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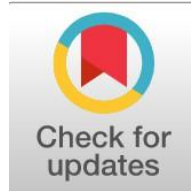
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Clinical and Demographic Factors Affecting Survival in Primary Biliary Cholangitis

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Abstract

General Background Primary biliary cholangitis is a chronic autoimmune liver disease that causes progressive bile duct destruction and liver failure. **Specific Background** Clinical laboratory markers and physical symptoms serve as key parameters for evaluating disease progression and patient outcomes. **Knowledge Gap** However, the precise prognostic impact of specific combined clinical symptoms and biochemical markers on long-term survival remains to be further clarified. **Aims** This study aimed to determine the impact of clinical laboratory variables and symptoms on survival rates in primary biliary cholangitis patients. **Results** Multiple Cox regression and Kaplan-Meier analyses of 312 patients showed that advanced histological stages, male sex, older age, elevated bilirubin, AST, copper, cholesterol, triglycerides, ascites, edema, hepatomegaly, and spider angiomas significantly reduce survival probability. **Novelty** These findings establish a comprehensive risk factor profile combining physical manifestations with biochemical indicators. **Implications** Monitoring these parameters enables timely clinical interventions and improved risk stratification for patient management.

Key Findings Highlights

Advanced histological stages and male sex significantly reduce survival probability in primary biliary cholangitis.

Physical manifestations including ascites, edema, hepatomegaly, and spider angiomas serve as strong indicators of mortality risk.

Elevated serum bilirubin, copper, cholesterol, and liver enzymes strongly correlate with diminished overall survival time.

Keywords: Primary Biliary Cholangitis, Survival Rate, Liver Biomarkers, Cox Regression, Disease Symptoms

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Introduction

Primary biliary cholangitis (PBC) is a one of most common rare progressive autoimmune liver disease that it is affected in middle and involved persistent chronic inflammation of interlobular bile duct which can lead to liver damage. If it is left untreated, PBC can lead to cirrhosis, decompensation and death. It requires novel therapies or liver transplantation [1] [2] [3]. PBC was formerly known as Primary Biliary Cirrhosis, but the designation was around 2015, because cirrhosis was not a necessary condition for the diagnosis of this disease [4].

PBC is classified into four stages: Stage I (portal stage) involves portal inflammation with granulomatous destruction of bile ducts; Stage II (periportal stage) shows periportal fibrosis, Stage III (septal stage) demonstrates bridging fibrosis, and Stage IV represents cirrhosis [5] [6]. The Biochemical markers play a central role in the diagnosis, monitoring, and prognostication of PBC. In PBC, patients have increased serum alkaline phosphatase enzyme (ALP), positive antimicrobial antibody (AMA) [7] in addition to slight to moderate elevation in aminotransferase enzymes, alanine aminotransferase (ALP), aspartate aminotransferase (AST) [8].

As a disease progress hyperbilirubinemia occur and significant hyperbilirubinemia indicates to advanced disease, and regard as reliable predictors of adverse outcome in PBC, when hyperbilirubinemia co-occur with thrombocytopenia, reduce albumin levels, and elevated international normalized rate (INR), it is indicated to development decompensated cirrhosis [9].

The relationship between these biochemical markers and survival rate is complex and clinically important, several prognostic models integrate biochemical markers to predict outcome including Mayo risk score, albumin-bilirubin (ALBI) score, UK-PBC and GLOBE scores [10]. The UK-PBC score includes measurements of AST, ALT, ALP, bilirubin at 12 months and albumin, platelets at baseline to estimate risk of liver transplant and liver-related death within 5,10, and 15 years [11], and GLOBE score includes age, ALP, bilirubin, albumin and platelets to estimate liver transplantation free survival at 3,5,10, and 15 years [12].

