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Multi-Organ Histopathological Changes in SARS COV2 Infection: A Systematic Review and Meta-analysis

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ABSTRACT

Background: *The World Health Organization has officially acknowledged the emergence of Coronavirus Disease 2019 (COVID-19), attributed to the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) virus, as a rapidly escalating global public health issue and declared it a pandemic. SARS-CoV-2 infection can lead to varied and multiorgan pathologies, with the most notable impacts occurring in the lungs (characterized by phases of diffuse alveolar damage, microthrombi, and bronchopneumonia), heart (involving lymphocytic myocarditis), kidney (resulting in acute tubular injury), and vasculature (involving microthrombi and deep vein thrombi).* ***Objectives:*** *To summarize, resolve contradiction and provide solid evidence on multiorgan histopathological changes caused by SARS-CoV2 infection.* ***Material and method:*** *Histological data obtained from autopsy and biopsy studies were gathered following the guidelines of the Preferred Reporting Items for Systematic Review (PRISMA). An extensive electronic search was conducted on databases such as PubMed, Science Direct, Scopus, and Google Scholar, covering the period from database inception to March 2022. The collected studies underwent a systematic literature search, and a thorough critical review was performed.* ***Result:*** *After excluding studies that did not meet the eligibility criteria, a total of 58 articles were included in the review. We estimate the histopathological findings of 13 organ. For the pool proportion of exudative, proliferative and fibrotic phase of diffuse alveolar damage of lung is (70.666%, 56.126% and 33.031%) respectively. For liver steotosis is 35.808%. For acute tubular injury of kidney is 74.872%. For adrenal cortical necrosis is 13.113%. For brain gliosis is 13.865%. For heart necrosis is 5.477%. For gastrointestinal tract the pool proportion of inflammatory cells infiltration is 6.171%. For placental infarction is 25.684%. For orchitis is 29.019%. For perivascular inflammation of skin is 35.176%. For lymphocytic depletion of white pulp of spleen is 69.204%. For hemophagiocytosis of lymph node is 7.022%. For bone marrow fibrosis is 8.473%.*

Conclusion: *COVID-19 is characterized as a multiorgan infection closely associated with a hyperinflammatory state, believed to initiate with diffuse alveolar damage and immuno-thrombotic microangiopathy. The extensive activation of the immune system and microvascular damage may contribute to indirect harm to other organs, although the direct impact of the virus on these tissues cannot be ruled out.*

Keywords: Covid 19, SARS-Cov2, Meta-Analysis and Review.

Article Information

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INTRUDUCTION

The global spread of the novel SARS-CoV-2 (severe acute respiratory syndrome coronavirus2) infection has prompted the World Health Organization to declare it a pandemic[1]. This virus easily transmits through droplets, fomites, or contact with the bodily fluids of infected individuals reaching another person's face, mouth, nose, or eyes. SARS-CoV-2 binds to Angiotensin-converting enzyme 2 (ACE2), highly expressed in the respiratory tract, initiating invasion into human cells. This invasion results in severe destruction and inflammation across various organs, potentially leading to fibrosis and affecting vascular supply. Clinical presentations primarily encompass fever, cough, fatigue, and shortness of breath, accompanied by less frequent symptoms such as headache, sore throat, and rhinorrhea. Approximately one-fifth of patients (20%) experience severe manifestations, including respiratory failure, multiorgan failure, and septic shock, necessitating intensive care[2,3,4].

The incubation period of covid19 range between 0–24 days[5]. COVID-19 predominantly affects the lungs and heart. In the lungs, the characteristic injury pattern is diffuse alveolar damage (DAD), representing a nonspecific interstitial pneumonia progressing through distinct phases. This pattern involves hyaline membranes in early stages and fibrosis in later stages, often with interstitial lymphocytic infiltrates featuring predominant CD4-positive T cells. Severe infections may display "acute fibrinous and organizing pneumonia (AFOP)," characterized by intra-alveolar fibrin balls without hyaline membranes. Other common findings include microvascular thrombi and hemorrhage. In the heart, a spectrum from mild interstitial chronic inflammation within the myocardium without necrosis to lymphocytic myocarditis with myonecrosis is observed. Additional organs involved in this disease are the liver, spleen, and kidney. The liver exhibits frequent sinusoidal dilatation with congestion and steatosis. The spleen typically shows lymphocytic depletion of the white pulp, leading to a decrease or absence of lymphoid follicles. Kidney involvement manifests as acute tubular necrosis (ATN), characterized by glomerular capillary thrombi, vacuolization, and dilatation of tubules[6].

MATERIAL AND METHOD

Histological data obtained from autopsy and biopsy studies adhered to Preferred Reporting Items for Systematic Review and Meta-Analysis (PRISMA) standards. A comprehensive electronic search spanning PubMed, Science Direct, Scopus, and Google Scholar, covering the period from the inception of databases from December 1st, 2021 to March 1st, 2022, was conducted, as illustrated in Figure 1.

Inclusion criteria encompassed articles that presented histopathological observations of organs in individuals diagnosed with COVID-19 following postmortem examinations or biopsies.

Exclusive Criteria: Articles that did not mention about histopathology of organs, unavailable full text studies on animal models and case report and reviews.

Statistical analysis involved the consolidation of data for each histopathological observation related to SARS-CoV-2 infection in different organs. Prevalence of event rates, presented as proportions with a 95% confidence interval, was calculated. Pooled proportions were determined through random-effects models, and heterogeneity was assessed using the Q statistic and I2. Using I-Squared test. Random effect model used when there is significant heterogeneity. In general, random effect model adopted to overcome heterogeneity between studies.

The lung: A total of 352 from 487 (72.2%) patients demonstrated exudative phase of diffuse alveolar damage. Upon meta-analysis, the data indicated a pooled proportion of exudative phase of 70.666%. 95% confidence interval (CI): 59.538 to 80.666 with notable heterogeneity observed among the studies (P = < 0.0001; I2 =86.10%) as showed in table 1 and figure 2.

