Chronic liver disease independently associated with COVID-19 severity: Evidence based on adjusted effect estimates

SUPPLEMENTARY FILE

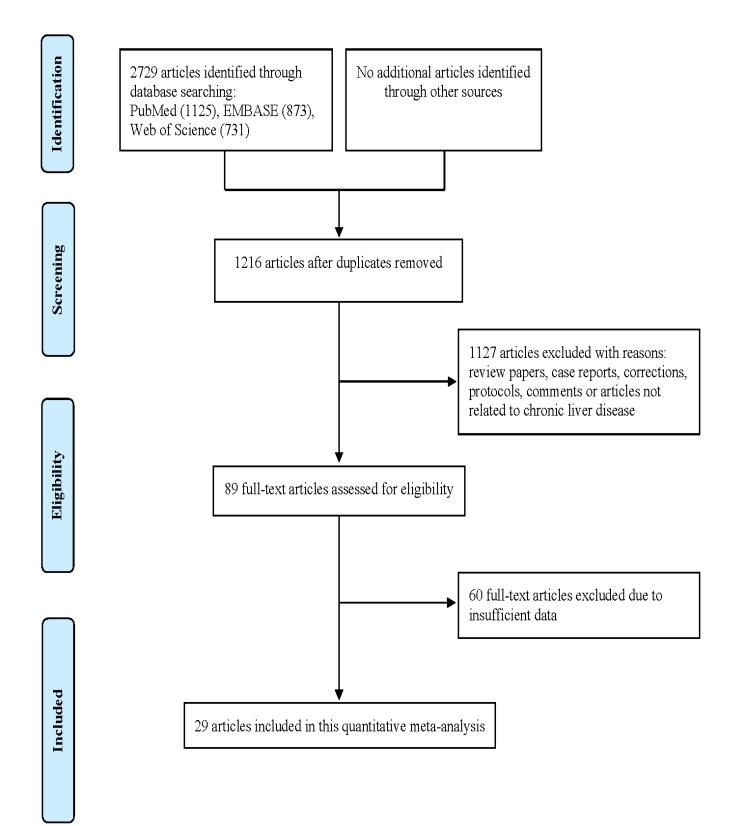
Tables & Figures

Variables	No of studios	Me	eta-regress	sion	Subgroup analy	ysis	H	leterogenei	ity
Variables	No. of studies	Tau ²	t-Value	P value	Pooled ES (95% CI)	P value	I^2	χ^2	P value
Sample size		0.128	1.37	0.182					
≥ 1000	16				1.36 (1.14-1.64)	0.001	38.3%	24.32	0.060
< 1000	13				1.73 (1.12-2.68)	0.014	66.9%	36.23	< 0.001
Age (years)		0.170	0.29	0.770					
≥ 60	18				1.53 (1.23-1.91)	< 0.001	47.3%	30.17	0.025
< 60	11				1.44 (0.88-2.36)	0.151	86.8%	75.58	< 0.001
Male (%)		0.167	0.10	0.918					
≥ 55	14				1.48 (1.17-1.88)	0.001	57.4%	30.52	0.004
< 55	15				1.51 (0.99-2.30)	0.057	78.2%	64.30	<0.001
Effect estimate		0.162		0.397					
HR	11		0.11	0.911	1.33 (1.03-1.72)	0.030	38.2%	16.18	0.095
OR	17		0.57	0.575	1.75 (1.19-2.58)	0.005	90.7%	172.18	<0.001
RR	1		-	-	1.19 (0.45-3.17)	0.728	-	-	-
Region		0.177		0.374					
Asia	14		0.44	0.660	1.28 (0.78-2.12)	0.330	86.2%	93.89	<0.001
North America	7		-	-	1.49 (1.18-1.87)	0.001	0.00%	4.43	0.619
Europe	8		0.76	0.454	1.82 (1.32-2.52)	<0.001	64.3%	19.62	0.006
Study design		0.169	0.46	0.646					
Retrospective	24				1.57 (1.13-2.18)	0.008	89.1%	211.61	< 0.001
Others	5				1.45 (1.15-1.83)	0.001	16.8%	4.81	0.308

Table S1 Subgroup analysis and meta-regression

Note: CI, confidence interval; HR, hazard ratio; OR, odds ratio; RR, relative risk; ES, effect size.

