

PRIMARY CARCINOMA OF THE GALL BLADDER: REVIEW AND STUDY  
OF EIGHTY CASES IN EMAM-KHOMEINI MEDICAL CENTER

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SUMMARY

In a retrospective study on the cancer of the gall bladder, done in Iran, it seems that it comprises 0.36% of all the malignant tumors. 1.75% of the patients were females and the maximum incidence was in the sixth decade of life. It was interesting to note that the age ratio between the males and females reverses with the advance of age, so at the 7th and 8th decade of life, the incidence of the disease in males was much higher than females. At the 8th decade, the number of male patients was twice as females.

The presenting symptoms in most cases were; pain, jaun-

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dice, loss of weight, and in a few cases there was a history of long lasting symptoms, referable to the biliary system. After admission and surgical opening of the abdomen, 60% of patients were considered inoperable. All the patients suffering from anaplastic carcinoma, which comprised 5% of all cases, were female and had a long lasting history of gall bladder infections. The prevalence of stone formation in gall bladder malignancies is a known fact but whether the cause of this coincidence is due to some factors, such as irritation dysplasia, or only combination of these, is not definitely known.

#### INTRODUCTION

Despite persistent curiosity on the part of surgeons, and introduction of various diagnostic procedures such as percutaneous cholangiography(1), selective angiography scintigraphy (2), ultrasonic scan, tomography of the gall bladder (3,6), and endoscopic retrograde cholangiopancreatography (ERCP) (4), malignancies of the gall bladder remain important problem in gastroenterology. This is because early diagnosis is difficult and prognosis disappointing (5).

We have reviewed the hospital records of eighty patients. In the proven cancer of the gall bladder admitted to the Emam-Khomeini Medical Center, between the years 1956 to 1975. The clinical, radiological and surgical findings were analysed and the results classified according to the sex, age, clinical symptoms, history of concomitant disorders, presence or absence of gall stones and histological findings.

#### RESULTS

Between 1956 and 1975 a total of 20387 cases of malig-

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nancies of various organ systems were diagnosed at Emam-Khomeini Medical Center. There were 80 cases of primary carcinoma of the gall bladder making up 0.36% of all the malignancies in our patients population. This malignancy ranks fifth among all gastrointestinal malignancies.

There were 29 men and 51 women in this group of patients. The average age of patients was 54 years in the female, and 56.5 in males. The sex ratio was 1.75 females for 1 male. The youngest patient was 34 and the oldest was 75 years.

The majority of patients were in their sixth decade of life demonstrates the age distribution of the patients (Figure.1). In the fourth decade, women were affected twice as often as men, and in the sixth decade three times as often as men, while in the seventh decade this ratio was equal between the two sexes, and in the eighth decade the number of men suffering from gall bladder malignancies were twice that of women. This shows that with increasing age and beyond 60 years of age, the incidence of cancer of gall bladder among men and women becomes reversed. (Figure.2 and 3).

The most frequent presenting symptom was abdominal pain which was either epigastric or located in the right upper quadrant. 34% of patients were admitted because of jaundice. (Figure.4). The average duration of symptoms was 4 months prior to hospitalization. In about one half of the patients this period was less than 4 months and in about 10% of cases this period was less than twenty days. (Figure.5). In most cases a sudden increase in the severity of abdominal pains, or a change in the type and quality of other primary symptoms had prompted patient's admission to hospital.

