

Supplementary table 1 ICD-9 codes for liver cirrhosis

ICD-9 CODE	
571	Chronic liver disease and cirrhosis
571.5	End stage chronic liver disease
	Cirrhosis of liver
	Cirrhosis of liver without mention of alcohol
	Cryptogenic cirrhosis

Supplementary table 2 International Classification of Diseases, 9th Revision codes for etiologies of thrombocytopenia other than liver cirrhosis

ICD-9 CODE	
287.31	Idiopathic thrombocytopenic purpura
287.4	Drugs induced thrombocytopenia
287.4	Viral induced thrombocytopenia (HIV, EBV, CMV)
710.0	Lupus associated thrombocytopenia (systemic lupus erythematosus)
742.59	Myelodysplasia
202.8, 202.0, 200.7, 200.8	Lymphoma
208.0, V10.6, 208.9	Leukemia
289.81	APLA (antiphospholipid syndrome)
284, 284.9	Aplastic anemia
289.83, 238.76	Myelofibrosis
286.4	Inherited thrombocytopenia (von Willebrand disease)

ICD-9: International Classification of Diseases, 9th Revision; HIV: Human immunodeficiency virus; EBV: Epstein-Barr virus; CMV: Cytomegalovirus; APLA: Antiphospholipid antibodies.

Supplementary table 3 Medications which excluded from the study

Medications which excluded from the study

Aazathioprine

Mercaptopurine

Inliximab

Adalimumab

Golimumab

Vedolizumab

Ustekinumab

Cyclosporine

Tacrolimus (Progr.FK506)

Sirolimus

Methotrexate

Everolimus

Rituximab

**Supplementary table 4 International Classification of Diseases, 9th
Revision codes for etiologies of liver cirrhosis and its complications**

ICD-9 CODE	Etiologies of liver disease
571.2-3	Alcoholic liver damage, unspecified; Alcoholic cirrhosis of liver
571.8	Other chronic nonalcoholic liver disease
070	Viral hepatitis
070.3	Viral hepatitis B without mention of hepatic coma
070.70	Unspecified viral hepatitis C without hepatic coma
571.42	Autoimmune hepatitis
576.1	Cholangitis
571.6	Biliary cirrhosis
275.1	Disorders of copper metabolism
ICD-9 CODE	Cirrhosis complications
456.0-1	Gastroesophageal varices; Esophageal varices with bleeding; Esophageal varices without bleeding
456.8	Gastric varices
456.2	Portal hypertensive gastrointestinal bleeding
789.59, 568.82, 276.6	Ascites due to Cirrhosis
572.2, 348.39	Hepatic encephalopathy; Portal-systemic encephalopathy; Hepatocerebral intoxication
567.23	Spontaneous bacterial peritonitis
155.0	Liver, primary carcinoma; Malignant neoplasm of liver and intrahepatic bile ducts
572.3	Portal hypertension
789.1-2	Hepatomegaly NOS; Splenomegaly
289.4	Hypersplenism
452	Portal vein obstruction

ICD-9: International Classification of Diseases, 9th Revision; NOS: Nitric oxide synthase.

Supplementary table 5 Laboratory values, normal ranges

Laboratory parameter	Normal range
White blood count	4-11
Hemoglobin	13.2-17
Platelets	150-450
Bilirubin (total)	0.1-1.2 (mg/dL)
AST	7-40 (U/L)
ALT	5-39 (U/L)
Alkaline Phosphatase	46-116 (U/L)
GGT	6-42 (U/L)
Albumin	3.5-5 (mg/dL)
INR	0.97-1.19
PT	10-12.42 sec
PTT	25-34 sec
Creatinine	0.7-1.3 (mg/dL)

AST: Aspartate aminotransferase; ALT: Alanine transaminase; GGT: Gamma-glutamyl transferase; INR: international normalized ratio; PT: Prothrombin time; PTT: Partial thromboplastin time.