PBC has early and advanced stages of progression. Physical examination in early stages is usually normal, although presence hepatomegaly, xanthoma. Jaundice is late finding of liver advanced disease in addition to many sings such as ascites, edema, spiders angiomas may be found in setting of portal hypertension [13]. The death is commonly due to complications of the disease or liver failure. PBC is a progress in most cases but the rate of progression varies greatly among individual patients asymptomatic have substantially longer life expectancies than symptomatic ones, but their survival is still less than the healthy individual. Median survival rate of asymptomatic patients was 10 to 16 years in the two large cohorts followed for up to 24 years and median survival rate of symptomatic patients is approximately 7 years [14]. Liver transplant (LT) is the only treatment option for end stage liver disease [15]. This study aims to determine the impact of certain factors such as sex, age, laboratory variables as AST, ALP liver enzymes, bilirubin, albumin, copper, prothrombin time, platelets count, cholesterol, triglyceride, ascites, hepatomegaly, spiders and edema on survival rate in PBC. Also, the survival rate between asymptomatic and symptomatic patients was studied.

Materials and methods

2.1 Data collection

The patient's population for development and testing survival rate in PBC models, consist of patients with primary biliary cirrhosis recently known as primary biliary cholangitis (PBC) those who were at Mayo Clinic between January 1974 to May 1984 which met the biochemical and histological criteria of PBC. Total patients sample were 424 patients qualified for the randomized placebo-controlled trial testing the drug D-penicillamine, 112 patients didn't join with study but agree to record basic metrics, 312 patients took part in the trial and have mostly comprehensive data [16]. Data of patients consist of 17 variables in addition to ID patients, time and status, the demographic variables as shown in Table 1, clinical laboratory variables shown in Table 2.

Table 1 Demographic variables

N O.	Variable name	Type	Description
1	sex	Categorical	M (male) or F (female)
2	Age	Integer	days
3	time	Integer (days)	number of days between registration and the earlier of death, transplantation, or study analysis time in July 1986
4	Status	Categorical	Status of the patient:1= C(censored),2=CL (censored due to liver transplantation), or 0=D (dead)
5	drug	Categorical	type of drug D-penicillamine or placebo
6	Ascites	Categorical	Existence of fluid in abdomen, 0 (No) or 1 (Yes)
7	Hepatomegaly	Categorical	Existence of enlarge liver, 0 (No) or 1 (Yes)
8	Spiders	Categorical	Existence of blood vessels malformations in skin ,0 (No) or 1 (Yes)
9	Edema	Categorical	Existence of fluid in body tissues,0=no edema and no diuretics therapy,0.5=presence edema without diuretics or edema resolved diuretics,1=edema despite diuretics therapy.

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Table 2 Clinical laboratory variables

No.	Variable name
1	Bilirubin: serum bilirubin in [mg/dl]
2	Albumin: serum albumin in [gm/dl]
3	Copper: urine copper in [μ g /day]
4	Alk Phos: serum alkaline phosphatase in [U/liter]
5	AST: serum aspartate aminotransferase in [U/liter]
6	Cholesterol: serum cholesterol in [mg/dl]
7	Triglycerides: serum triglycerides in [mg/dl]
8	Platelets: platelets per cubic [ml/1000]
9	Prothrombin: prothrombin time in seconds [s] to evaluate the extrinsic pathway of coagulation
10	Stage: histologist stage of disease (1, 2, 3, 4)

Statistical analysis

Study data are concerned with knowing the probability of the PBC patient remaining before the appearance of a certain event (liver transplantation or death), where the result of the disease is linked to the number of days spent by the patient in the days from the beginning of the diagnosis until the appearance of an outcome event, when outcome takes three cases, namely (0 censored, 1 censored due to liver transplantation, and 2 dead). From the nature of the data, the appropriate statistical method for analysis is (cox-regression) and Kaplan-Meier [17], [18], all results from this study we depended on python 3.13 program to import data and clean it from missing and outlier values.

Cox-Regression analysis:

Cox-regression is characterized by a set of advantages in statistical analysis, including are:

- Don't need to specify the shape of the latency distribution (non-parametric)
- We can apply in Quantitative and categorical variables
- Very useful for identifying the factors that affect survival the most

The 17 independent variables for the Cox model as in a multiple regression, the P-value was used as a criterion to decide whether a variable was statistically significant ($P \leq 0.05$) by Z-statistic and also to determine which variable is most informative other criteria such as OR and Hazard rate (HR); if $HR > 1$ this mean variable(feature) increase danger of disease with ratio $(HR-1) \times 100$; and if $HR < 1$ feature decrease with ratio $(1-HR) \times 100$.

