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CIRRHOSIS AND PRIMARY (LIVER CANCER) CARCINOMA INCIDENCE IN IRAN

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The incidence of cirrhosis and hepatoma varies greatly in different parts of the world.

Although many contributions and advances have been made on this subject during the last decades, there are still many obscurities in the knowledge of the etiology, pathogenesis, and pathology of these disorders.

The discoveries which have been made up to the present do not cover all the problems of these disorders throughout the world. To help towards a solution of these problems, cirrhosis and hepatoma in each country should be studiedd and controlled, separately, taking into consideration geographical, environmental, and living conditions in the country.

We have based our studies on the autopsy findings of the case materials of Tehran University hospitals.

Material and Methods

The autopsy materials correspond to the files of the pathology Department of the Medical Faculty of Teheran University from 1960-1968. from 4389 autopsies performed during this period, there were 653 cases of Hepatic lesions.

We studied in detail the illnesses antecedent, especially previous hepatitis or jaundice, the first clinical manifestetion in the last admittance to the hospital, and the cause of death. Then, each liver was studied grossly and microscopically. For histologic studies hematoxylin-

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eosin, trichrome, and silver stains were used. In the cases of primary hepatic carcinoma, we tried to find out if any previous cirrhosis was present

RESULTS

In 4389 autopsies during the last 9 years we found 653 cases of different types of hepatic lesions. Table No. 1 shows the frequency and different types of hepatic lesions.

Table No. 1

THE DIFFERENT TYPES OF HEPATIC LESIONS AND THEIR FREQUENCY IN OUR 653 AUTOPSY CASES

Type of Lesion	Acute and Chronic Inflammatory Lesion	Metastatic Lesion	Cirrhosis	Primary Hep. Car.	Total Number
Number	245	250	134	24	653
Percent	37.5%	20.5%	20.5%	3.7%	100%

Table No. 2 shows the frequency and percentage of tumor metastasis in the liver. There were 250 liver metastatic cases.

CIRRHOSIS

In this report, the term cirrhosis is used only for when the liver is grossly modular and microscopically showing cell proliferation (Hepatocyte, Kupfer cell, cholangiscyte) and collagen formation (fibrous band, membrane, septum).

of 134 cases of cirrhosis, 90 cases correspond to the portal type, 24 cases to the post necrotic type, 12 to the biliary type 6 to the post hepatic type and 2 to the cardiac type.

Table No. 3 shows the type, frequency and percentage of cirrhosis in 134 cases regard being given to the sex and age.

Table No. 2

FREPUENCY AND PERCENTAGE OF MALIGNANT TUMORS METASTIZED TO THE LIVER IN 250 AUTOPSY CASES

Primry Site	Number		Total Number	Average Age Incidnce	Primary Site	Number		Total Number	Average Age Incidence
	M	F				M	F		
Blood and R.E.S.					Uro_Genital Tract				
Lymphosareoma and leukemia	97	7	104	20-40	Kidney	3	2	5	3-60
Hodgkin's Disease	10	2	12	20-40	Uter. Choriocarcinoma	0	2	2	18-45
Erythroblatosis	2	1	3	Under Year	Urinary Bladder	1	0	1	41
Respiratory Tract					Prostate	1	0	1	58
Lung	30	9	39	40-60	Testis	1	0	1	30
Nasoparynx	1	0	1	50	Ovary	0	1	1	60
Gastro-Intestinal Tract					Bone				
Stomach	30	8	38	40-60	Multiple Myeloma	3	0	3	45-50
Gall Bladder	21	1	22	40-60	Ewing Sarcoma	1	0	1	12
Esophagus	1	1	2	37-46	Osteo-Sarcoma	1	0	1	35
Pancreas	0	2	2	47-50	Adrenal Gland				
Appendix	0	1	1	55	Cortical	2	2	4	36-37
Water. Amp	1	0	1	55	Medullan	3	1	4	3-21
					Malignan Melanoma	0	1	1	50
TOTAL	193	32	225		TOTAL	16	9	25	

Table No. 3

TYPES OF CIRRHOSIS IN 134 AUTOPSY CASES

Type of Cirrhosis	Sex		Ratio of M to F	Age	Total	%
	M	F				
Portal	80	10	8 to 1	2.5 Y-79Y	90	67
Post Necrotic	22	2	11 to 1	1.5 Y-64Y	24	18
Post Hepatic	3	3	1 to 1	3Y-55Y	6	4.5
Biliary	11	1	11 to 1	2M-60Y	12	9
Cardiac	2	-	2 to 0	30Y-35Y	2	1.5
Total Cases	118	16	8 to 1		134	

Nineteen of our 134 cases of cirrhosis occurred in children between the ages of 2 months and 13 years. Table No. 4 shows the frequency and percentage of each type of these 19 cases with regard to sex and age.