A total of 205 from 487 (42%) patients demonstrated proliferative phase of diffuse alveolar damage. Upon meta-analysis, the data indicated a pooled proportion of proliferative phase of 56.126%. 95% confidence interval (CI): 37.322 to 74.059 with notable heterogeneity observed among the studies (P =< 0.0001; I2 =94.97%) as showed in table 2 and figure 3.

A total of 161 from 487 (33%) patients demonstrated fibrotic phase of diffuse alveolar damage. Upon meta-analysis, the data indicated a pooled proportion of fibrotic phase of 33.031%. 95% confidence interval (CI): 19.972 to 47.586 with notable heterogeneity observed among the studies (P =< 0.0001; I2 =91.67%) as showed in table 3 and figure 4.

The liver: A total of 168 from 516 (32.5%) patients demonstrate steotosis of the liver. Upon meta-analysis, the data indicated a pooled proportion of steotosis of 35.808%. 95% confidence interval (CI): 20.478 to 52.798 with notable heterogeneity observed among the studies (P =< 0.0001; I2 =92.78 %).

The Kidney: A total of 217 from 409 (53%) patients demonstrate acute tubular injury (ATI). Upon meta-analysis, the data indicated a pooled proportion of ATI of 74.872 %. 95% confidence interval (CI): 57.095 to 89.133 with notable heterogeneity observed among the studies (P =< 0.0001; I2 = 92.34%).

Adrenal gland: A total of 8 from 140 (5.7%) patients demonstrate cortical necrosis of the adrenal gland. Upon meta-analysis, the data indicated a pooled proportion of cortical necrosis of 13.113 %. 95% confidence interval (CI): 0.805 to 36.741 with notable heterogeneity observed among the studies (P =< 0.0001; I2 =89.40 %).

The brain: A total of 17 from 177 (9.6%) patients demonstrates gliosis. Upon meta-analysis, the data indicated a pooled proportion of gliosis of 13.865 %. 95% confidence interval (CI): 1.071 to 37.535 with notable heterogeneity observed among the studies (P < 0.0001; I2 =92.36%)

The heart: A total of 17 from 415 (4%) patients demonstrate necrosis in the heart. Upon meta-analysis, the data indicated a pooled proportion of necrosis of 5.477 %. 95% confidence interval (CI): 2.341 to 9.825 with notable heterogeneity observed among the studies (P = 0.0035; I2 =53.86 %) as showed in table 4 and figure 5.

Gastrointestinal tract (GIT): A total of 7 from 146 (4.7%) patients demonstrate inflammatory cells infiltration of GIT. Upon meta-analysis, the data indicated a pooled proportion of inflammatory cells infiltration of 6.171 %. 95% confidence interval (CI): 0.00698 to 22.460 with notable heterogeneity observed among the studies (P < 0.0001; I2 =85.24 %).

The placenta: A total of 16 from 109(14.6%) patients demonstrates placental infarction. Upon meta-analysis, the data indicated a pooled proportion of placental infarction of25.684 %. 95% confidence interval (CI): 0.346 to 71.178 with notable heterogeneity observed among the studies (P < 0.0001; I2 =94.95 %).

The testis: A total of 7 from 23(30.4%) patients demonstrate orchitis. Upon meta-analysis, the data indicated a pooled proportion of orchitis of29.019 %. 95% confidence interval (CI): 0.588 to 76.189 with notable heterogeneity observed among the studies (P = 0.0018; I2 =84.12 %).

Skin: A total of 41 from 99(41.4%) patients demonstrate perivascular inflammation in the skin. Upon meta-analysis, the data indicated a pooled proportion of perivascular inflammation of 35.176 %. 95% confidence interval (CI): 2.182 to 81.139 with notable heterogeneity observed among the studies (P < 0.0001; I2 =95.88 %).

Spleen: A total of 124 from 168(73.8%) patients demonstrate lymphocytic depletion of white pulp of the spleen. Upon meta-analysis, the data indicated a pooled proportion of lymphocytic depletion of white pulp of 69.204 %. 95 % confidence interval (CI): 30.300 to 96.482 with notable heterogeneity observed among the studies (P < 0.0001; I2 =95.61 %).

Lymph node (LN): A total of 4 from 94(4.2%) patients demonstrate absence of hemophagiocytosis in the LN. Upon meta-analysis, the data indicated a pooled proportion of hemophagiocytosis of7.022 %. 95 % confidence interval (CI): 0.121 to 23.118 with notable heterogeneity observed among the studies (P= 0.0019; I2 =73.71 %).

Bone marrow: A total of 12 from 79(15.1%) patients demonstrate fibrosis of bone marrow. Upon meta-analysis, the data indicated a pooled proportion of the fibrosis of 8.473 %. 95 % confidence interval (CI): 0.00105 to 31.320 with notable heterogeneity observed among the studies (P < 0.0001; I2 = 87.01%).