To drawing the curves of the survival function according to each descriptive variable by Kaplan-Meier analysis.

Kaplan-Meier analysis:

Kaplan-Meier analysis (or Kaplan-Meier estimates) are a statistical tool used in Survival Analysis to represent the probability that a group of individuals will survive (or that a particular event such as disease relapse or organ failure will not occur) over time. Kaplan-Meier curve: Purpose: Estimates the Survival Function and shows the probability of survival at each point in time. Input data: Depends on survival times considering "censored" cases, i.e. individuals who did not have the event until the end of the follow-up. Instructions: Whenever an "event" occurs (such as death or treatment failure), the Step Function curve drops abruptly. Times when an event does not occur remain stable (horizontal line). Comparison between groups: More than one Kaplan-Meier curve can be compared using the Log-rank test (chi-square criteria) to see if there is a substantial difference between the groups. Graphic Representation: Horizontal axis (X) = time. Vertical axis (Y) = probability of survival, the curve starts at a value of 1 (100% survival) and decreases as events occur.

Results

Descriptive statistics

Overall, 312 patients with PBC were included, their mean age was 50.19 (26.28-78.44) years, among them 276 were female and 36 were male. Also average of time variable (survival rate) in sample was 2006.362 days, it ranges from (41-4556) days. All variables (features) are shown in as following Tables 3 to 5.

Table 3 Some Descriptive statistics of variables

Variables	Mean $\pm$ SD	min	max	International Standards (normal ranges)
Time(days)	2006.362 $\pm$ 1123.281	41	4556	
Age	50.019 $\pm$ 10.581	26.278	78.439	
Bilirubin	2.676 $\pm$ 3.151	0.3	28	0.1 – 1.2 mg/dL
Cholesterol	201.247 $\pm$ 98.069	100	636	< 200 mg/dL
Albumin	3.935 $\pm$ 1.035	2.54	8.9	3.5 – 5 g/dL
Copper	79.648 $\pm$ 85.338	40	588	$\leq 30 \mu$ g/day
ALP	145.981 $\pm$ 115.028	30	761	40 – 129 U/L
AST	48.509 $\pm$ 36.370	1.91	238	8 – 48 U/L
Triglycerides	124.702 $\pm$ 61.927	33	598	<150 mg/dL
Platelets count	295.063 $\pm$ 96.888	97	650	140 – 440 $\times 10^9$ /L
Prothrombin time	11.343 $\pm$ 1.645	9	17.1	9.5 – 12.5 seconds

Normal ranges according to internationally recognized clinical laboratory standards such as Mayo Clinic Laboratories and Merck Manual (MSD).

Table 4 Numbers of patients according features (disease symptoms)

Feature	categorical	count	feature	categorical	count
Sex	Male	36	Edema	Level_0	263
	Female	276		Level_0.5	29
Drug	D-penicillin	158		Level_1	20
	Placebo	154	Stage	1	16

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Ascites	No	288		2	67
	Yes	24		3	120
Hepatomegaly	No	160		4	109
	Yes	152			
Spiders	No	222			
	Yes	90			

Table 5 Numbers of patients according status category and features (disease symptoms)

Variable	Category	Censored	Censored due to transplantation	Dead	P-value	Si g.
Drug	Penicillamine	83 (49.4%)	10 (52.6%)	65 (52.0%)	0.8935	n s
Drug	placebo	85 (50.6%)	9 (47.4%)	60 (48.0%)	0.8935	n s
Sex	Female	157 (93.5%)	16 (84.2%)	103 (82.4%)	0.0115	*
Sex	Male	11 (6.5%)	3 (15.8%)	22 (17.6%)	0.0115	*
Ascites	No	166 (98.8%)	19 (100.0%)	102 (81.6%)	<0.00001	**
Ascites	Yes	2 (1.2%)	0 (0.0%)	23 (18.4%)	<0.00001	**
Hepatomegaly	No	108 (64.3%)	7 (36.8%)	37 (29.6%)	<0.00001	**
Hepatomegaly	Yes	60 (35.7%)	12 (63.2%)	88 (70.4%)	<0.00001	**
Spiders	No	134 (79.8%)	14 (73.7%)	73 (58.4%)	0.0004	**
Spiders	Yes	34 (20.2%)	5 (26.3%)	52 (41.6%)	0.0004	**
Edema	Level_o	157 (93.5%)	17 (89.5%)	89 (71.2%)	<0.00001	**
Edema	Level_o.5	10 (6.0%)	2 (10.5%)	17 (13.6%)	<0.00001	**
Edema	Level_1	1 (0.6%)	0 (0.0%)	19 (15.2%)	<0.00001	**
Stage	1	15 (8.9%)	0 (0.0%)	1 (0.8%)	<0.00001*	**
Stage	2	48 (28.6%)	3 (15.8%)	16 (12.8%)	<0.00001	**
Stage	3	69 (41.1%)	8 (42.1%)	43 (34.4%)	<0.00001	**
Stage	4	36 (21.4%)	8 (42.1%)	65 (52.0%)	<0.00001	**