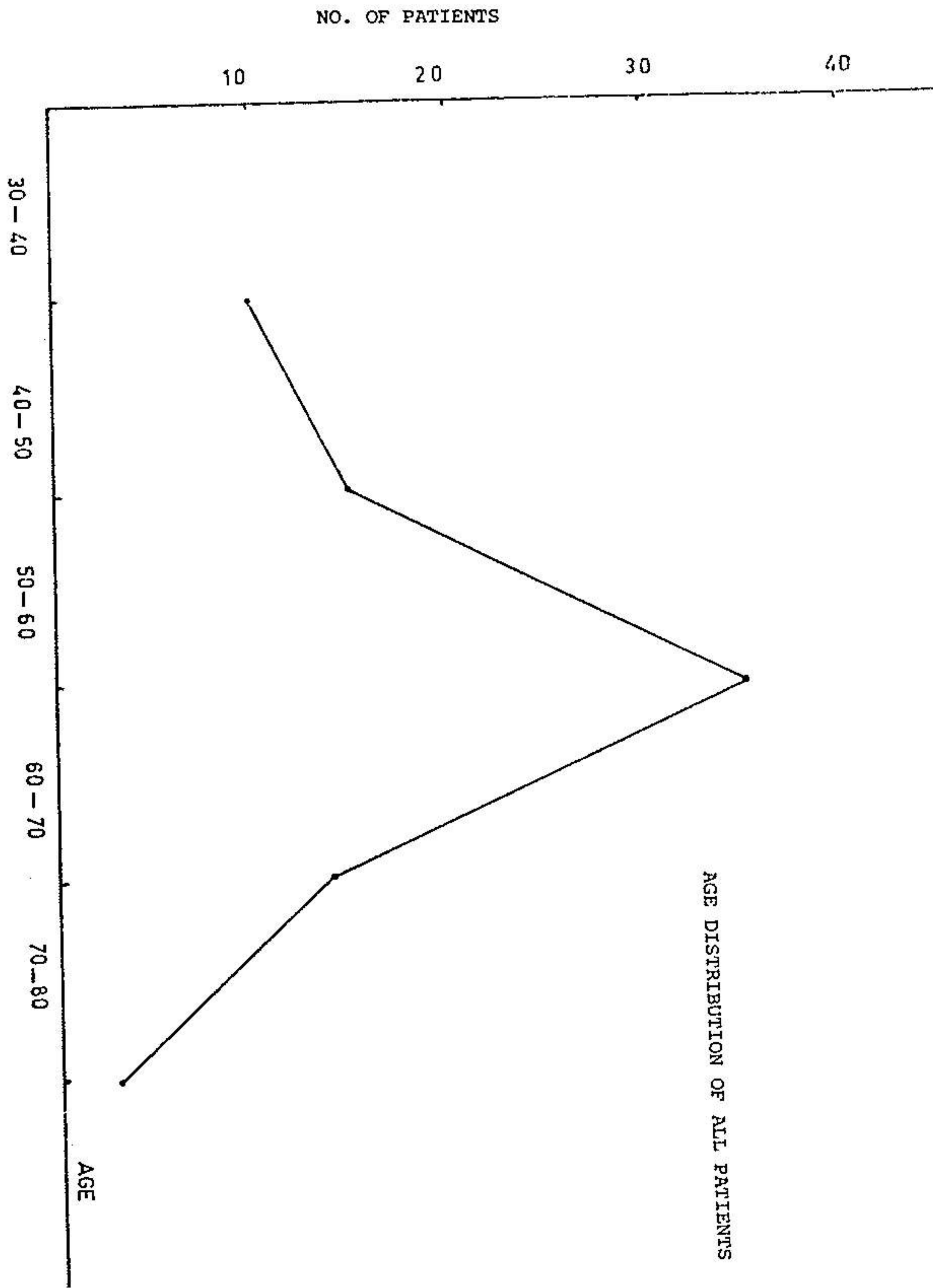


FIG 1