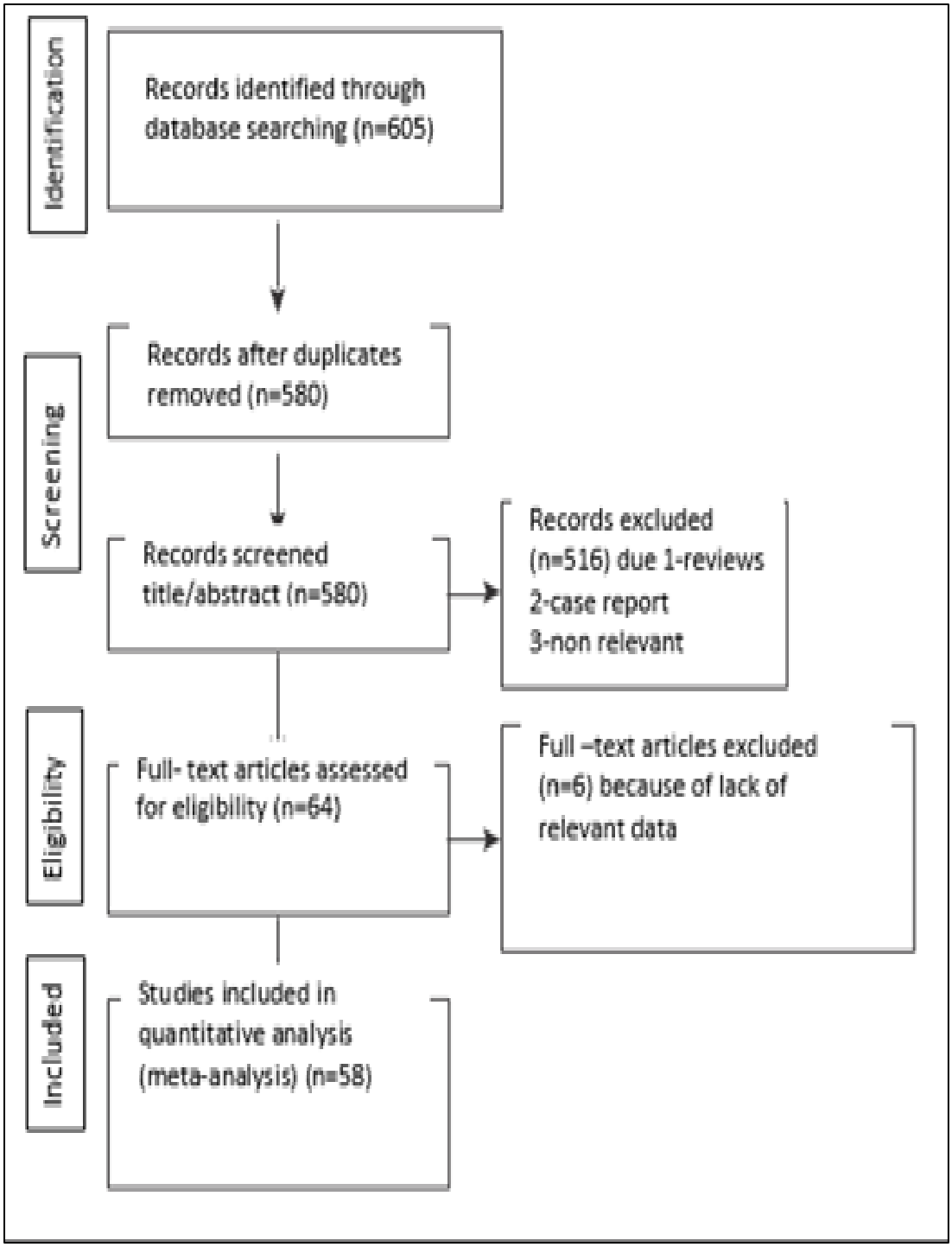


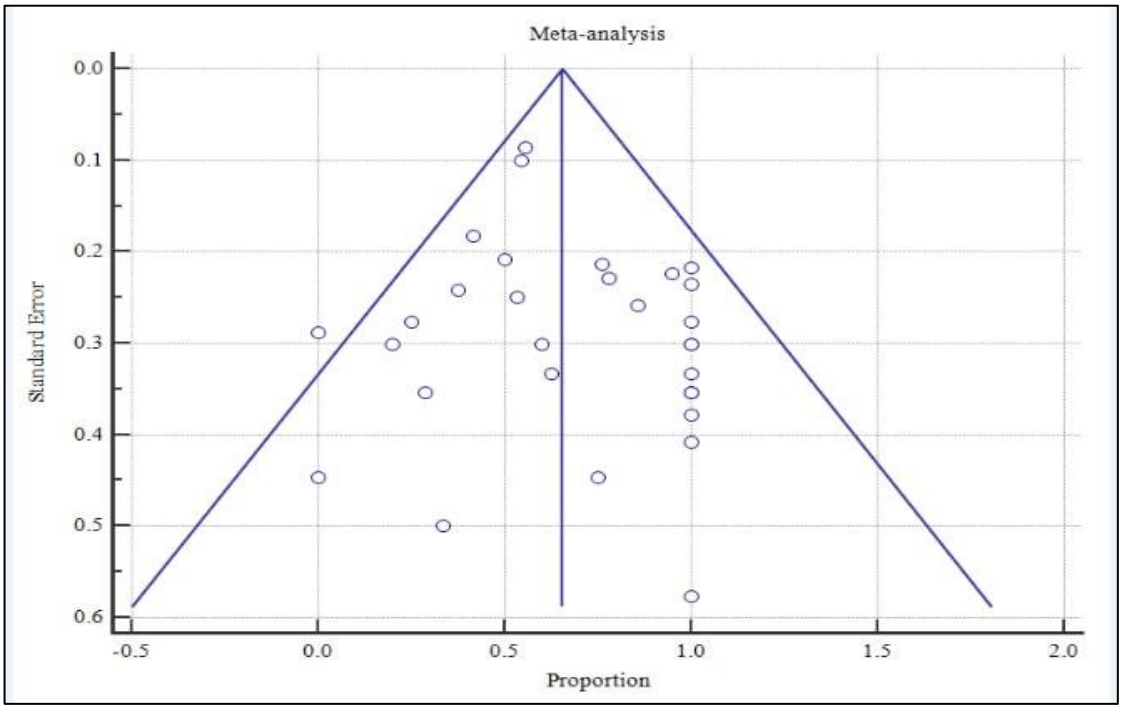
Figure 1. The PRISMA flow diagram, outlining the process of literature search and selection, adheres to the PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-analyses) guidelines.