Figure S1 Flow diagram of study selection



Study ID	adjusted–effect (95% CI)	% Weigh
<1000		
Liu et al	0.56 (0.23, 1.36)	3.53
Tang et al	0.94 (0.29, 3.02)	2.81
Feng et al	1.00 (0.13, 7.76)	1.41
Li et al	1.19 (0.45, 3.19)	3.28
Posso et al	1.24 (0.39, 3.95)	2.84
Shang et al	1.37 (0.45, 4.12)	2.97
Forlano et al	1.47 (0.57, 3.90)	3.33
Shah et al	1.89 (0.23, 15.44)	1.36
Hashemi et al	2.00 (0.94, 4.28)	3.89
Guo et al	2.30 (0.48, 10.90)	2.05
Salacup et al	> 2.61 (0.39, 17.43)	1.58
Mahamid et al*	 3.28 (3.16, 3.39) 	5.38
Galiero et al	♦ 5.88 (2.39, 14.46)	3.50
Subtotal (I-squared = 66.9%, p = 0.000)	1.73 (1.12, 2.68)	37.94
>=1000		
Yu et al	0.75 (0.23, 2.44)	2.79
An et al	0.76 (0.37, 1.57)	3.99
Emami et al	0.81 (0.35, 1.15)	4.35
Gupta et al	0.92 (0.49, 1.71)	4.28
Ji et al*	0.96 (0.46, 1.99)	3.97
Lee SG et al	1.01 (0.58, 1.74)	4.48
Rubio–Rivas et al	1.20 (1.00, 1.44)	5.26
loannou et al	1.55 (1.16, 2.07)	5.10
Clift et al*	1.59 (1.12, 2.25)	4.98
Reilev et al	1.80 (1.00, 3.30)	4.35
Yan et al	1.84 (0.44, 7.73)	2.27
Berenguer et al	- 2.03 (1.31, 3.13)	4.78
Bauer et al	2.14 (0.76, 6.07)	3.13
Omrani et al	2.46 (0.72, 8.47)	2.67
Lee YR et al	2.86 (1.04, 9.30)	2.99
Kolhe et al	◆ 4.37 (1.27, 15.10)	2.66
Subtotal (I–squared = 38.3% , p = 0.060)	1.36 (1.14, 1.64)	62.06
	1.50 (1.14, 1.04)	02.00
Overall (I–squared = 89.6%, p = 0.000)	1.52 (1.14, 2.02)	100.00
NOTE: Weights are from random effects analysis		
I I .0574 1	І 17.4	

Figure S2 The association between chronic liver disease and COVID-19 severity: Subgroup analysis by sample size. * indicates combined value calculated from subgroups.