In Table (5) there is high significant difference in the number of patients with symptoms (ascites, hepatomegaly, spiders and edema) for each of three groups (censored, censored due to transplantation, dead), we see absence of ascites and edema level 1 in transplant group. The incidence of these symptoms in liver transplant group is low compared with censored and dead group. For example: transplant patients with hepatomegaly are 12(63.2%), spiders 5(26.3%), edema level (0.5) 2(10.5%). Also, incidence of patients with advanced histological stage (3,4) is 8(42.1%) patients it is consider is low compared to the censored and dead group. in Table (6) there is high significant difference in all laboratory variables among three groups, the bilirubin is slightly elevated in transplant group it is value 3.13, albumin 5.05 is high compared with other two groups, AST within normal range in transplant group but ALP is slightly elevated.

Table 6 Comparison between clinical laboratory variables under type of status

Variable	Censored	Censored due to transplantation	Dead	p-value	Sig.
Age	48.62 ± 10.49	41.18 ± 6.06	53.24 ± 10.11	0.0000	***
Bilirubin	1.50 ± 1.75	3.13 ± 2.02	4.18 ± 4.00	0.0000	***
Cholesterol	187.46 ± 66.28	241.84 ± 62.61	293.48 ± 105.49	0.0000	***
Albumin	3.63 ± 0.33	5.05 ± 1.53	4.17 ± 1.35	0.0003	***
Copper	66.80 ± 56.93	124.00 ± 100.08	135.11 ± 98.16	0.0000	***
ALP	127.25 ± 69.21	146.74 ± 62.30	193.50 ± 153.70	0.0059	**
AST	34.65 ± 21.92	45.91 ± 29.83	67.53 ± 43.77	0.0000	***
Triglycerides	113.09 ± 45.92	133.46 ± 68.59	138.97 ± 75.47	0.0055	**
Platelets count	272.37 ± 88.73	298.84 ± 79.60	324.98 ± 102.07	0.0001	***
Prothrombin time	10.38 ± 0.85	10.37 ± 0.59	12.78 ± 1.51	0.0000	***

Cox-Regression analysis

Univariate cox-regression analyses showed that presence disease symptoms such as (Ascites_(yes),Hepatomegaly(yes), Spiders_ yes, Edema level_o.05) advanced histological stage (3,4),Prothrombin time, Bilirubin ,age, sex-male, Copper, AST, Triglycerides, Cholesterol) are high

statistical significant (P-value<0.0001) and have risk factors for death and diminished survival rate, while variables (sex female, stage1,2, spiders_ no, Hepatomegaly(No),edema no, ascites_(no),hypoalbuminemia, thrombocytopenia are statistical significant but Hazard risk(HR) are Protective , as for the variables as (drug-penicillamine ,ALP, drug-placebo) are not significant for death (p-value>0.05) see following Table 7.