Table 1. Show how the Forest plots of exudative phase of DAD of coronavirus patients.

Study	Standard deviation	Proportion (%)	95% CI
DUAN et al., 2020	6	100.000	54.074 to 100.000
Núñez-Torrón et al., 2020	16	37.500	15.198 to 64.565
Bösmüller et al., 2020	4	75.000	19.412 to 99.369
Falleni et al., 2021	7	100.000	59.038 to 100.000
Pessolani et al., 2020	4	0.000	0.000 to 60.236
Rapkiewicz et al., 2020	7	100.000	59.038 to 100.000
Schurink et al., 2020	18	77.778	52.363 to 93.591
Wang et al., 2021	2	100.000	15.811 to 100.000
Recalde-Zamacona et al., 2020	10	100.000	69.150 to 100.000
Haberecker et al., 2021	15	53.333	26.586 to 78.733
Wong et al., 2021	8	100.000	63.058 to 100.000
Hirschbu¨ hl et al., 2021	19	94.737	73.972 to 99.867
Remmelink et al., 2020	17	100.000	80.494 to 100.000
Bryce et al., 2021	99	54.545	44.225 to 64.586
Diaz et al., 2021	11	0.000	0.000 to 28.491
Williams et al., 2021	5	100.000	47.818 to 100.000
Magro et al., 2020	12	100.000	73.535 to 100.000
Bradley et al., 2020	14	85.714	57.187 to 98.221
Merdji et al.,2021	22	50.000	28.221 to 71.779
Flikweert et al., 2020	7	28.571	3.669 to 70.958
Felix et al., 2021	12	25.000	5.486 to 57.186
Buja et al., 2021	3	33.333	0.840 to 90.570
Himware et al., 2021	29	41.379	23.524 to 61.064
Fox et al., 2020	10	20.000	2.521 to 55.610
Hanley et al., 2020	10	60.000	26.238 to 87.845
Duarte-Neto et al., 2020	10	100.000	69.150 to 100.000
Menter et al., 2020	21	76.190	52.834 to 91.782
Roden et al.,2020	8	62.500	24.486 to 91.477
Hooper et al., 2021	135	55.556	46.761 to 64.101
Prieto-Pérez et al., 2020	20	100.000	83.157 to 100.000
Total (fixed effects)	561	65.272	61.280 to 69.111
Total (random effects)	561	70.666	59.538 to 80.666

Test for heterogeneity

Q	208.6007
DF	29
Significance level	P < 0.0001
I^2 (inconsistency)	86.10%
95% CI for I^2	81.23 to 89.70



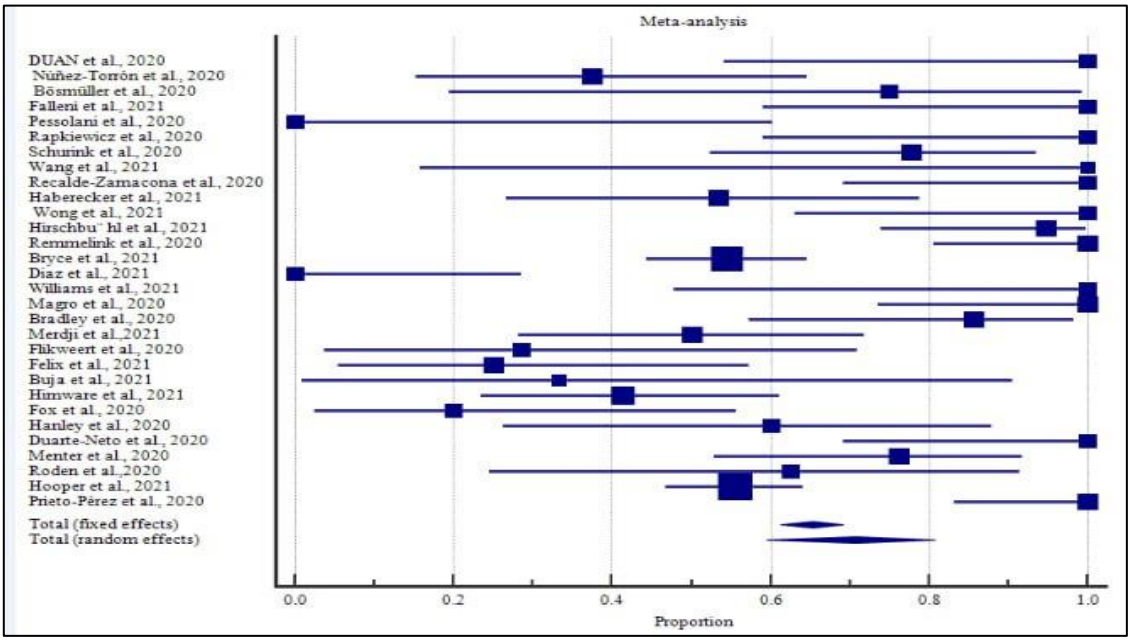


Figure 2. Show the Forest and funnel plots of exudative phase of DAD of coronavirus patients.

Table 2. Show the Forest plots of proliferative phase of DAD of coronavirus patients.