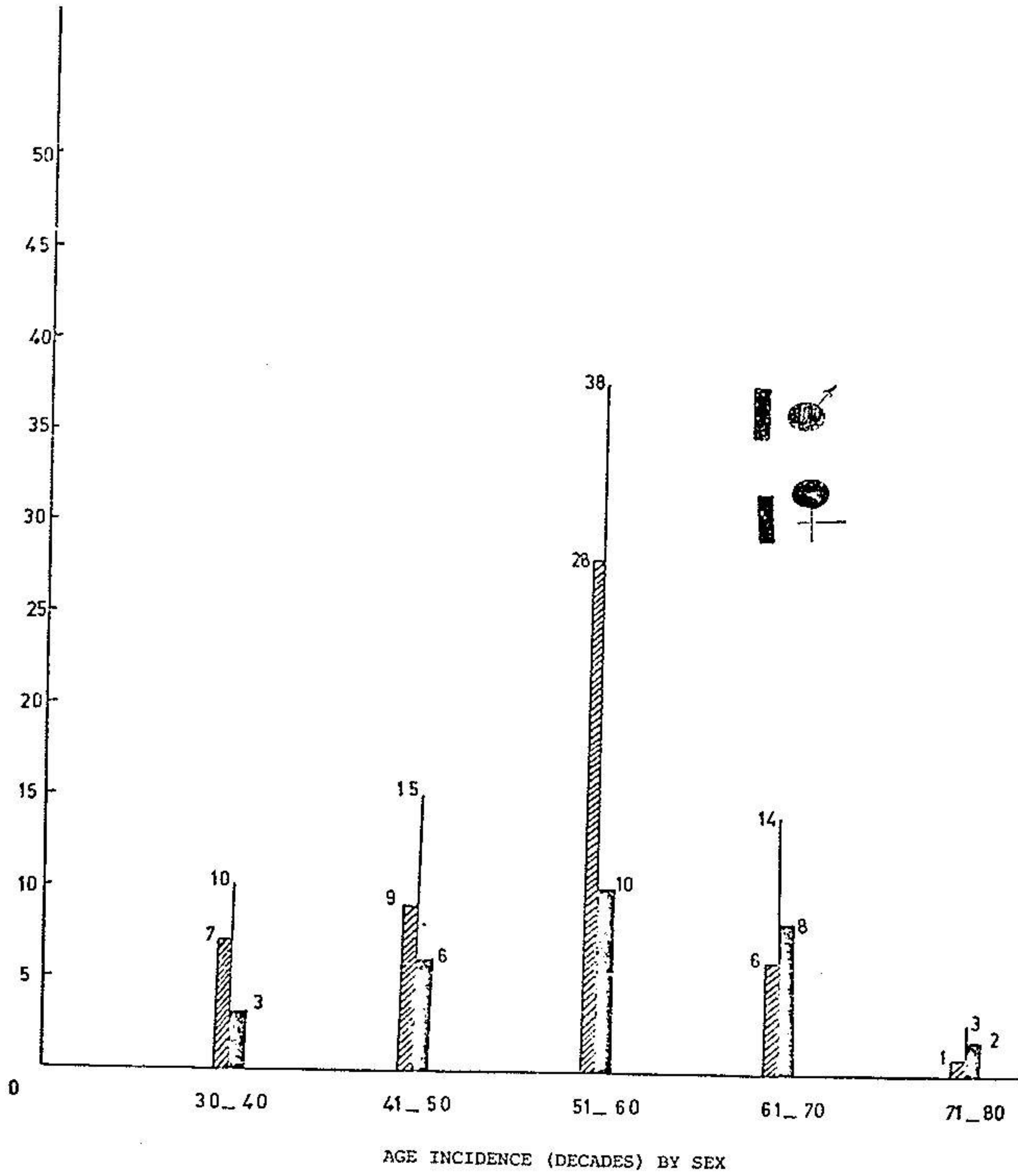