Table (7): Results of Cox-regression analysis

Variable	Original variable	Coef.	HR	p-value	Interpretation
Ascites Yes	ascites	2.053	7.790	5.332E-18	Risk factor
Hepatomegaly Yes	Hepatomegaly	1.186	3.275	1.955E-09	Risk factor
Stage_4	stage	1.185	3.269	5.797E-11	Risk factor
Spiders Yes	spiders	0.974	2.649	1.134E-07	Risk factor
Edma_0.5	Edma	0.686	1.986	8.667E-03	Risk factor
Sex male	sex	0.484	1.622	4.075E-02	Risk factor
Prothrombin time	Prothrombin time	0.380	1.462	1.208E-12	Risk factor
Stage_3	stage	0.280	1.323	1.378E-02	Risk factor
Bilirubin	Bilirubin	0.149	1.161	2.579E-30	Risk factor
drug-penicillamine	drug	0.057	1.059	7.494E-01	Not significant
Age	age	0.040	1.041	5.651E-06	Risk factor
Copper	copper	0.007	1.007	2.009E-18	Risk factor
AST	AST	0.006	1.006	4.412E-08	Risk factor
Triglycerides	Triglycerides	0.004	1.004	2.732E-04	Risk factor
Cholesterol	Cholesterol	0.001	1.001	1.331E-03	Risk factor
ALP	ALP	0.000	1.000	1.098E-01	Not significant
Thrombocytopenia	platelet	-0.003	0.997	2.372E-03	Protective
drug placebo	drug	-0.057	0.944	7.494E-01	Not significant
Sex female	sex	-0.484	0.616	4.075E-02	Protective
Stage_2	stage	-0.870	0.419	1.192E-03	Protective
Spiders No	spiders	-0.974	0.377	1.134E-07	Protective
Hepatomegaly No	Hepatomegaly	-1.186	0.305	1.955E-09	Protective
Edema_0.0	Edema	-1.388	0.250	3.054E-12	Protective
Hypoalbuminia	albumin	-1.796	0.166	9.835E-18	Protective
Ascites No	ascites	-2.053	0.128	5.332E-18	Protective
Stage_1	stage	-2.378	0.093	1.794E-02	Protective

Kaplan-Meier analysis

Using Kaplan-Meier analysis for the data to diagnostic the time(days) and survival probability for each categorical variable (see Table 8).

Table (8): Survival probability according four times

Variable	Group	Event Time	Survival prob.	Max (time)	Median Survival
Sex	Female	3853	0.39	4556	3428
	Male	4191	0.206	4459	2386
Drug	D-penicillamine	4191	0.319	4556	3282
	placebo	3853	0.361	4523	3428
Stage	4	3762	0.187	4523	1682
	3	4191	0.330	4500	3428
	2	4079	0.397	4556	4079
	1	2386	0.909	4459	----
Edema	Level_1	3428	0.000	3428	264
	Level_0	4191	0.375	4556	3584
	Level_0.5	3282	0.316	4232	1576
Hepatomegaly	Yes	4191	0.159	4523	2256
	No	3853	0.565	4556	----

Spiders	Yes	3762	0.149	4500	1847
	No	4191	0.403	4556	3839
Ascites	yes	3222	0.000	3222	388
	No	4191	0.377	4556	3584

From the results in Table (8), there are two times according to each variable, the first of these times is event (time) represents the time of the appearance of the event (death) under study with a certain probability while Max (time) represents the last possible time of the event (death) to occur, which is always less than or equal to the continuation of the examination for the patients in the study (4556 days), for example in sex (female) the first time of death is 3853 day and max time is 4556 with survival probability 39%, while median survival is 3428 days. The patient's survival probability varies according to the disease status such as sex, histological stage and disease symptom, the highest probability of survival is 0.91 in patients with first histological stage of disease and the first time of death (2386) while the lowest probability of survival is (0.000) for patients with presence (Edema level 1 and Ascites) and first time of event (death) 3428 ,3222 day respectively. and the median survival for edema 1 and ascites is 264 ,388 day respectively, survival decreasing according to time from disease detection until the end of the period; as shown in column (3) and column (4) of the table, and this can be observed through the Kaplan-Meier curves shown in the following figures:

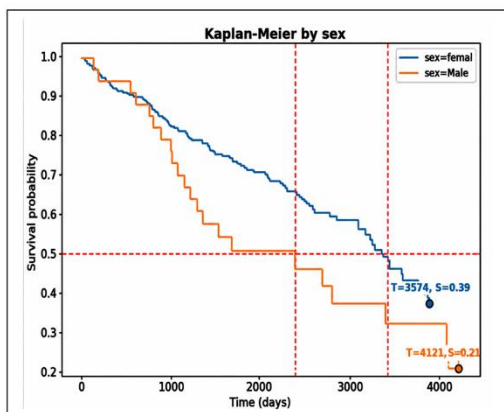


Fig.(a): Survivals probability curve of Sex

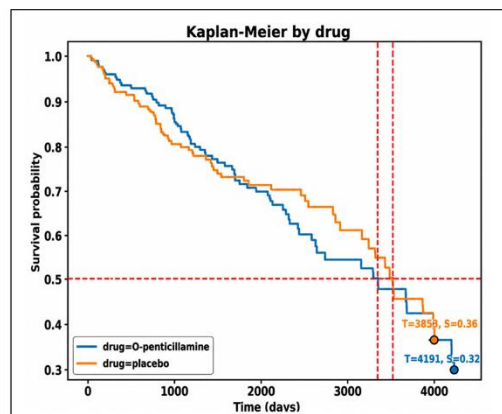


Fig.(b): Survivals probability curve of Drug

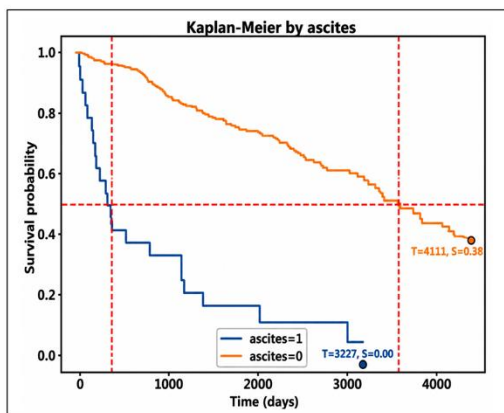


Fig.(c): Survivals probability curve of ascites

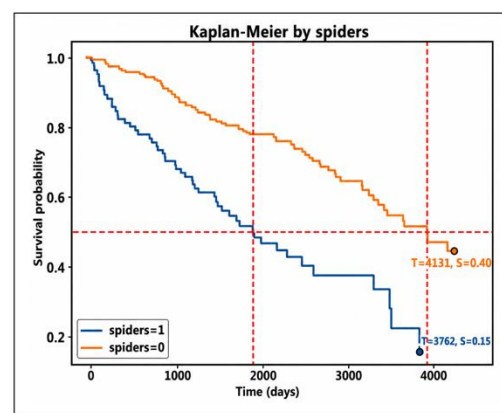


Fig.(d): Survivals probability curve of Spiders

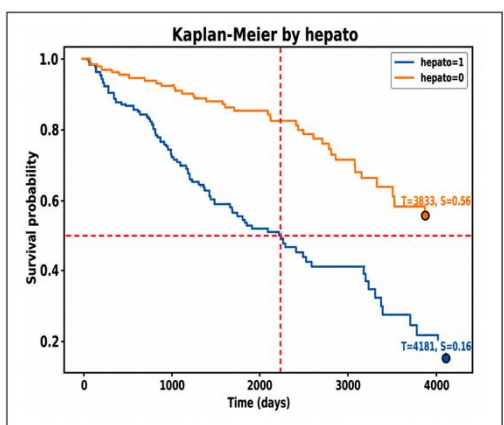


Fig.(e): Survivals probability curve of hepatomegaly

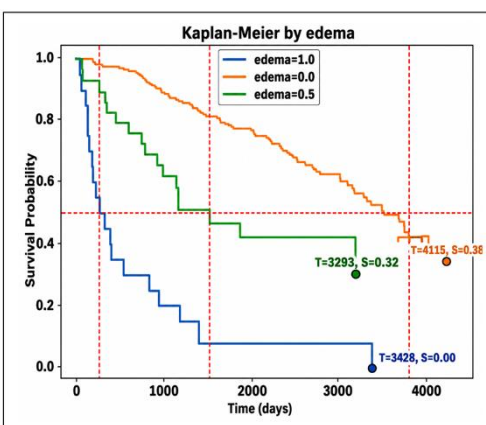


Fig.(f): Survivals probability curve of edema

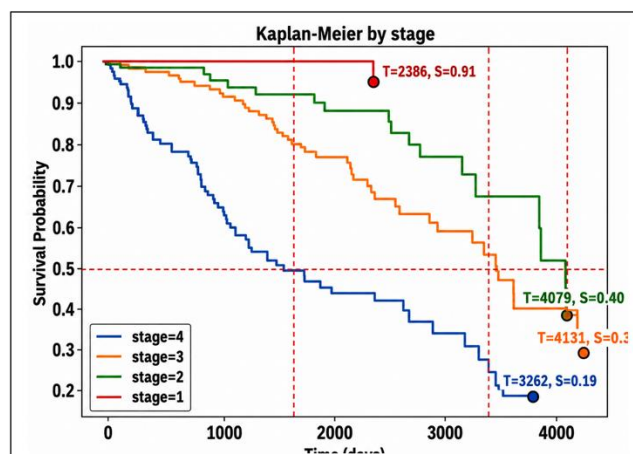


Fig.(g): Survivals probability curve of histological stage

From the previous graphs it can be seen that the decreases in the lines represent events (deaths or failures of the event). Every plan line means that an event has occurred to an individual. Plane distances also mean that during that period no new events occurred (it continued to remain constant). Also, higher curve means a higher probability of long-term survival compared to low curves, and a decrease rate can be taken advantage of when the level is less than the median probability (0.50), for one curve faster than the other curve, indicating that this group has a lower survival rate or more early mortality.

Typically, not depend only curves diagnostic in such an analysis, but depend on statistical test such as a log-rank test is performed to ascertain whether the difference between the two curves is statistically significant or not (see Table (9)).

Table (9): Comparison between Variables Level according Chi-square test

Variables	Chi-square	p-value
Drug (D-penicillin vs placebo)	0.120814	0.728154
Sex (male vs female)	4.850086	0.027645
Histological stages (1,2,3,4)	58.34948	1.32E-12
Edema (0,0.5,1)	112.2748	4.17E-25
Spiders (0 vs 1)	28.37678	9.99E-08
Hepatomegaly (0 vs 1)	43.61176	4E-11
Ascites (0 vs 1)	87.67252	7.72E-21

From Table (9), it can be noted that the type of drug isn't significant on survival. (p-value=0.728>0.05), but all other variables levels (histological stage, edema, spiders, hepatomegaly, and ascites) are significant differences in their impact on survival rate (p-value<0.001) only sex levels are low significant differences on survival (p-value<0.05).

Discussion

PBC is slowly progressive disease with natural history from 10-15 years that lead to end stage liver disease and high risk cases can progress to decompensated cirrhosis and death [19], [20], the study found that the symptoms of the disease such as (ascites, hepatomegaly, edema and spiders) are high risk factor of death and diminished survival rate and this consistent with the results previous studies [21] that show the (ascites, hepatomegaly) as important predictors of diminished survival rate. ascites is a one of major complications of liver cirrhosis and patients with ascites have lower survival rate as the disease progresses, therefore survival at 10-years after diagnosis 52% [22].