Study	Standard deviation	Proportion (%)	95% CI
DUAN et al., 2020	6	100.000	54.074 to 100.000
Núñez-Torrón et al., 2020	16	62.500	35.435 to 84.802
Bösmüller et al., 2020	4	100.000	39.764 to 100.000
Falleni et al., 2021	7	100.000	59.038 to 100.000
Pessolani et al., 2020	4	75.000	19.412 to 99.369
Rapkiewicz et al., 2020	7	100.000	59.038 to 100.000
Schurink et al., 2020	18	83.333	58.582 to 96.421
Wang et al., 2021	2	50.000	1.258 to 98.742
Recalde-Zamacona et al., 2020	10	100.000	69.150 to 100.000
Haberecker et al., 2021	15	53.333	26.586 to 78.733
Wong et al., 2021	8	100.000	63.058 to 100.000
Hirschbu¨ hl et al., 2021	19	78.947	54.435 to 93.948
Remmelink et al., 2020	17	100.000	80.494 to 100.000
Bryce et al., 2021	99	28.283	19.686 to 38.222
Diaz et al., 2021	11	0.000	0.000 to 28.491
Williams et al., 2021	5	60.000	14.663 to 94.726
Magro et al., 2020	12	100.000	73.535 to 100.000
Bradley et al., 2020	14	0.000	0.000 to 23.164
Merdji et al.,2021	22	72.727	49.778 to 89.271
Flikweert et al., 2020	7	100.000	59.038 to 100.000
Felix et al., 2021	12	0.000	0.000 to 26.465
Buja et al., 2021	3	33.333	0.840 to 90.570
Himware et al., 2021	29	0.000	0.000 to 11.944
Fox et al., 2020	10	70.000	34.755 to 93.326
Hanley et al., 2020	10	40.000	12.155 to 73.762
Duarte-Neto et al., 2020	10	80.000	44.390 to 97.479
Menter et al., 2020	21	38.095	18.107 to 61.565
Roden et al.,2020	8	0.000	0.000 to 36.942
Hooper et al., 2021	135	0.000	0.000 to 2.696
Prieto-Pérez et al., 2020	20	0.000	0.000 to 16.843
Total (fixed effects)	561	31.421	27.695 to 35.334
Total (random effects)	561	56.126	37.322 to 74.059

Test for heterogeneity

Q	576.0321
DF	29
Significance level	P < 0.0001
I^2 (inconsistency)	94.97%
95% CI for I^2	93.71 to 95.97

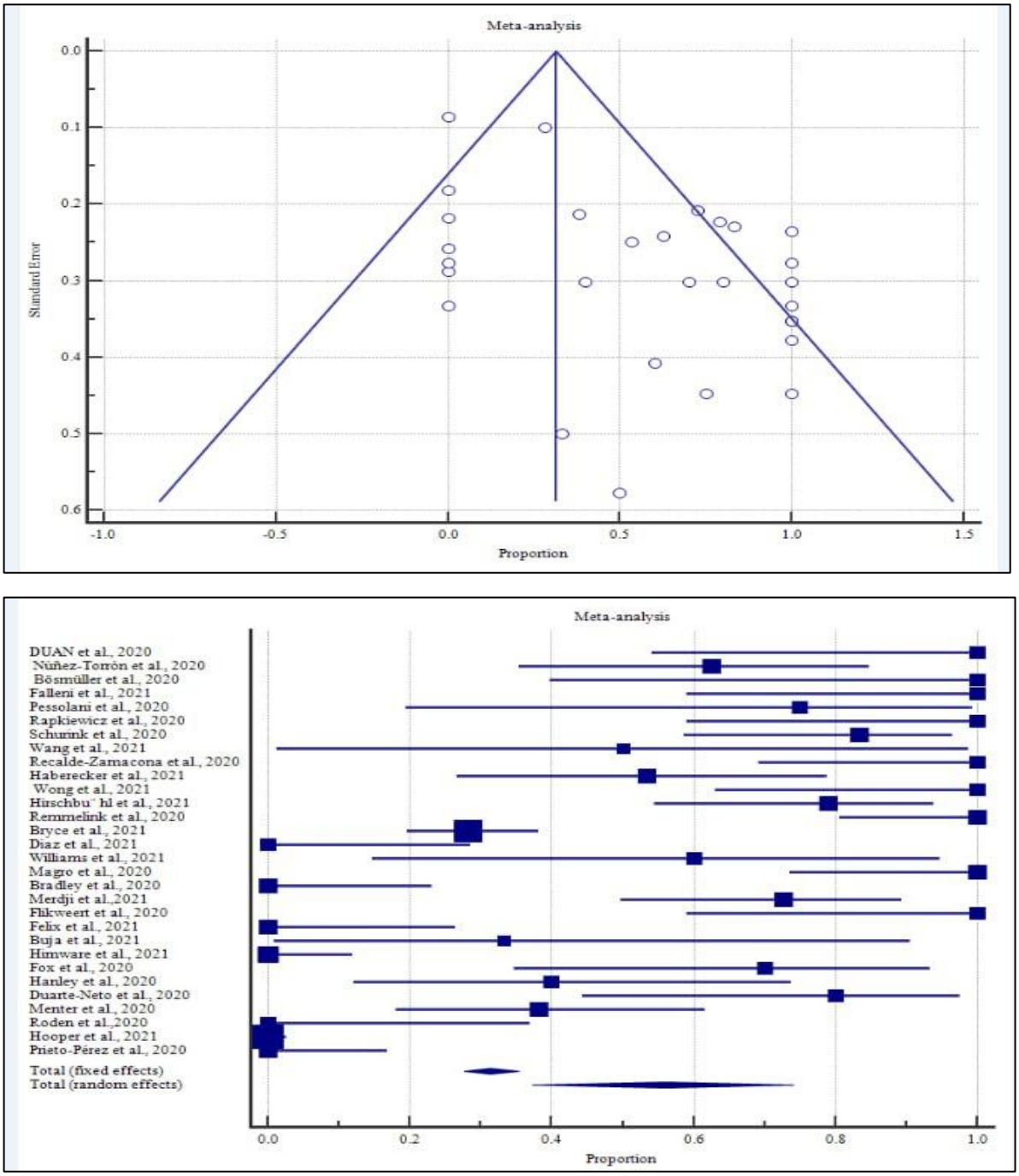


Figure 3. Show the Forest and funnel plots of proliferative phase of DAD of coronavirus patients.

