 year which is less than the mean age of Scc (57.5 year),the male to female ratio in Tcc was 3:1 while for Scc was 5:3(Scc more common in female than Tcc).

Muscle invasion was present in 13 case of TCC(18:3%) at time of diagnosis while all cases of SCC were muscle invading at time of diagnosis .

Associated schistosomiasis was present in 1 case of TCC & 1 case of SCC.

Discussion:-

In the present study , the transitional cell carcinoma is the most common bladder tumor (87.6%) in Hilla city , while squamous cell carcinoma constitute only 9,8% of the cases seen over a period of 3 years duration . in countries endemic with schistosomiasis, the incidence of squamous cell carcinoma is much higher and may reach about 75% in Egypt (9) and 65% in south of Iraq (10).

- The mean age in this study was 52.5 year in Tcc and 57.5 year in Scc, the male: female ratio in Tcc 3:1 while it is 5:3 in Scc , the relatively younger age incidence and male predominance of Tcc are in agreement with other reports (9,11,12,13).

-Tumor grading show that Tcc grade **I, II, III & IV** frequency were 8 (11.2%), 50 (70.4%), 11 (15.4%) and 2 (2.8 %) respectively, while for Scc the frequency of well differentiated was 3 (37.5%) & of moderately differentiated scc were 5 (62.5%). these results may be slightly different from other studies ,this discrepancy may be attributed to individual variation of interpretation of tumors grade.(14).

-Muscle invasion is present in 13 case (18.3%) with Tcc while all cases of Scc were muscle invading at time of diagnosis this may be attributed that Scc are presented at advanced stage. this findings are in agreement with other reports((9,11,,15,16).

-Histological grading and clinical staging were done for all cases and this is important in determination of mode of treatment and to know the prognosis of tumor

-Superficial tumors were treated by transurethral resection with or without chemotherapy while for deeply invasive tumors with regional or distant metastasis, the standard treatment is radical cyctectomy with or without radiation therapy or by combined chemotherapy-radiation therapy(17,18)

-Intravesical therapy with bacillus Calmette Guerin(BCG) is often used for treatment of patients with multiple tumors or recurrent tumors or as prophylactic measures in high risk patients after TUR.(19,20).

In concern to schistosomiasis, it is found that only one case of Tcc and one case of Scc was associated with schistosomiasis, while in other studies, a close relation ship was found between schistosomiasis and bladder cancer and this was supported by many investigation (21,22) but rejected by others.

Conclusion:

Urinary bladder carcinoma is a common malignant tumor in Babylon city(it is the third malignant tumor in Babylon city)(23) , mainly in male and its require complete evaluation and early detection as quick as possible in order to identify and treat the high risk patients in order to decrease the incidence of urinary bladder tumor.

Recommendation :-

It is important to try to reduce the incidence of bladder tumor by prevention and early detection. .

Prevention is by public education

Early detection of localized early stages by different methods that have been focused on investigating tumor cells in urine and these include urine cytology , flow cytometry ABO (H) cell surface iso antigen or detection of tumor products in urine such as bladder tumor antigen test that detect the presence of basement membranes complex in urine (24,25).

Urine cytology is a specific , non invasive technique which can be useful in screening Of high risk group (26 , 27) .