Study ID	adjusted–effect (95% CI)	% Weight
Retrospective study		
Liu et al	0.56 (0.23, 1.36)	3.53
Yu et al	0.75 (0.23, 2.44)	2.79
An et al	0.76 (0.37, 1.57)	3.99
Gupta et al	0.92 (0.49, 1.71)	4.28
Tang et al	0.94 (0.29, 3.02)	2.81
Ji et al*	0.96 (0.46, 1.99)	3.97
Lee SG et al	1.01 (0.58, 1.74)	4.48
Li et al	1.19 (0.45, 3.19)	3.28
Rubio–Rivas et al	1.20 (1.00, 1.44)	5.26
Posso et al	1.24 (0.39, 3.95)	2.84
Shang et al	1.37 (0.45, 4.12)	2.97
Forlano et al	1.47 (0.57, 3.90)	3.33
Yan et al	1.84 (0.44, 7.73)	2.27
Shah et al	1.89 (0.23, 15.44)	1.36
Hashemi et al	2.00 (0.94, 4.28)	3.89
Berenguer et al	2.03 (1.31, 3.13)	4.78
Bauer et al	2.14 (0.76, 6.07)	3.13
Guo et al	2.30 (0.48, 10.90)	2.05
Omrani et al	2.46 (0.72, 8.47)	2.67
Salacup et al	> 2.61 (0.39, 17.43)	1.58
Lee YR et al	♦ 2.86 (1.04, 9.30)	2.99
Mahamid et al*	♦ 3.28 (3.16, 3.39)	5.38
Kolhe et al	♦ 4.37 (1.27, 15.10)	2.66
Galiero et al	♦ 5.88 (2.39, 14.46)	3.50
Subtotal (I-squared = 89.1%, p = 0.000)	1.57 (1.13, 2.18)	79.81
Others		
Emami et al	0.81 (0.35, 1.15)	4.35
Feng et al	1.00 (0.13, 7.76)	1.41
oannou et al	1.55 (1.16, 2.07)	5.10
Clift et al*	1.59 (1.12, 2.25)	4.98
Reilev et al	1.80 (1.00, 3.30)	4.35
Subtotal (I–squared = 16.8%, p = 0.308)	1.45 (1.15, 1.83)	20.19
Overall (I-squared = 89.6%, p = 0.000)	1.52 (1.14, 2.02)	100.00
NOTE: Weights are from random effects analysis		
.0574 1	 17.4	

Figure S3 The association between chronic liver disease and COVID-19 severity: Subgroup analysis by study design. * indicates combined value calculated from subgroups.

Study ID	adjusted–effect (95% CI)	% Weigh
		weigh
>=60		
Liu et al	0.56 (0.23, 1.36)	3.53
Yu et al	0.75 (0.23, 2.44)	2.79
Gupta et al	0.92 (0.49, 1.71)	4.28
Tang et al	0.94 (0.29, 3.02)	2.81
Feng et al	1.00 (0.13, 7.76)	1.41
Rubio–Rivas et al	1.20 (1.00, 1.44)	5.26
Posso et al	1.24 (0.39, 3.95)	2.84
Forlano et al	1.47 (0.57, 3.90)	3.33
loannou et al	1.55 (1.16, 2.07)	5.10
Clift et al*	1.59 (1.12, 2.25)	4.98
Yan et al	1.84 (0.44, 7.73)	2.27
Shah et al	1.89 (0.23, 15.44)	1.36
Hashemi et al	2.00 (0.94, 4.28)	3.89
Berenguer et al	2.03 (1.31, 3.13)	4.78
Salacup et al	> 2.61 (0.39, 17.43)	1.58
Lee YR et al	2.86 (1.04, 9.30)	2.99
Kolhe et al	• 4.37 (1.27, 15.10)	2.66
Galiero et al	♦ 5.88 (2.39, 14.46)	3.50
Subtotal (I–squared = 43.7%, p = 0.025)	1.53 (1.23, 1.91)	59.37
<60		
An et al	0.76 (0.37, 1.57)	3.99
Emami et al	0.81 (0.35, 1.15)	4.35
Ji et al*	0.96 (0.46, 1.99)	3.97
Lee SG et al	1.01 (0.58, 1.74)	4.48
Li et al	1.19 (0.45, 3.19)	3.28
Shang et al	1.37 (0.45, 4.12)	2.97
Reilev et al	1.80 (1.00, 3.30)	4.35
Bauer et al	2.14 (0.76, 6.07)	3.13
Guo et al	2.30 (0.48, 10.90)	2.05
Omrani et al	2.46 (0.72, 8.47)	2.67
Mahamid et al*	3.28 (3.16, 3.39)	5.38
Subtotal (I–squared = 86.8%, p = 0.000)	1.44 (0.88, 2.36)	40.63
		10.05
Overall (I–squared = 89.6%, p = 0.000)	1.52 (1.14, 2.02)	100.00
NOTE: Weights are from random effects analysis		
I I .0574 1	 17.4	

Figure S4 The association between chronic liver disease and COVID-19 severity: Subgroup analysis by age. * indicates combined value calculated from subgroups.