Table 3. Show the Forest plots of fibrotic phase of DAD of coronavirus patients.

Study	Standard deviation	Proportion (%)	95% CI
DUAN et al., 2020	6	0.000	0.000 to 45.926
Núñez-Torrón et al., 2020	16	25.000	7.266 to 52.377
Bösmüller et al., 2020	4	50.000	6.759 to 93.241
Falleni et al., 2021	7	100.000	59.038 to 100.000
Pessolani et al., 2020	4	50.000	6.759 to 93.241
Rapkiewicz et al., 2020	7	0.000	0.000 to 40.962
Schurink et al., 2020	18	22.222	6.409 to 47.637
Wang et al., 2021	2	0.000	0.000 to 84.189
Recalde-Zamacona et al., 2020	10	100.000	69.150 to 100.000
Haberecker et al., 2021	15	53.333	26.586 to 78.733
Wong et al., 2021	8	100.000	63.058 to 100.000
Hirschbu" hl et al., 2021	19	5.263	0.133 to 26.028
Remmelink et al., 2020	17	58.824	32.925 to 81.556
Bryce et al., 2021	99	0.000	0.000 to 3.658
Diaz et al., 2021	11	27.273	6.022 to 60.974
Williams et al., 2021	5	20.000	0.505 to 71.642
Magro et al., 2020	12	100.000	73.535 to 100.000
Bradley et al., 2020	14	78.571	49.202 to 95.342
Merdji et al.,2021	22	45.455	24.386 to 67.790
Flikweert et al., 2020	7	14.286	0.361 to 57.872
Felix et al., 2021	12	0.000	0.000 to 26.465
Buja et al., 2021	3	33.333	0.840 to 90.570
Himware et al., 2021	29	0.000	0.000 to 11.944
Fox et al., 2020	10	10.000	0.253 to 44.502
Hanley et al., 2020	10	30.000	6.674 to 65.245
Duarte-Neto et al., 2020	10	0.000	0.000 to 30.850
Menter et al., 2020	21	0.000	0.000 to 16.110
Roden et al.,2020	8	12.500	0.316 to 52.651
Hooper et al., 2021	135	34.815	26.825 to 43.487
Prieto-Pérez et al., 2020	20	70.000	45.721 to 88.107
Total (fixed effects)	561	24.546	21.126 to 28.222
Total (random effects)	561	33.031	19.972 to 47.586

Test for heterogeneity

Q	348.1990
DF	29
Significance level	P < 0.0001
I^2 (inconsistency)	91.67%
95% CI for I^2	89.21 to 93.57

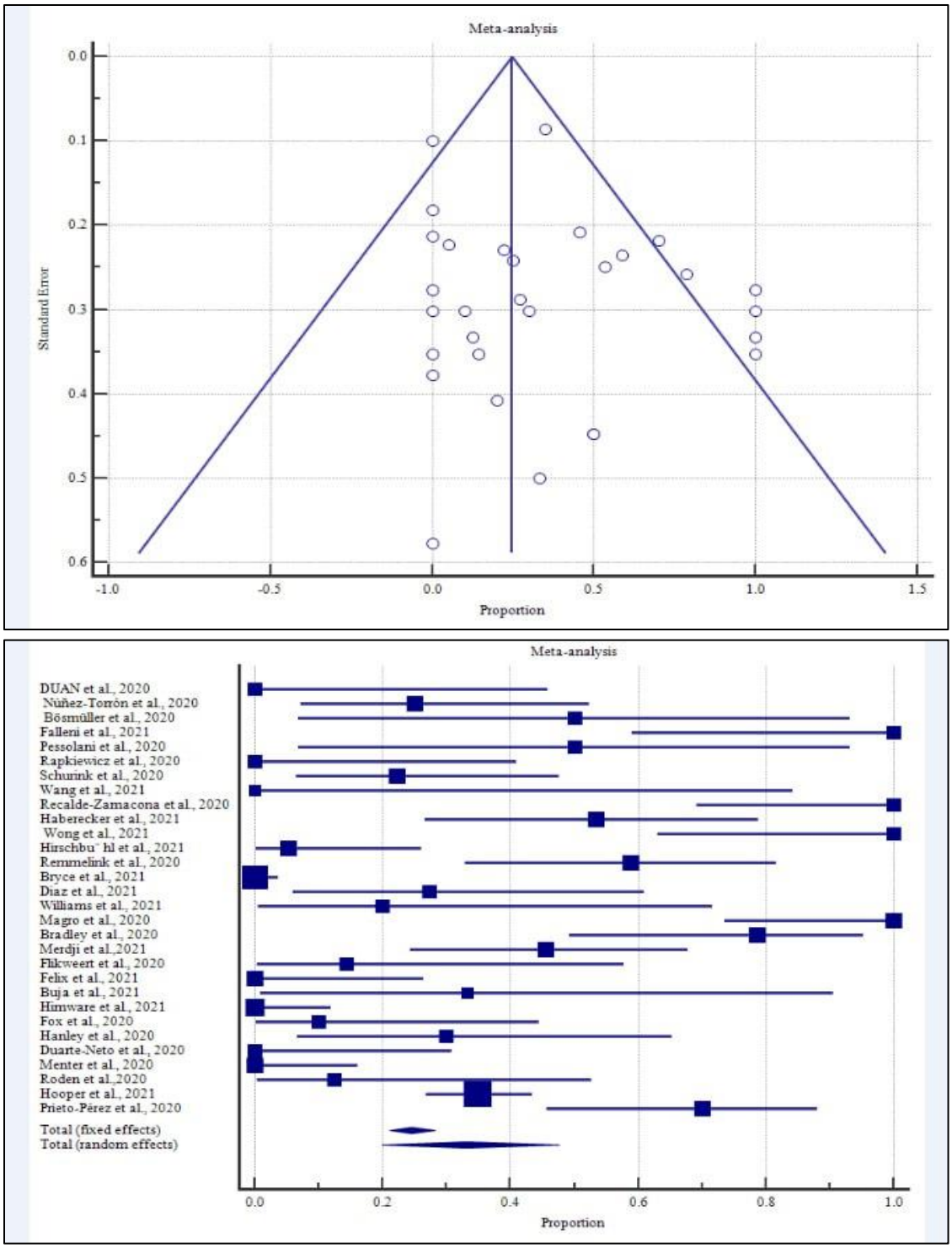


Figure 4 Show the Forest and funnel plots of fibrotic phase of DAD of coronavirus patients.