Also results of our study shows that the histological stages as stage 3 (portal bile stasis) and stage 4 (advanced fibrosis) are high risk factors of death and diminished survival rate that is consistent with study of Martini [23] which concluded that the advanced fibrosis and portal bile stasis are risk factors for diminished survival rate in PBC patients.

The older age plays central in decreasing survival rate according to findings study that conducted by [24] showed the prevalence of PBC increase with age and it is identified in middle age individual (40-60) years.

And sex-male is risk factor of death and decline survival rate as shown in the results of current study and this is consistent with pervious study by [25], which concluded that the sex male is independent poor prognostic factor for death and transplantation in PBC, because PBC is advanced in male and associated with greater progression to cirrhosis and hepatocellular carcinoma (HCC),

The clinical laboratory markers play important role in diagnosis and predication of PBC outcome, results of the current study found that each of the following laboratory parameters such as bilirubin, prothrombin time, AST, cholesterol, triglyceride and, copper are risk factors for death in PBC, the bilirubin level is high risk factor of death, this consistent with previous study [26] which proved that the hyperbilirubinemia independent markers for death and impaired chance of survival. also, AST, prothrombin time and presence spiders in current study are high risk factor for of death and this consistent with results of study [27]. In pervious investigation [28] which show the prolonged elevation in AST, total bilirubin, ALP, fibrosis score 4, (APRI) may increase risk of negative outcomes in PBC patients. Other investigation [29] revealed that the AST, bilirubin, albumin, ascites, organomegaly, and cirrhosis stage 4 are significantly impact on PBC patients' survival rate. also, hyperlipidemia is main complications of PBC, our study shows high cholesterol, triglyceride levels are risk factors of death and diminished survival rate, Hypercholesterolemia is risk factor of death because cholesterol led to development ductopenia in early stages of PBC according to previous study [30].