Table No. 4

TYPE OF CIRRHOSIS IN 19 CHILDREN

Type of Cirrhosis	Sex		Age	Total
	M	F		
Portal	7	3	5M-13Y	10
Post Necrotic	3	1	18M-11Y	4
Post Hepatic	-	1	- 3Y	1
Biliary	3	1	2M-5M	4
Total Cases	13	6		19

In Table No. 5 the first clinical manifestations of our 90 cases of portal Cirrhosis are shown.

Table No. 5

THE MORE COMMON CLINICAL MANIFESTATIONS IN 90 CASES OF PORTAL CIRRHOSIS

The Main Complaints	Sex		Total	Percent
	M	F		
Edema and Ascites	41	7	48	53
Coma	7	1	8	9
Hematemesis	7	—	7	8
Ascites and Jaundice	6	1	7	8
Ascites and Hemorrage	6	—	6	4
Jaundice and Hematemesis	4	—	4	7
Jaundice	3	1	4	4
Miscellaneous	6	—	6	7

Table No. 6 (A) shows that 37 percent of our 90 cases of portal cirrhosis had esophageal varice, and 13 percent stomach ulcer.

Table No. 6 (B) shows that 9 of our cases had artoriosclerosis, and 2 had ulcerative colitis.

Table No. 6

6-A COMMON COMPLICATIONS IN 90 CASES OF PORTAL CIRRHOSIS

Type of Complication	Sex		Total Number	%
	M	F		
Esophageal Varice	31	2	33	36.7%
Stomach Ulcer	12	—	12	13.3%

6-B CONCURRENT DISORDERS IN 90 CASES OF PORTAL CIRRHOSIS

Type of Lesion	Sex		Total Number	%
	M	F		
Arterosclerosis	9	—	9	10%
Ulcerative Cnlitis	2	1	3	33%

PAST HISTORY OF PATIENTS

As the table No. 7 shows, 2.2 percent of patiens suffering from portal cirrhosis in our cases were alcholic, 1.5. percent opiomane and 1.5 percent had previous syphilis, 5.2 percent Malaria.

Pathological Findings

Portal Cirrhosis. The liver of 90 cases diagnosed portal cirrhosis, were characterized grossly by weights ranging from 510-2800 grams, and a fine uniformly nodular surface.

Microscopically, the hepatic cells seemed to be swollen, mostly vacuolated, disorderly arranged, showing fatty change. In some cases, the fat globules were free, and accumulated between the cells. In the majority of cases, hepatic cell necrosis was seen, and focal necrosis and spotty necrosis were observed. The neo-formed nodules were surrounded by a thick fibrous band, and were divided by tiny connective tissue strands, giving a pseudolobule appearance.

The delicate fibrillary tongues, interconnecting triad and central vein were seen. Intralobular ductuls showed no specific change, but instead pseudo-ductals were numerous.

In some cases, around the portal spaces as well as their expansions, the epithelial cells were seen. Basically, the fatty micronodules showed no central vein and were one of the most prominent histological patterns in our cases. The liver of 7 cases were characterized grossly by a yellowish greasy appearance and had a fine, uniform nodulaa surface. In these cases, the hepatic cell as well as the kupfer cells, and other phagocytes contained a fine granular pigment, cytes centained a fine corresponding to the amount of intra-cellular fat.

Considering the classification of portal cirrhosis to the type A, B, C, D and Florid cases, as proposed by paul E. Steiner, our 90 cases could be arranged as shown in Table No. 8.

postnecrotic cirrhosis. of our 24 postnecrotic cirrhosis, four (16%) had antecedent hepatitis and jaundice. Grossly, the livers were inorderly shrunken, yellowish, presenting broad scarring, and coarse areas of collapse of the lobules, containing three or more closely arranged portal spaces, infiltrated by inflammatory cells. These selerotic areas contained also many dilated vessels, bearing a thin wall sinusoidal varices).