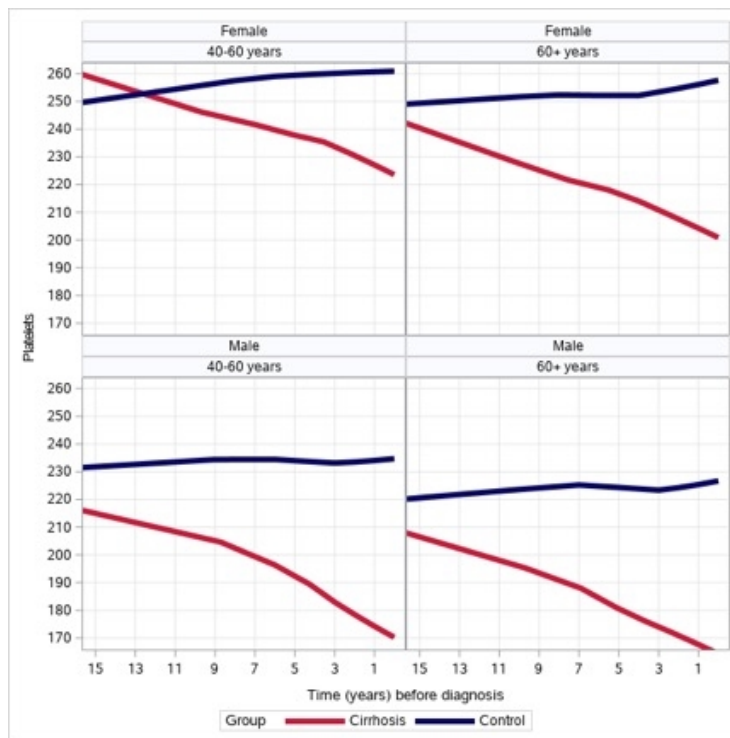
Supplementary table 6-Mean platelets count per year.

Time (years) before diagnosis	Group	N	Mean	Std Dev	Minimum	Median	Maximum	P- value
1	Cirrhosis	4903	206.06	84.31	23	204	759.6	< 0.0001
	Control	15774	246.34	65.46	18	240.5	1166	
2	Cirrhosis	4118	209.29	82.5	28.5	207.5	769.8	< 0.0001
	Control	9533	243.42	65.08	27.33	237	1186	
3	Cirrhosis	3686	212.68	79.72	33	210	736.56	< 0.0001
	Control	8665	243.34	64.8	27	237	1102	
4	Cirrhosis	3328	215.26	78.56	35.33	212.2	861.5	< 0.0001
	Control	7526	243.73	64.69	30.5	238	1007	
5	Cirrhosis	2922	217.96	76.72	29.5	214.75	932.5	< 0.0001
	Control	6878	244.7	66.95	4	239	1649	

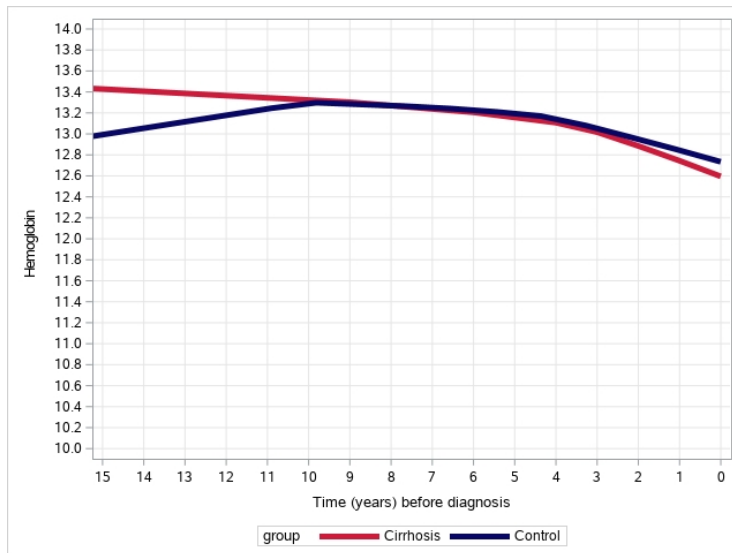
6	Cirrhosis	2590	220.29	76.48	17	216	794	<0.0001
	Control	6298	244.39	63.01	5	239	1306	
7	Cirrhosis	2273	221.56	73.26	42	217	761	<0.0001
	Control	5507	243.69	62.47	48	238.25	950.5	
8	Cirrhosis	1940	225.1	73.2	31	219.35	715	<0.0001
	Control	4549	244.62	61.41	44.17	238	782	
9	Cirrhosis	1753	225.37	71.36	49	220	691.5	<0.0001
	Control	4195	243.32	60.65	32	238	783.5	
10	Cirrhosis	1478	225.89	70.08	58	220	742	<0.0001
	Control	3581	245.49	63.2	44	237.5	1115	
11	Cirrhosis	1258	226.66	75.73	52	221.75	1192	<0.0001
	Control	3144	244.12	59.53	46.86	239	641	
12	Cirrhosis	1026	227.3	70.3	48	220	947	<