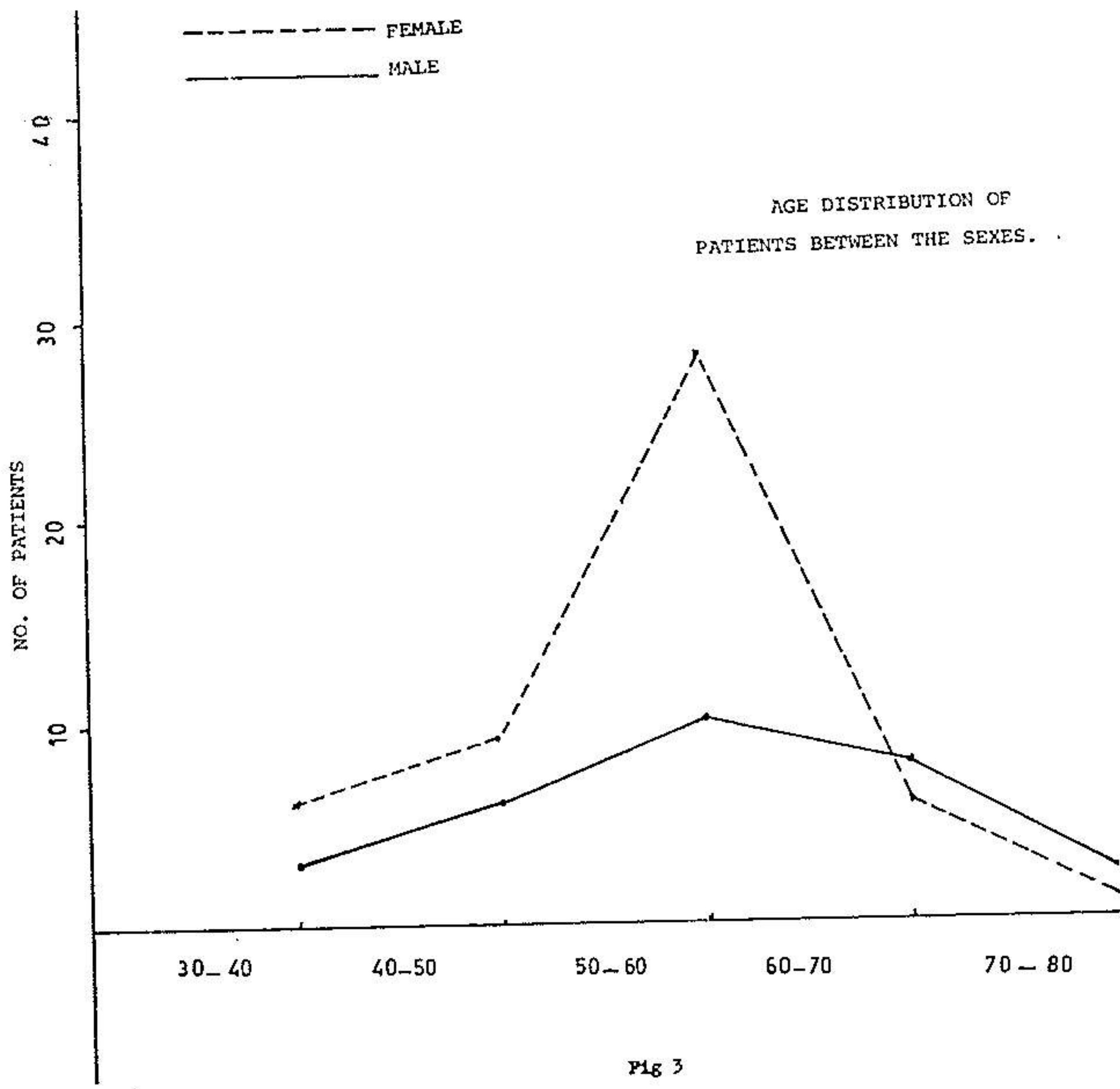
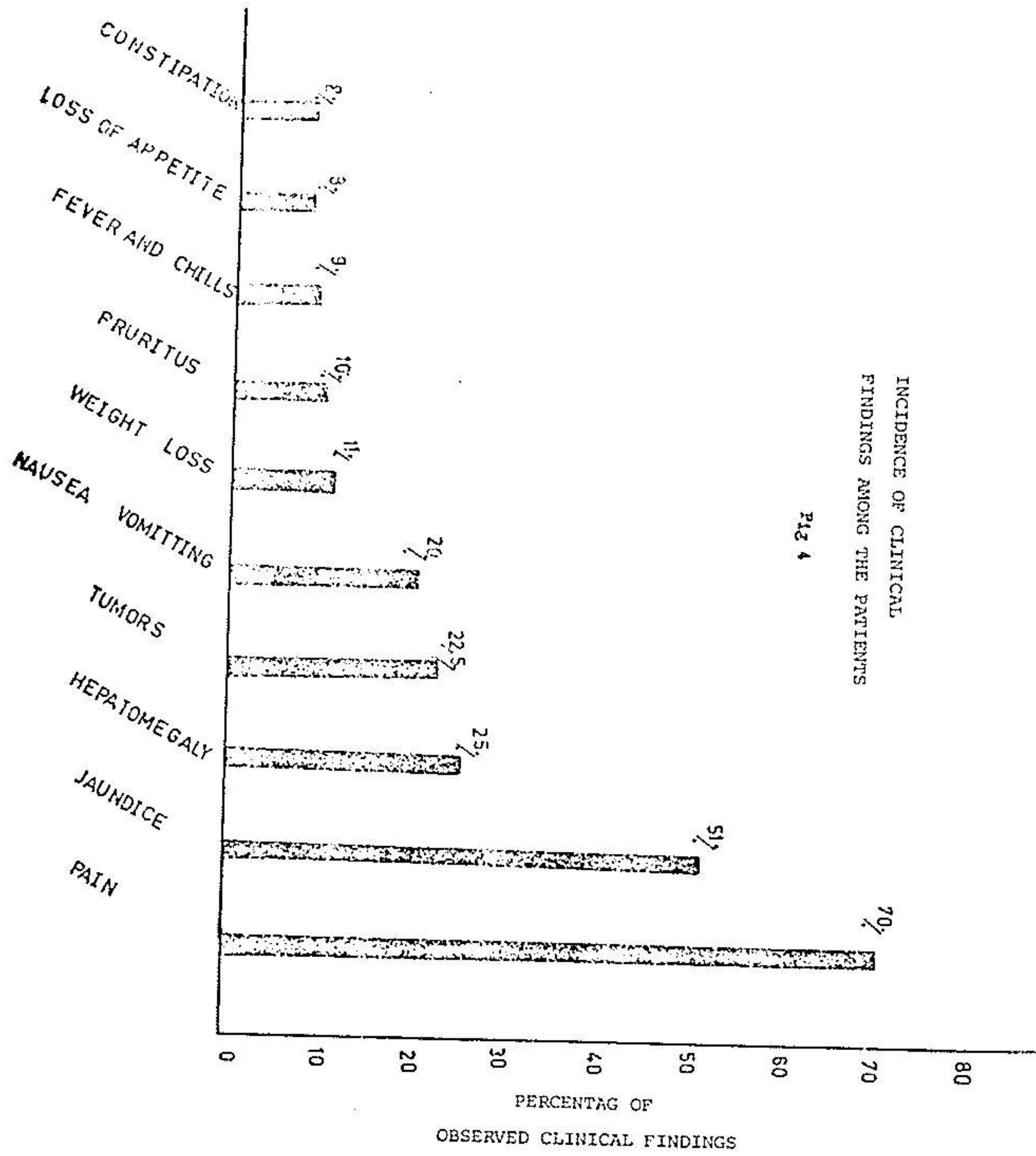