Post hepatitic cirrhosis. Grossly, the livers of this group were reddish-brown, nodules of 0.5 to 1.5 cm in diamete microscopically, in these livers fibrous septum was narrow, Crossing filirouthe hepatic parenchyma from portal to portal areas, enclosing some lobules. The hepatic cells show no fatty change and the central veins were normal, in position.

Biliary cirrhosis. of twelve cases of biliary cirrhosis seven were of extra-hepatic type and five were of intra-hepatic type.
We found that the majority (75%) of the patients were from north-west and western parts of the eountry and 60% of the patients were farmers.

PRIMARY LIVER CANCER

The incidence of Primary Liver Cancer among all autopsy cases (4389) was 24 and that among cirrhosis cases was fifteen.

Cirrhosis, therefore, was complicated by hepatic cancer in fifteen of 134 cases (11.19 percent). The age incidence in the present series is indicated in Table No. 9.

The average age of those with Hepatic Cancer and cirrhosis was 48 years and those with carcinoma of the liver without cirrhosis was 36 years. Most of those with hepatic cancer (22 out of 24) were male.

Pathological : findings

In our 24 cases of primary hepatic cancer the gross patholgical findings did not differ significantly between the hepatic and the bile duct types of carcinoma. Gross appearance of individual tumors varied considerably in terms of size, degree of nodularity, and color. Table No. 10 indicates the gross pathology aspect of 24 cases studied.

In three cases, tumors were located in the right lobe, and one case was located in the left lobe. The remaining cases were diffusely spread throughout the liver.

Among twentyfour cases, five livers were actually less than 1500 grams, eleven livers were between 1500-2500 grams, six between 2500-5000 grams, one 7000 grams, and one case 11,000 grams.

Table No. 11 shows the incidence weight in our 24 primary liver cancer cases,

Histological classification of tumors of the liver, studied in this series, is indicated in Table No. 12,

No instances of carcincsarcoma or squamous cell carcinoma were encountered. Hepato-cellurar carcinoma occured in seventeen patients, fifteen of whom were male.

Coexistent cirrhosis. There was a coexistent cirrhosis in eleven patients out of seventeen cases of hepato-cellular type (65%). Cholangiocarcinoma was diagnosed in five primary malignant hepatic tumors, all of whom were male, and coexistent cirrhosis was found in three of these cases.

Post necrotic cirrhosis. In one case post necrotic cirrhosis was complicated by bile-duct carcinoma.

Portal cirrhosis was associated with hepatoma in nine cases and with hepato-biliar carcinoma in one case.

In two cases the type of cirrhosis could not be determined generally because most of the liver tissue was iovolved by tumor (one case cholangio-carcinoma and one case hepetoma).

Table No. 13 shows the coexistent cirrhosis in twenty four cases of primay liver cancer,

Incidence of metastasis. The site and frequency of metastasis in the study are lsted in Table No. 14

In both types of tumor, the high frequency of lung metastasis was observed.

Lymph nodes at the liver hilus in five cases were involved. The brain was examined in in all 24 cases, but no intra-cranial metastasis was found. In one case only there was a small tumor emboli lodged in the pulmonary bilood vessels. Extension of tumor into the portal veins was seen in two cases and in three cases to the hilus and even spleen.

In three cases regional lymph nodes were invloved, and local extension of tumors involving the diaphragm, peritoneal cavitiy, pancreas, and adrenal glands was noted in seven cases.

Metastasis in the skull was noted in one patient (a seven-year-old boy).

The Physical Findings

The physical findings frequently did not lead to the correct diagnosis. The correct diagnosis was made before death in only three cases in the present study,

The complaints of all 24 patients with primary malignant hepatic neoplasm are grouped in Table No. 15