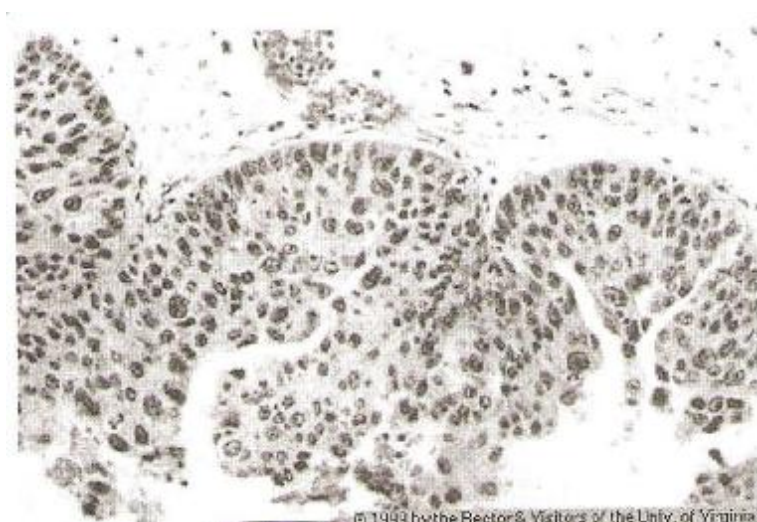
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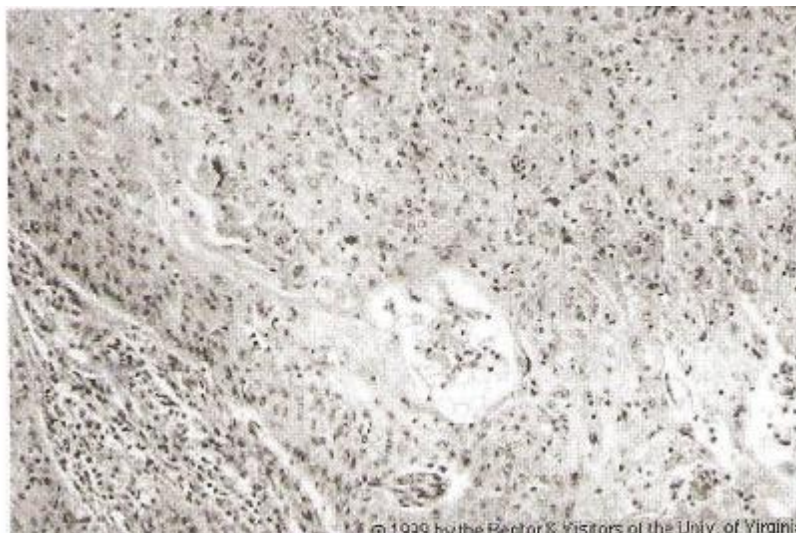
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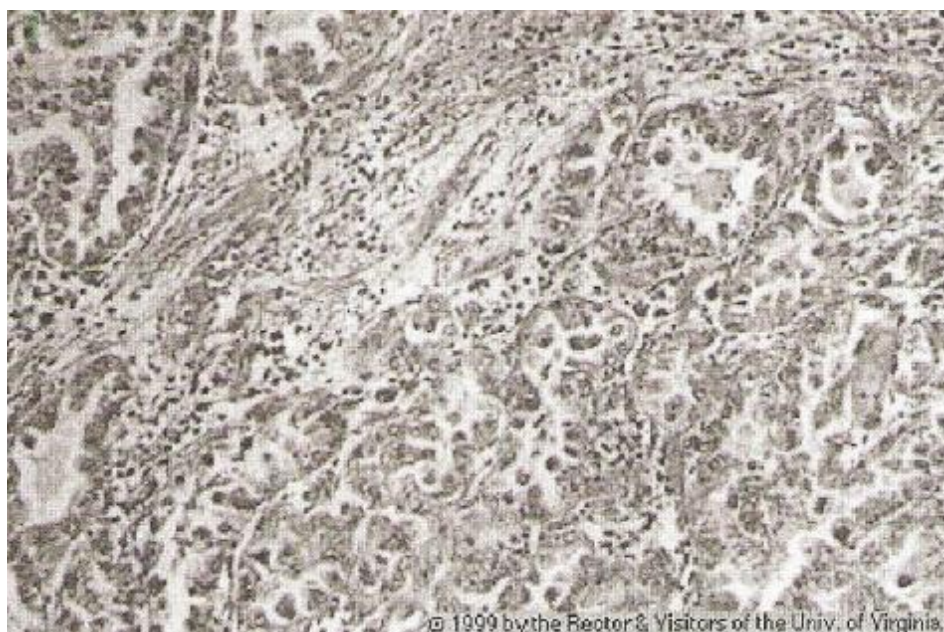
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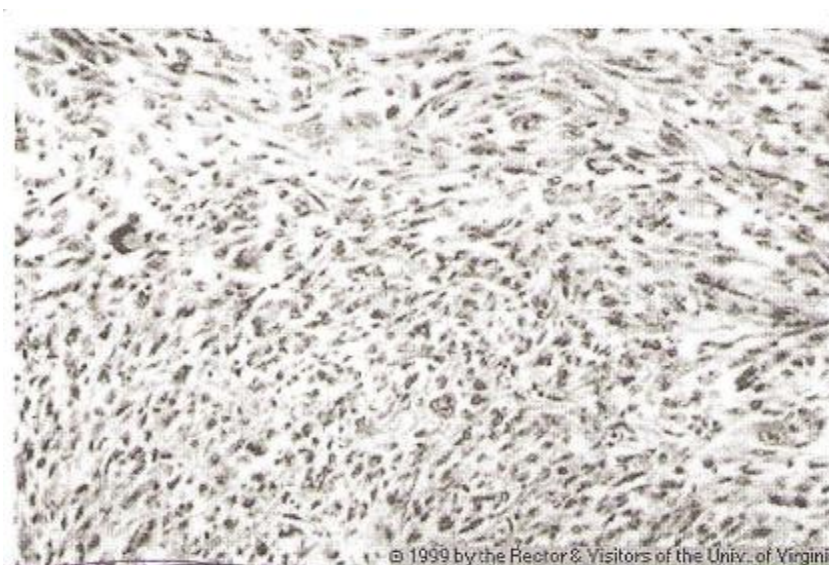
Picture (1)
Non-papillary carcinoma grade **III**.