	adjusted–effect (95% CI)	Weigh
>=55		
Liu et al	0.56 (0.23, 1.36)	3.53
Emami et al	0.81 (0.35, 1.15)	4.35
Gupta et al	0.92 (0.49, 1.71)	4.28
Feng et al	1.00 (0.13, 7.76)	1.41
Li et al	1.19 (0.45, 3.19)	3.28
Rubio–Rivas et al	1.20 (1.00, 1.44)	5.26
Forlano et al	1.47 (0.57, 3.90)	3.33
loannou et al 🛛 🚽 🔶 🚽	1.55 (1.16, 2.07)	5.10
Clift et al*	1.59 (1.12, 2.25)	4.98
Hashemi et al	2.00 (0.94, 4.28)	3.89
Berenguer et al	2.03 (1.31, 3.13)	4.78
Omrani et al	2.46 (0.72, 8.47)	2.67
Kolhe et al	4.37 (1.27, 15.10)	2.66
Galiero et al	• 5.88 (2.39, 14.46)	3.50
Subtotal (I–squared = 57.4%, p = 0.004)	1.48 (1.17, 1.88)	53.03
Yu et al	0.75 (0.23, 2.44)	2.79
An et al	0.76 (0.37, 1.57)	3.99
Tang et al	0.94 (0.29, 3.02)	2.81
Ji et al*	0.96 (0.46, 1.99)	3.97
Lee SG et al	1.01 (0.58, 1.74)	4.48
Posso et al	1.24 (0.39, 3.95)	2.84
Shang et al	1.37 (0.45, 4.12)	2.97
Reilev et al	1.80 (1.00, 3.30)	4.35
Yan et al	1.84 (0.44, 7.73)	2.27
Shah et al	1.89 (0.23, 15.44)	1.36
Bauer et al	2.14 (0.76, 6.07)	3.13
Guo et al	2.30 (0.48, 10.90)	2.05
Salacup et al	> 2.61 (0.39, 17.43)	1.58
Lee YR et al	2.86 (1.04, 9.30)	2.99
Mahamid et al*	3.28 (3.16, 3.39)	5.38
Subtotal (I–squared = 78.2%, p = 0.000)	1.51 (0.99, 2.30)	46.97
Overall (I–squared = 89.6%, p = 0.000)	1.52 (1.14, 2.02)	100.00
NOTE: Weights are from random effects analysis		
.0574 1	I 17.4	

Figure S5 The association between chronic liver disease and COVID-19 severity: Subgroup analysis by male percentage (%).* indicates combined value calculated from subgroups.

Figure S6 The association between chronic liver disease and COVID-19 severity: Subgroup analysis by effect estimates. HR, hazard ratio; OR, odds ratio, RR, relative risk. * indicates combined value calculated from subgroups.