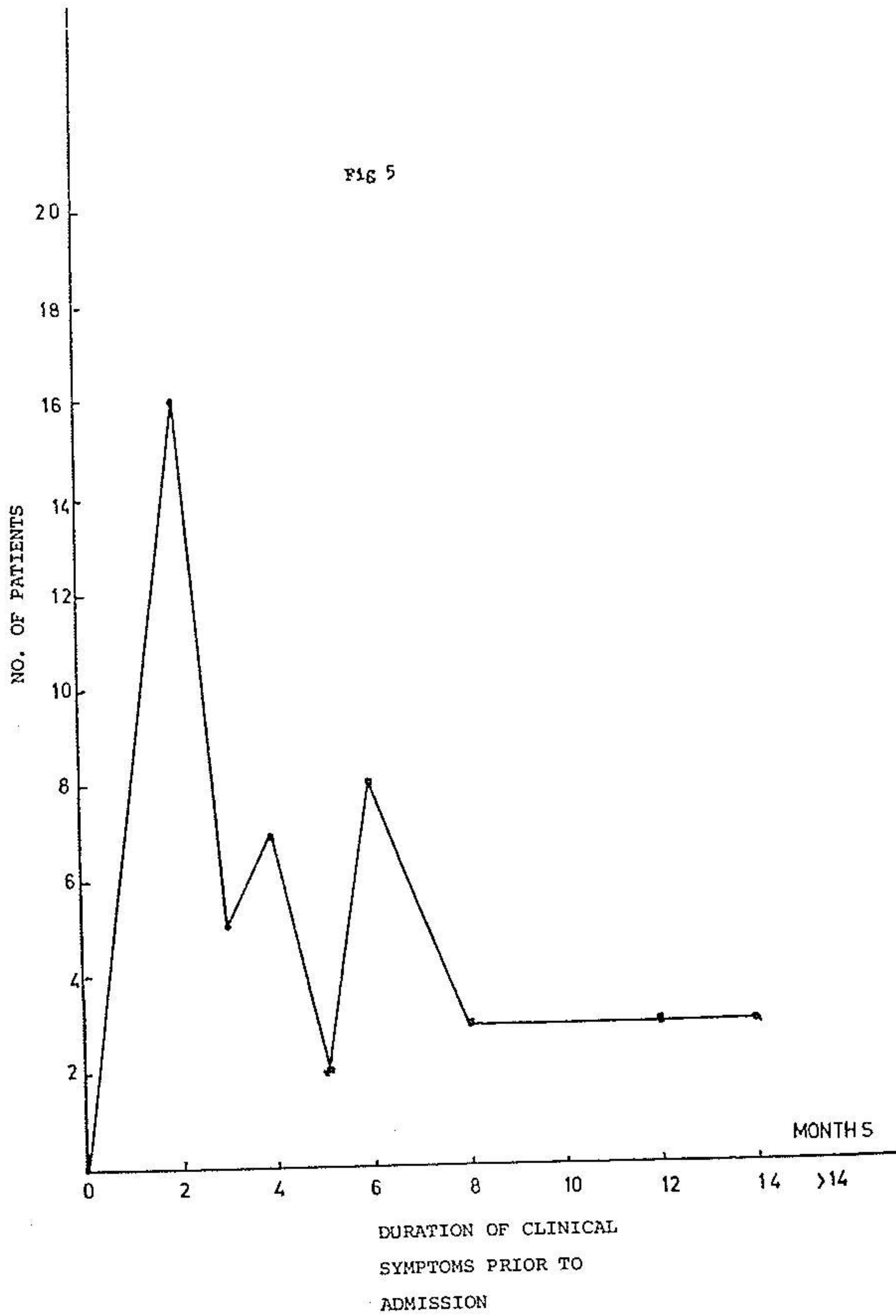