Picture (2)
Squamous cell carcinoma with focal keratinization & necrosis.



Picture (3)
Adenocarcinoma of the bladder .



Picture (4)
Undifferentiated carcinoma .

Table No -1-

Clinico – pathological Features in 71 patients with Tcc

- No .men / women	53 / 18
- Male to Female ratio	3 : 1
- Mean age at time of diagnosis	52 .5 year
- Histological grade	
Grade I	8 (11.27%)
Grade II	50 (70.45%)
Grade III	11 (15.43%)
Grade IV	2 (2.85%)
Clinical Stage-	
Stage A (No muscle invasion)	58 (81.7%)
Stage B (with muscle invasion)	13(18.3%)

Table No - 2-

A comparison between transitional and squamous cell Carcinoma .

<u>Feature</u>	<u>Tcc</u>	<u>ScC</u>
- No. of patients	71 (87.61.)	8 (9.8%)
- Mean age	52.5year	57.5 year
- Male : Female ratio	3 : 1	5 : 3
- Tumor Stage		
Stage A (No muscle invasion)	58 (81. 7%)	0 (non)
Stage B (with muscle invasion)	13 (18. 3%)	8 (100%)
- Associated Schistosomiasis	1	1

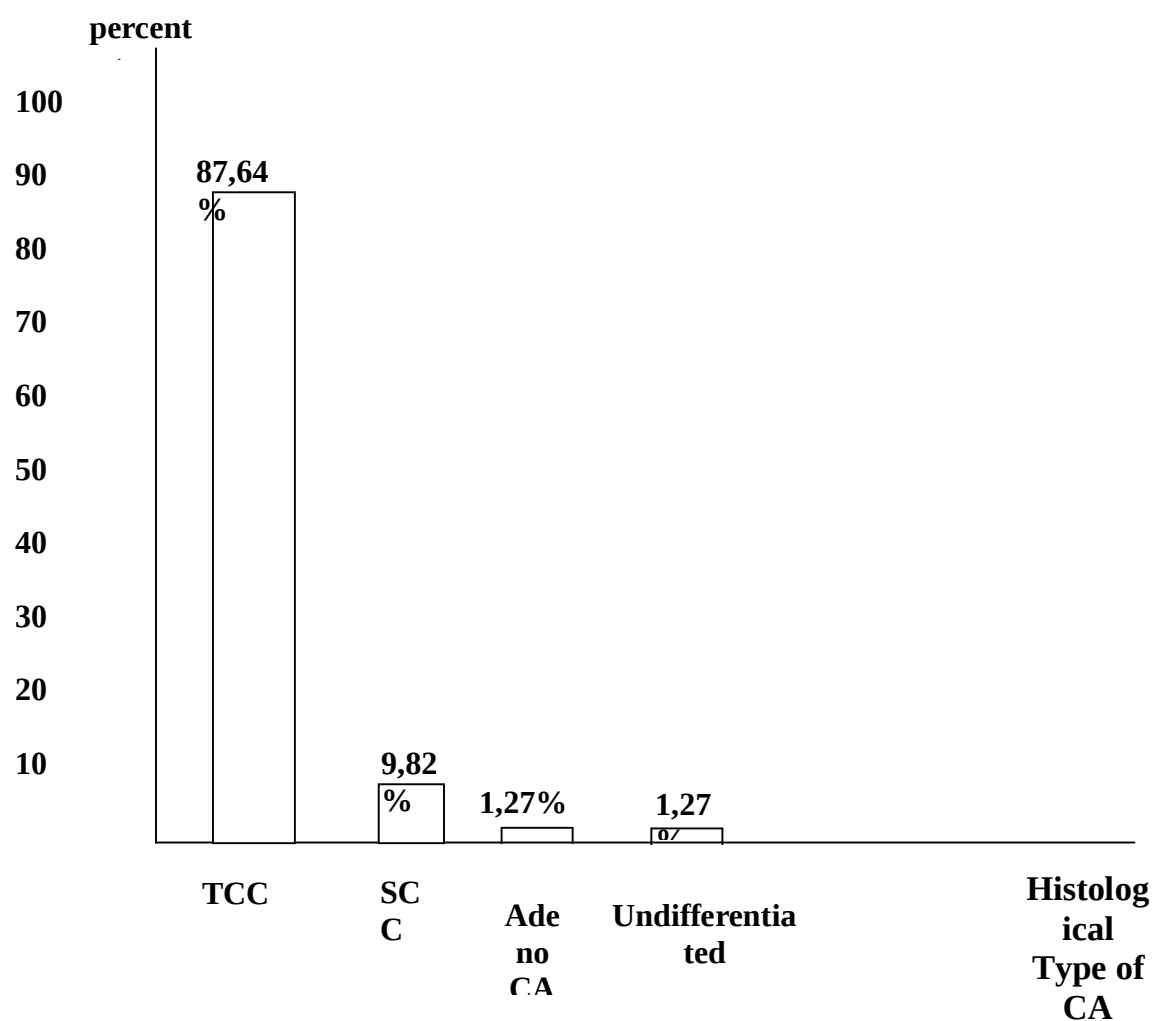


Figure No.1
Frequency of various histological type of
primary CA bladder in 81 patients