Table 4. Show the Forest plots of necrosis of the heart of coronavirus patients.

Study	Standard deviation	Proportion (%)	95% CI
Pessolani et al., 2020	3	33.333	0.840 to 90.570
Rapkiewicz et al., 2020	7	42.857	9.899 to 81.595
Schurink et al., 2020	21	0.000	0.000 to 16.110
Nikkhoo et al., 2021	25	0.000	0.000 to 13.719
Wang et al., 2021	1	100.000	2.500 to 100.000
Recalde-Zamacona et al., 2020	10	0.000	0.000 to 30.850
Haberecker et al., 2021	15	0.000	0.000 to 21.802
Wong et al., 2021	5	0.000	0.000 to 52.182
Remmelink et al., 2020	17	11.765	1.458 to 36.441
Bryce et al., 2021	97	0.000	0.000 to 3.732
Magro et al., 2020	12	0.000	0.000 to 26.465
Bradley et al., 2020	14	7.143	0.181 to 33.868
Buja et al., 2021	3	0.000	0.000 to 70.760
Fox et al., 2020	10	0.000	0.000 to 30.850
Hanley et al., 2020	9	11.111	0.281 to 48.250
Duarte-Neto et al., 2020	10	0.000	0.000 to 30.850
Menter et al., 2020	21	4.762	0.120 to 23.816
Hooper et al., 2021	135	5.185	2.110 to 10.392
Total (fixed effects)	415	3.834	2.233 to 6.100
Total (random effects)	415	5.477	2.341 to 9.825

Test for heterogeneity

Q	36.8426
DF	17
Significance level	P = 0.0035
I^2 (inconsistency)	53.86%
95% CI for I^2	21.30 to 72.95

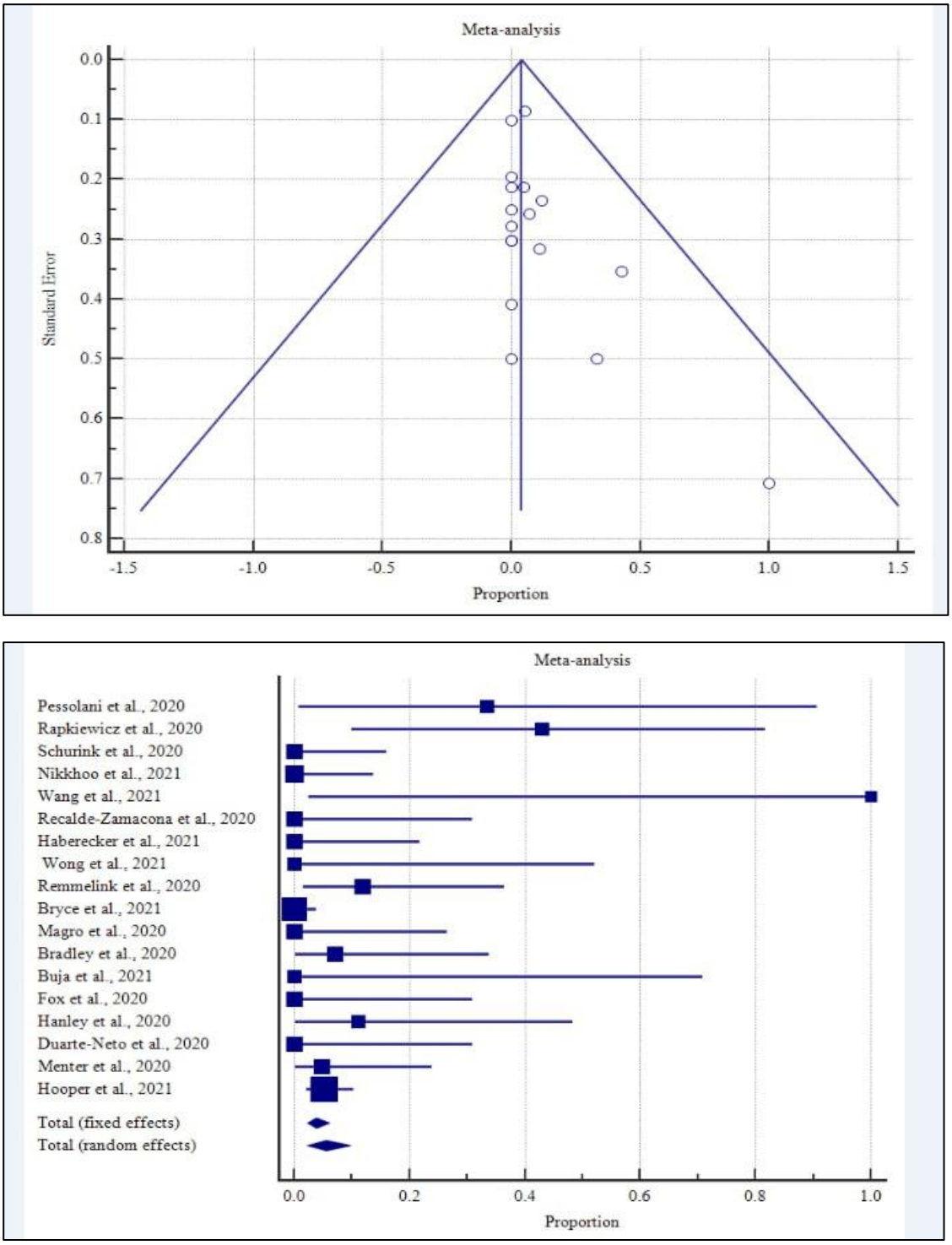


Figure 5. Show the Forest and funnel plots of necrosis of the heart coronavirus patients.