Fig 2









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On physical examination a tumor was palpable in the region of gall bladder in 22.5% of patients. Loss of weight was noted in 11% of patients. 25% of patients had splenomegaly.

During the period of hospitalization abdominal pain was present in 70% of patients and jaundice was noted in 5%. Other clinical findings such as pruritus, tenderness, over the hepatic area, constipation, diarrhea, hematemesis, melena and ascites were present in a few cases.

At past history of a serious illness, except in a 60 year old lady with empyema of the gall bladder, was usually not present. Special dietary habits, addictions and possible occupational hazards were noted in the patient population. In one case the diagnosis of ulcerative colitis was made by radiologic studies. Without the patient having specific symptoms of the disease.

The total number of the patients with gall bladder stone diagnosed on the basis of plain radiography of the abdomen, oral cholecystography, I.V. cholangiography, retrograde cholangiography or on surgical exploration of the gall bladder, was 42 cases, or an average of 52% (Table.1).

The percent age of patients with malignancy of the gall bladder who had concomitant stone was 63% in the 50 to 60 year age group, and 58% beyond the age of 60. No significant difference in the incidence of gall stones could be found between the two sexes.

Radiologic studies did not help in the diagnosis of malignancy of the gall bladder. In 83% of cholangiogram cases the gall bladder was not visualized. In one patient the pattern of "porcelain" gall bladder could be seen. Laboratory data revealed slight leukocytosis and ane-

emia. In addition, derangement of the liver function tests due to obstruction were noted in most cases. In only one case was the serum alkaline phosphatase markedly elevated without any other derangements in liver function studies.

The initial clinical diagnosis was confirmed in 16% of cases. In 60% of cases benign lesions of the gall bladder, such as cholelithiasis or cholecystitis, were suggested as preliminary diagnosis. In only 6% of patients were pancreatic tumors suggested in the differential diagnosis. Tumors of colon were next in the order of differ-

Table 1)- Number of cases in whom gallbladder stones were diagnosed by various diagnostic methods.

	No.of cases	Positive results	Percentage
Plain film of the abdomen	13	5	38.5%
Oral cholangiography	12	2	12.5%
i.v. Cholangiography.	3	-	-
E.R.C.P.	1	-	-
Laparotomy	73	35	48%
<b>Total</b>		<b>42</b>	<b>52%</b>

Table 2)- The conditions which were suggested as initial diagnosis on admission.

initial diagnosis	Number	Percentage
Gall bladder & biliary tract stones.	24	30%
Cholecystitis	22	28%
Tumor of the head of Pancreas.	5	6%
Tumor of the colon	5	6%
Empyema	3	4%
Gastric and duodenal ulcers	3	4%
Hepatic abcess	1	1.25%
Hydatid cyst	1	1.25%
Hepatic tumors	1	1.25%
Mucocele	1	1.25%
Gall bladder tumor (Correct diagnosis)	13	16%

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ential diagnoses. The definitive diagnosis was made after laparotomy in all cases. (Table.2).

Sixty percent of patients were found to be inoperable, and in 24% of cases simple cholecystectomies were performed. In a few cases radical surgical procedures were performed, i.e. cholecystectomy and choledochojejunostomy. The average survival was 2/5 months post-operatively for patients who could be followed up.