Study ID	adjusted-effect (95% CI)	% Weight
HR		
Liu et al	0.56 (0.23, 1.36)	3.53
An et al	0.76 (0.37, 1.57)	3.99
Emami et al		4.35
Tang et al	0.81 (0.35, 1.15) 0.94 (0.29, 3.02)	4.55 2.81
		2.01 1.41
Feng et al	1.00 (0.13, 7.76)	
Shang et al	1.37 (0.45, 4.12)	2.97
loannou et al	1.55 (1.16, 2.07)	5.10
Clift et al*	1.59 (1.12, 2.25)	4.98
Yan et al	1.84 (0.44, 7.73)	2.27
Berenguer et al	2.03 (1.31, 3.13)	4.78
Lee YR et al	2.86 (1.04, 9.30)	2.99
Subtotal (I–squared = 38.2%, p = 0.095)	1.33 (1.03, 1.72)	39.19
OR		
Yu et al	0.75 (0.23, 2.44)	2.79
Gupta et al	0.92 (0.49, 1.71)	4.28
Ji et al*	0.96 (0.46, 1.99)	3.97
Lee SG et al	1.01 (0.58, 1.74)	4.48
Rubio–Rivas et al	1.20 (1.00, 1.44)	5.26
Posso et al	1.24 (0.39, 3.95)	2.84
Forlano et al	1.47 (0.57, 3.90)	3.33
Reilev et al	1.80 (1.00, 3.30)	4.35
Shah et al	1.89 (0.23, 15.44)	1.36
Hashemi et al	2.00 (0.94, 4.28)	3.89
Bauer et al	2.14 (0.76, 6.07)	3.13
Guo et al	2.30 (0.48, 10.90)	2.05
Omrani et al	2.46 (0.72, 8.47)	2.67
Salacup et al	> 2.61 (0.39, 17.43)	1.58
Mahamid et al*	3.28 (3.16, 3.39)	5.38
Kolhe et al	♦ 4.37 (1.27, 15.10)	2.66
Galiero et al	• 5.88 (2.39, 14.46)	3.50
Subtotal (I–squared = 90.7%, p = 0.000)	1.75 (1.19, 2.58)	57.53
RR		
Li et al	1.19 (0.45, 3.19)	3.28
Subtotal (I–squared = .%, p = .)	1.19 (0.45, 3.17)	3.28
	1.17 (0.43, 3.17)	5.20
Overall (I-squared = 89.6%, p = 0.000)	1.52 (1.14, 2.02)	100.00
NOTE: Weights are from random effects analysis		
I I .0574 1	I 17.4	

Study ID	adjusted–effect (95% CI)	% Weigh
		Weigh
Asia		
Liu et al	0.56 (0.23, 1.36)	3.53
Yu et al	0.75 (0.23, 2.44)	2.79
An et al	0.76 (0.37, 1.57)	3.99
Emami et al	0.81 (0.35, 1.15)	4.35
Ji et al*	0.96 (0.46, 1.99)	3.97
Feng et al	1.00 (0.13, 7.76)	1.41
Lee SG et al	1.01 (0.58, 1.74)	4.48
Li et al	1.19 (0.45, 3.19)	3.28
Shang et al	1.37 (0.45, 4.12)	2.97
Yan et al	1.84 (0.44, 7.73)	2.27
Guo et al	2.30 (0.48, 10.90)	2.05
Omrani et al	2.46 (0.72, 8.47)	2.67
Lee YR et al	2.86 (1.04, 9.30)	2.99
Mahamid et al*	♦ 3.28 (3.16, 3.39)	5.38
Subtotal (I–squared = 86.2%, p = 0.000)	1.28 (0.78, 2.12)	46.15
Americas		
Gupta et al	0.92 (0.49, 1.71)	4.28
Tang et al	0.94 (0.29, 3.02)	2.81
Ioannou et al 🛛 🚽 🔶	1.55 (1.16, 2.07)	5.10
Shah et al	1.89 (0.23, 15.44)	1.36
Hashemi et al	2.00 (0.94, 4.28)	3.89
Bauer et al	2.14 (0.76, 6.07)	3.13
Salacup et al	> 2.61 (0.39, 17.43)	1.58
Subtotal (I–squared = 0.0%, p = 0.619)	1.49 (1.18, 1.87)	22.15
Europe		
Rubio–Rivas et al	1.20 (1.00, 1.44)	5.26
Posso et al	1.24 (0.39, 3.95)	2.84
Forlano et al	1.47 (0.57, 3.90)	3.33
Clift et al*	1.59 (1.12, 2.25)	4.98
Reilev et al	1.80 (1.00, 3.30)	4.35
Berenguer et al	2.03 (1.31, 3.13)	4.78
Kolhe et al	♦ 4.37 (1.27, 15.10)	2.66
Galiero et al	• 5.88 (2.39, 14.46)	3.50
Subtotal (I–squared = 64.3%, p = 0.006)	1.82 (1.32, 2.52)	31.70
Overall (I–squared = 89.6%, p = 0.000)	1.52 (1.14, 2.02)	100.00
NOTE: Weights are from random effects analysis		
	 17.4	

Figure S7 The association between chronic liver disease and COVID-19 severity: Subgroup analysis by region. * indicates combined value calculated from subgroups.