The results of current study showed that some variables such as (sex-female, platelets, albumin, histological stage 1,2 and absence of ascites, edema, hepatomegaly and spiders) are statically significant risk of death but hazard risk (HR) are protective, this means that they could potentially high-risk factor of death in future and that it needs to be monitored to prevent the situation from worsening. Thrombocytopenia lower platelets count in current study has protective hazard risk for death, pervious study by [31] show that the platelets are prognostic factor and impaired survival rate in PBC. and albumin as protective hazard risk for death, hypoalbuminemia is significant risk factor for decline survival rate [32].

Other some variables as drug-D-penicillamine, drug-placebo and alkaline phosphatase (ALP) are not significant of death. ALP is not risking factor for death that is inconsistent with pervious study [32] which show higher ALP levels associated with an increased risk of disease progression. according Table (6) in present study use Kaplan -Meier analysis (median survival) with days And survival probability for each categorical variable, since the sex-male is a risk factor of death, the probability of survival rate for male is 20%, with median survival 2386 day,

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while in female survival probability 39% with median survival probability 3428 day as shown in fig(a), there is low significant difference between sex-male and female in the effect on survival rate according Chi-square test Table (7). also, patients with histological stages (3,4) have lower survival probability 33%, 18% with lower median survival rate is approximately 3428 day and 1682 day respectively compared to histological stage (1,2) as shown in fig(G), there is high significant difference between stages (1,2,3,4) for risk factor of death. according Chi-square test (Table 9)

Patients suffering from (edema, hepatomegaly, spiders and ascites) have lower survival probability and median survival in days than patients who do not have these symptoms, as shown in figures (c,d,e,f), there are high significant differences between presence or absence (edema, hepatomegaly, spiders, ascites) in its effect on survival rate according Chi-square test Table (9).

From this we conclude that patients with symptomatic patients have lower survival rate than asymptomatic patients, this like previous study [14] which show asymptomatic patients have survival rate 10-16 years and symptomatic patients is approximately 7 years, also study by [23] show the presence of these symptoms increase risk of disease.

There is high significant difference in all clinical laboratory variables and symptoms of disease as (ascites, hepatomegaly, edema, spiders) among three patients' groups: censored, transplant and censored, dead), previous study [33] which show there was presence significant difference in some laboratory variables as (bilirubin, albumin, prothrombin time) between UDCA treated patients with good outcome group and transplant or dead group. but ALP enzyme was not significant different. Other study [29] found the significant different between bilirubin, albumin, mayo risk score among alive patients and dead or transplant patients also cirrhosis stage 4, ascites and jaundice high in dead patients' groups.

Transplant patients in current study have AST within normal range but bilirubin and ALP are slightly elevated after liver transplant, and incidence of transplant patients with histological stage (3,4) is 42.1%. Findings study of Carols et al [34] showed that 13 from 52 surviving patients have abnormalities liver functions tests at the time of last follow up, though none were jaundiced. In previous study that show that the last follow up for all patients hold marked symptomatic improvement compared with their pretransplant condition and 91% of patients had normal hepatic laboratory markers including serum ALP, bilirubin, ALT, 41 from 60 patients had near normal liver histological appearance, 5 patients had histological feature of florid duct lesion, although normal hepatic biochemical value this suggest recurrent of PBC after transplantation.

Conclusion

This study concluded that age, sex-male, ascites, hepatomegaly, spiders, edema, bilirubin, cholesterol, triglyceride, aminotransferase level, copper, advanced histological stages are significant impact on survival rate in PBC, also mean survival rate lower in symptomatic patients compared with asymptomatic patients.

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