Histological examination of the specimens obtained during surgery, revealed that out of 80 cases of gall bladder malignancies, 88% were adenocarcinomas, 6.25% epidermoid carcinomas, 5% anaplastic carcinomas. There was also one case of adeno-acanthoma. The average age of the patients diagnosed as anaplastic carcinoma was 57 years and all these patients were females. Also in this group of patients, the beginning of symptoms dated an average of 7 months prior to admission. In half of this group of patients there was a long history of gall bladder disease, manifested mainly by pain.

In those patients who had epidermoid carcinoma of the gall bladder the ratio between female and male patients was 4:1, and their average age was 55 years. Symptoms were noted 2 months prior to admission by these patients. The epidermoid type of carcinoma was in 80% of cases of the anaplastic variety 50% of these cases had also gall stones. (Table.3).

The only case diagnosed as adenoacanthoma of the gall bladder was also suffering from cavernous angioma of the liver.

#### DISCUSSION

The overall incidence of gall bladder carcinoma, accor-

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ding to different sources, varies between 0.09 to 19 percent of all carcinoma. (7,8). Arminsky reported an incidence of 0.36 percent of all his autopsies (9). Other reports indicate an incidence of 1 to 1.4 percent of cancers of the gall bladder among the cholecystectomies (10-11).

After the age of 65, the percentage of cancers of gall bladder seen goes up to 10 percent. The average incidence has been reported to be between 2 to 2.3 percent of all cholecystectomies (12).

During the period of present study 6785 cholecystectomies were performed at one hospital, providing a figure of 1.17% for the 80 cases with proven malignancy of the gall bladder. Blalock has reported an incidence of 0.71 percent (13). Black and co-workers (14), have reported an incidence of 2.3 percent of all operative procedures involving the gall bladder and bile ducts among American Indians.

Malignancies of gall bladder rank fifth or sixth among the malignant tumors of the gastro-intestinal tract. (15-16). In Iran it ranks sixth after cancer of the esophagus stomach, colon, rectum and primary cancer of the liver (17) .

Some workers have reported the average age of patients with gall bladder malignancy as 63.9 years (17,18,19, 20,21,22, and 23). Some British and Swedish workers have reported a substantially higher average age (24,25,26).

It seems that we have had the lowest average age incidence for this disease in our country. This may be a reflection of the average tumor age among the general population.

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Out of eighty cases studied, ten cases were in their 4th decade of life (12%), fifteen cases in their 5th decade (12%) and thirty eight cases in the 6th decade (30.4 percent). In the 7th decade there were fourteen cases (11.2%) and in the 8th decade there were only three cases (2.4%).

#### PRESENTING SYMPTOMS

percent). In the 7th decade there were fourteen cases as pain, jaundice etc.....(Table.4).The average duration of symptoms prior to hospitalization was four months and its two extremes were ten days and three years prior to the admission. (Table.5).

In comparing the present data with those of Blalock (13), we did not notice much difference. The symptoms included abdominal pains, jaundice, nausea and vomiting and the signs were jaundice of the conjunctive and skin, hepatomegaly, right upper quadrant mass and tenderness. As was previously mentioned, the average incidence of cholelithiasis in the present patient population was 52 percent. This figure reached to 63 percent in the sixth decade of life.

The incidence of cholelithiasis accompanying the gall bladder malignancies has been reported to be between 54 to 90 percent, by various authorities(20,25,27).

On the whole, the prevalence of stone formation in gall bladder malignancies is a known fact, but whether the cause of this coincidence is due to some factors, such as irritation, dysplasia, or any combination of these, is not definitely known.(13).

Table 4) - Summary and percentage of clinical symptoms and signs in the group of 80 patients.

Clinical findings	No. of cases	Percentage
pains	56	70%
Jaundice	41	51%
hepatomegaly	20	25%
RUQ tumor	18	22%
nausea	16	20%
loss of weight	9	11%
pruritus	8	10%
tenderness of the hepatic region	7	9%
constipation	6	8%
ascites	2	3%
splenomegaly	1	1%
hematemesis-melena	1	1%
Arrest gas or feces	1	1%

1) Table 5 Duration of symptoms before hospitalization

2) Rime	1 months	2 months	3 months	4 months	5 months	6 months	8 months	One year	Total
3) No of cases	11	16	5	7	2	8	3	3	66
4) Percent	13%	16%	5	7	2	10%	4%	4%	82.



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