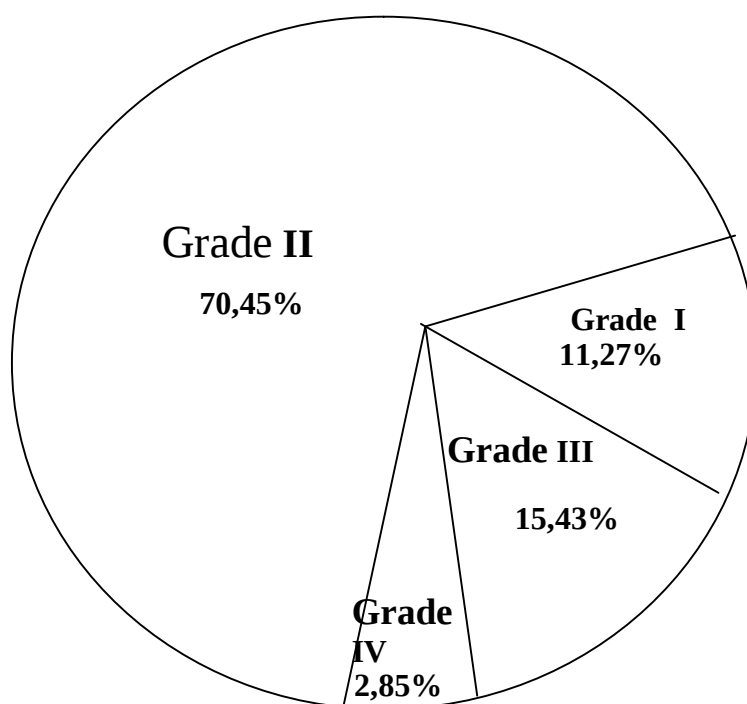


Figure No.2
Frequency of histological grades of Tcc In 71 case

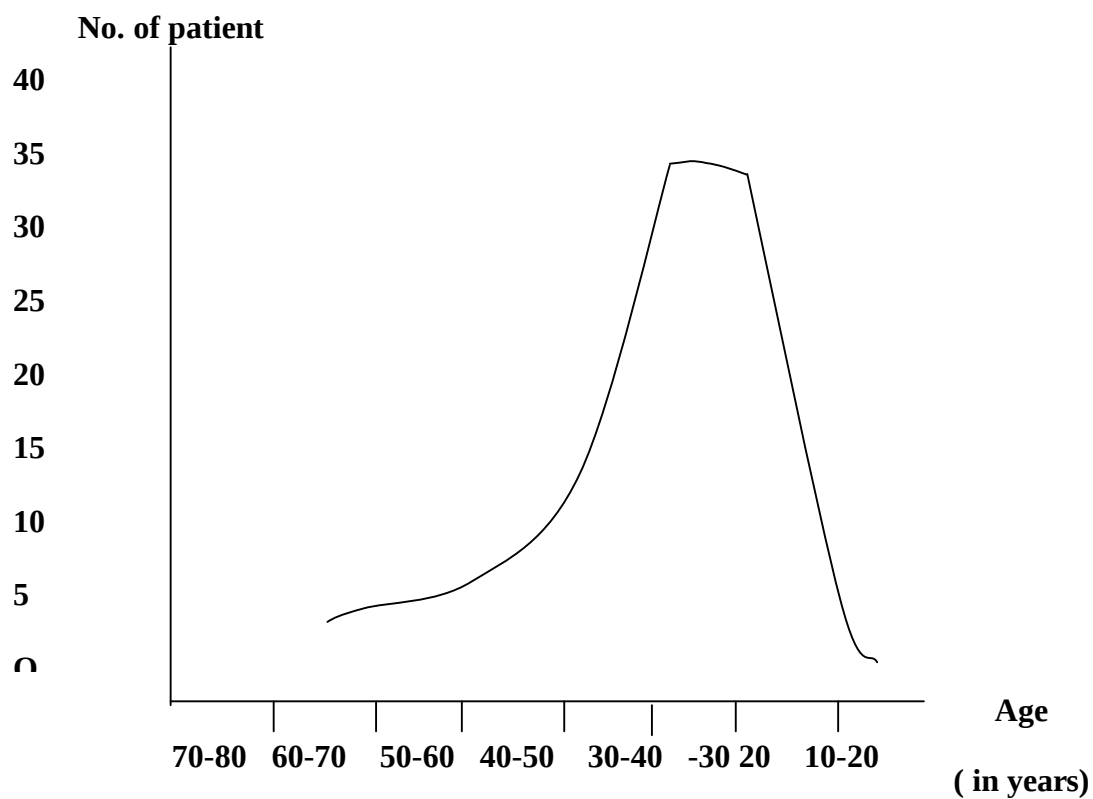