	is		8	6				0.000
								1
	Control	2382	244.3	59.2	34.67	238	649.67	
				4				
13	Cirrhosis	801	231.9	79.2	15	224	1317.33	0.002
			6	3				7
	Control	1841	241.3	57.9	38	237	484	
			1	1				
14	Cirrhosis	628	231.7	69.9	48	227.13	662.4	0.026
			8					1
	Control	1481	238.9	62.9	70	234	1233	
			9	9				
15	Cirrhosis	467	235.6	65.5	70.67	232	629.5	0.138
			3	3				7
	Control	1060	240.8	57.8	89	235	587	
			4	3				

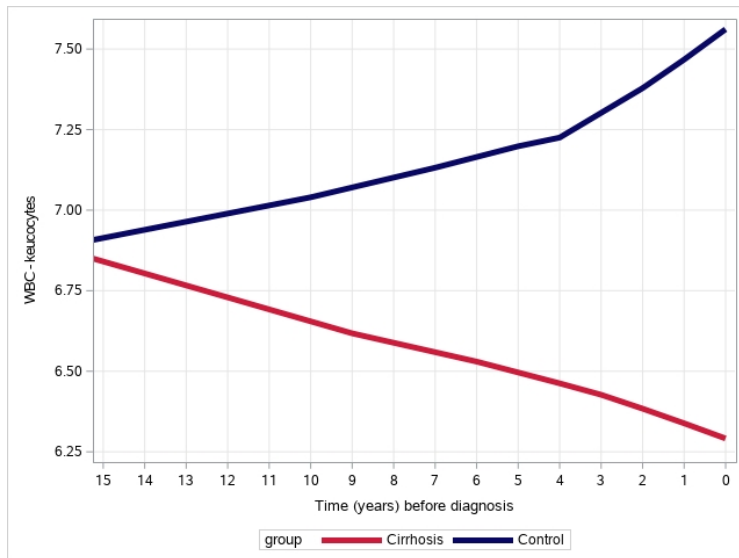
For each subject for each year prior to cirrhosis diagnosis/sampling date, the mean platelets count was calculated. For each year, a comparison of the average platelet's distribution was made using *t*-test.



Supplementary figure 1 Platelets trends along the years prior to cirrhosis diagnosis compared to controls, stratified by age and gender with locally weighted scatterplot smoothing trend.

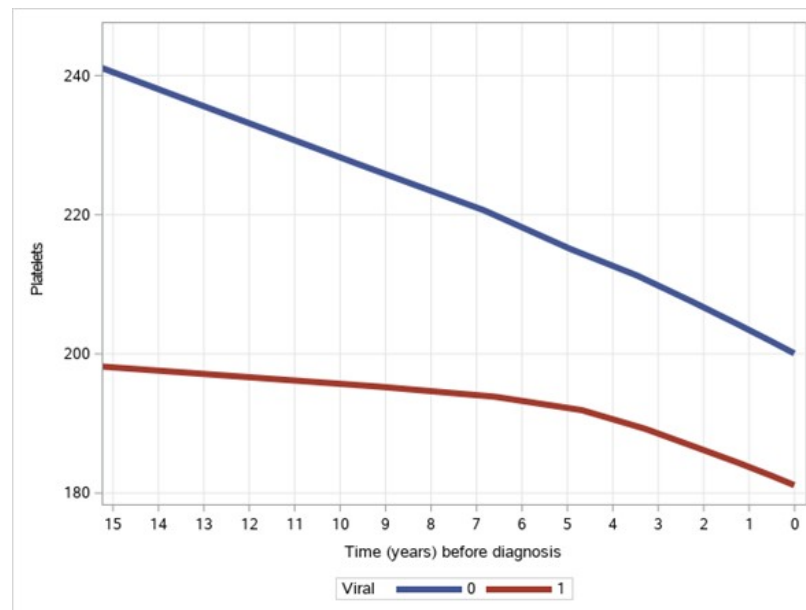


Supplementary figure 2 Association between time and Hemoglobin level among 21032 patients (5258 in cirrhosis group and 15744 controls; 295153 Hemoglobin measurements stratified by study group with locally weighted scatterplot smoothing trend.