Summary

The incidence of cirrhosis and primary hepatic carcinoma in the autopsy material is studied. in 4389 autopsies performed, during the last 9 years we found 134 (3%) cases of cirrhosis and 24 (0.5%) cases of primary hepatic carcinoma. The majority of the patients were from North-West and west part of the city. of the 134 cases of cirrhosis 90 correspond to the portal type, 24 to the post-necrotic type, 12 to the biliary cirrhosis, 6 to the post-hepatitis cirrhosis and two cardiac cisrhosis. 19 of our 134 cases of cirrhosis, occured in children between the age of 4

months to 13 years. The liver of the 90 cases diagnosed, Portal cirrhosis were characterized grossely by weights from 510-2800 Gr and fine uniformly nodular surface. Micscopically there was marked, fatty change of hepatic cells, focal and spotty necrosis and delicated fibriliary tongue, interconnecting portal spaces. of the 24 cases post-necrotic cirrhosis 4 had had (26%) an antecedent jaundice. The liver ranged, from 700-2500 gr., presenting broad scarring and coars nodules. In our six cases, Post-hepatitic cirrhosis, the liver were redish brown, and presented uniform nodules, 0,5 to 1.5 Cm. in diameter. Liver weights varried form 850 to 1200 Gr. Microscopically 17 cases of carcinoma were hepato-carcinoma, two presented mixed structures of hepatoma and 5 cases were cholangio Carcinoma. Six of hepatomas showed previous portal cirrhosis and one mixed carcinoma showed previous portal cirrhosis.

TABLE No. 7

PAST HISTORY OF PATIENTS IN 90 CASES OF PORTAL CIRRHOSIS

Habit and Illness Antecedents		Sex M	Sex F	Total Number	Per Cent
Habit :	Alcoholic	3	—	3	2.2%
	Opioman	2	—	2	1.5%
Illness Ant.	Paludisme	7	—	7	5.2%
	Syphilis	2	—	2	1.5%

TABLE No. 8

HISTOLOGICAL ASPECTS OF 90 CASES OF PORTAL CIRRHOSIS

Type of Portal Cirrhosis	Sex M	Sex F	Total Number	Percent
A	21	4	25	28%
B	49	5	54	60%
C	3	2	5	5.5%
Florid	5	1	6	6.5%
Total	78	12	90	

Table No. 9

AGE INCIDENE OF 24 PATIENTS WITH PRIMARY LIVER TUMOR

Histological Type	Number of Patients Listed According to Age (years)							Total
	Under30	30-40	40-50	50-60	60-70	70-80	over 80	
Hepatic Cell	4	1	4	3	4	—	—	17
Bile-duct	3	—	2	—	—	—	—	5
Hep-Biliary	—	—	—	2	—	—	—	2
Total								24

TABLE No. 10

GROSS PATHOLOGY

Type	Number	Percent
Nodular	14	58.3%
Massive	6	25%
Diffuse	4	16.6%
Total	24	

TABLE No. 11

THE WEIGHT INCIDENCE IN 24 CASES OF PRIMARY LIVER CANCER

Liver Cancer Type	weight				Total
	less than 1500 g.	1500-5000g	2500-5000g	5000-11000	
Hepatic Cell	4	7	4	2	17
Bile-duct	—	3	2	—	5
Hep. Bile	1	1	—	—	2
Total	5	11	6	2	24

TABLE No. 12

MICRSCOPIC PATHOLOGY

Cell Type	Number of Cases	Percent of Total Cases
Hepatic Cell	17	71
Bile-duct Cell	5	21
Hepato-biliary	2	8
Total	24	

TABLE No. 13

COEXISTENT CIRRHOSIS IN 24 CASES OF PRIMARY LIVER CANCER

Liver Caneer Type	With Cirrhosis					Without Cirrhosis	Total
	Port	Post. N.	Post. H.	Nutr	Indet.		
Liver Cell	9	—	—	1	1	6	17
Bile-duct Cell	—	1	1	—	1	2	5
Hepato-biliary	1	—	—	—	—	1	2
Total	10	1	1	1	2	9	24

TABLE No. 14

LOCATION AND FREQUENCY OF METASTASIS IN

Site of Metastasis	Type of Cancer						Total Number
	Hepatic Cell		Bile-duct		Hepato-bili.		
	No.	%	No.	%	No.	%	
Lung	9	37.5%	1				10
Lymph Node	9	37.5%	1				10
Adrenal	3	12.5%					3
Spleen	3	12.5%					3
Bone	1	4.1%					1
Peritoneal Surface	4	17.0%					4

TABLE No. 15
SHYSICAL FINDINGS

Findings	Number of Cases	Percent
Abdominal Mass	9	37.5
Ascite	19	79
Abdominal Pain	17	71
Icterus	8	33
Splenomegaly	17	71
Fever	11	46
Ankle Edema	11	46
Gastro-nitestinal Beelding	6	25

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