Figure No.3
Age distribution & peak age of incidence of CA
bladder in Babylon city.

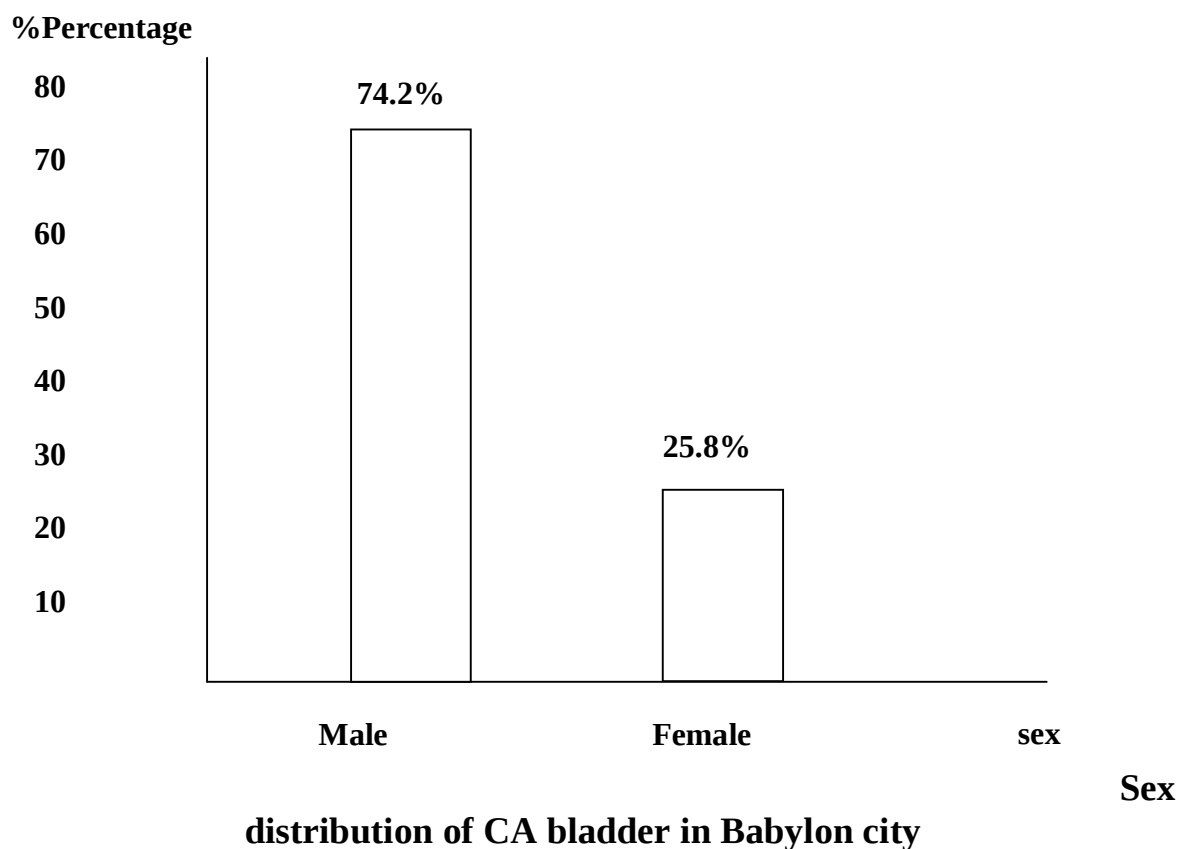


Figure No.4