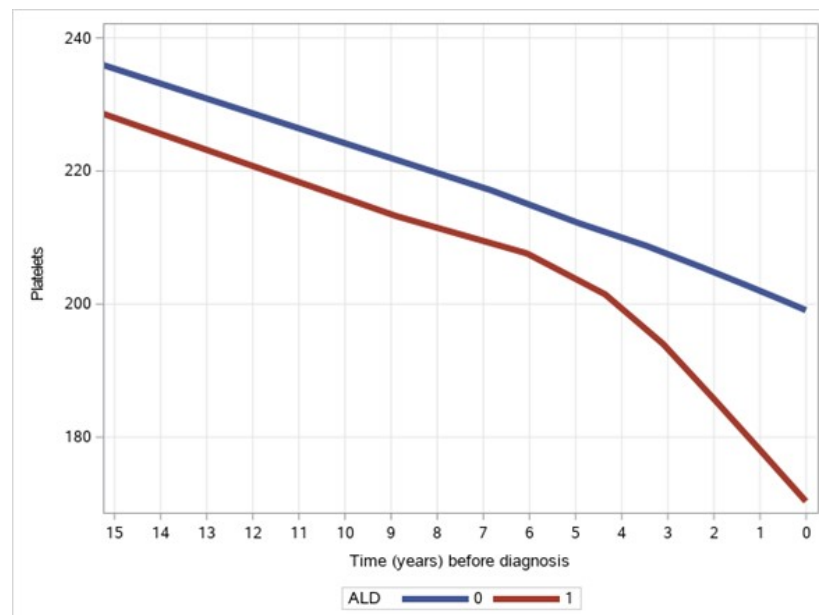


Supplementary figure 3 Association between time and white blood count level among 21032 patients (5258 in cirrhosis group and 15744 controls; 295153 WBC measurements stratified by study group with locally weighted scatterplot smoothing trend.

A

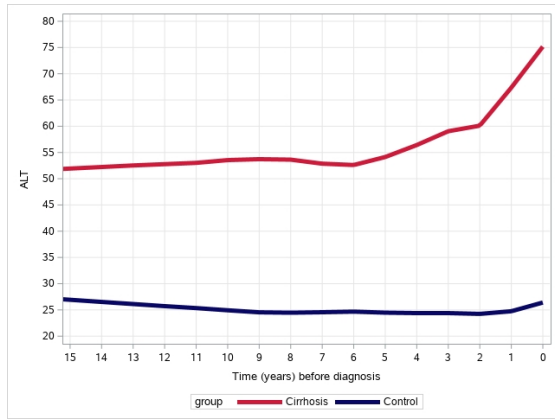


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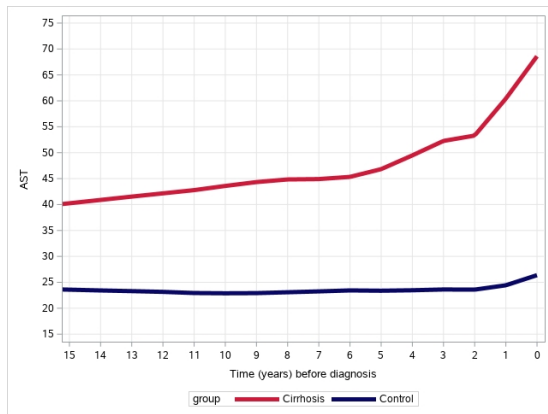


Supplementary figure 4 Platelets trends along the years prior to cirrhosis diagnosis, stratified by cirrhosis etiology. A: The association between time and platelets among cirrhotic patients with viral liver disease (987 patients; 12285 platelets measurements) compared to cirrhotic patients without viral liver disease (4271 patients; 69672 platelets measurements), with locally weighted scatterplot smoothing (LOWESS) for trend; B: The association between time and platelets among cirrhotic patients with alcoholic liver

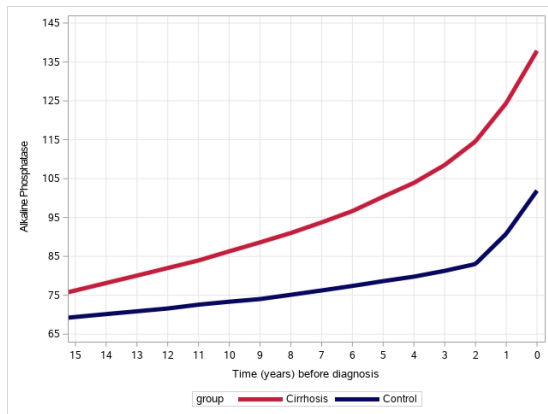
disease (488 patients; 4918 platelets measurements) compared to cirrhotic patients without alcoholic liver disease (4770 patients; 77039 platelets measurements), with LOWESS smooth for trend.



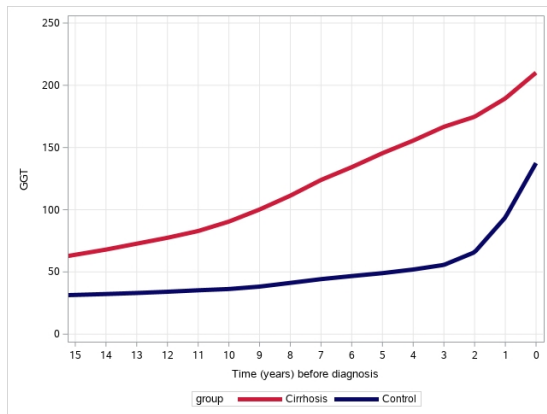
Supplementary figure 5 Association between time and ALT levels among cirrhotic patients compared to controls, stratified by study group with locally weighted scatterplot smoothing trend. There was a gradual increase in both hepatocellular and cholestatic enzymes during the 15 years preceding the diagnosis of liver cirrhosis.



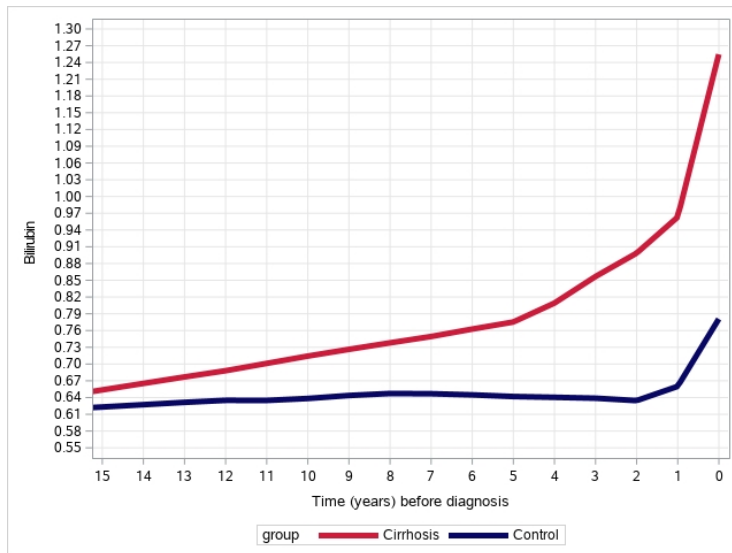
Supplementary figure 6 Association between time and AST levels among cirrhotic patients compared to controls, stratified by study group with locally weighted scatterplot smoothing trend. There was a gradual increase in both hepatocellular and cholestatic enzymes during the 15 years preceding the diagnosis of liver cirrhosis.



Supplementary figure 7 Association between time and alkaline phosphatase levels among cirrhotic patients compared to controls, stratified by study group with locally weighted scatterplot smoothing trend. There was a gradual increase in both hepatocellular and cholestatic enzymes during the 15 years preceding the diagnosis of liver cirrhosis.



Supplementary figure 8: Association between time and GGT levels among cirrhotic patients compared to controls, stratified by study group with locally weighted scatterplot smoothing trend. There was a gradual increase in both hepatocellular and cholestatic enzymes during the 15 years preceding the diagnosis of liver cirrhosis.



Supplementary figure 9 Association between time and bilirubin levels among cirrhotic patients compared to controls, stratified by study group with locally weighted scatterplot smoothing trend. There is a gradual increase in bilirubin levels, within the normal range, in the cirrhosis group compared to controls.