DISCUSSION

In our investigation, we presented key observations pertaining to COVID-19 tissues. We examined studies that documented microscopic (histopathological) data obtained from various organs through both biopsies and autopsies. Post-mortem evidence offers crucial information that contributes to an enhanced comprehension of the pathophysiology of COVID-19 infection. This understanding aids clinicians in identifying optimal and effective treatments to mitigate mortality. Autopsy series reveal the involvement of multiple systems in COVID-19, with respiratory symptoms and findings predominantly observed.

Our study is the first meta-analysis study including histopathological changes of 13 organs with Covid19 (lung, liver, kidney, adrenal gland, brain, heart, GIT, placenta, testis, skin, spleen, lymph node and bone marrow).

Lung histopathological findings in 561 patients show DAD (exudative phase, proliferative phase and fibrotic phase) which agreed with systemic review of (Hariri et al.) [7], (Pandey et al.)[8] and (Pannone et al.)[9]. The pool proportion of exudative phase of DAD is 70.666%, proliferative phase is 56.126%, fibrotic phase is 33.031% , there is only single meta-analysis that shows the proportion of DAD without dividing it in to three phases[10].

Liver histopathological findings in 516 patients show steotosis which agreed with systemic review of (Idalsoaga et al.)[11]

The pool proportion of steotosis is 35.808%, which disagree with (Díaz et al.)[12] which show it 55.1%[13].

Kidney histopathological findings in 409 patients show acute tubular injury which is agreed with systemic review of (Jeyalan et al.)[13].

The pool proportion of ATI is 74.872% which disagree with (Shao et al., Yang et al., Silver et al., and Oliveira et al.) which show (0.10%,0.123%,0.28%,0.12%) respectively [14] [15] [16] [17].

Adrenal histopathological findings in 140 patients show cortical necrosis which agree with the systemic review of (Kanczkowski et al.)[18].

The pool proportion of cortical necrosis is 13.113%, there is no data to compare with it

Brain histopathological findings in 177 patients show gliosis which agree with systemic review of (Pajo et al.)[19].

The pool proportion of gliosis is 13.865%, there is no data to compare with it.

Heart histopathological findings in 415 patients show necrosis which are agree with systemic review of (Almamlouk et al.)[20], (Maiese et al.)[21] and (Roshdy et al.)[22].

The pool proportion of necrosis is 5.477% there is no data to compare with it.

GIT histopathological findings in 146 patients show inflammatory cells infiltration which agree with a systemic review of (Singh et al.)[23] and, (Deshmukh et al.) [24].

The pool proportion of inflammatory cells infiltration is 6.171%, there is no data to compare with it.

Placental histopathological findings in 109 patients show placental infarction which agree with systemic review of (Gesaka et al.)[25], (Sharps et al.)[26], (Almohammadi.)[27] and (Ghazi et al.)[28].

The pool proportion of placental infarction is 25.684%, there is no data to compare with it.

Testicular histopathological findinds in 23 patients show orchitis which agree with systemic review of (Kloping et al.)[29] and (Sengupta et al.)[30].

The pool proportion of orchitis is 29.019%, there is no data to compare with it.

Skin histopathological findings in 99 patients show perivascular inflammation which agree with systemic review of (Nobari et al.)[31] and (Rongioletti et al.)[32].

The pool proportion of perivascular inflammation is 35.176%, there is no data to compare with it.

Splenic histopathological findings in 168 patients show lymphocytic depletion of white pulp which agree with systemic review of (Hammoud et al.)[33], (Malik et al.)[34] and (Octavius et al.)[35].

The pool proportion of lymphocytic depletion of white pulp is 69.204%, there is no data to compare with it.

Lymph node histopathological findings in 94 patients show hemophagiocytosis which agree with systemic review of (Vasquez-Bonilla et al.)[36], and (Octavius et al.)[35].

The pool proportion of hemophagiocytosis is 7.022%, there is no data to compare with it.

Bone marrow histopathological findings in 79 patients show fibrosis which disagree with systemic review of (Octavius et al.)[35], (Vasquez-Bonilla et al.)[36] and (Menezes et al.)[37]

The pool proportion of fibrosis is 8.473%, there is no data to compare with it.

CONCLUSION

COVID-19, characterized by a myriad of symptoms, is increasingly recognized as a systemic disease. Although it primarily affects the respiratory system, evidence of SARS-CoV-2 has been found in various organs, accompanied by organ damage.

REFERENCE

1. Maiese A, Manetti AC, La Russa R, Di Paolo M, Turillazzi E, Frati P, Fineschi V. Autopsy findings in COVID-19-related deaths: a literature review. Forensic Science, Medicine and Pathology. 2021 Jun;17:279-96.doi:10.1007/s12024-020-00310-8
2. Hammoud H, Bendari A, Bendari T, Bougmiza I. Histopathological findings in COVID-19 cases: A Systematic Review. Cureus. 2022 Jun 1;14(6).doi:10.7759/cureus.25573
3. Guo G, Ye L, Pan K, Chen Y, Xing D, Yan K, Chen Z, Ding N, Li W, Huang H, Zhang L. New insights of emerging SARS-CoV-2: epidemiology, etiology, clinical features, clinical treatment, and prevention. Frontiers in cell and developmental biology. 2020 May 22;8:410. doi:10.3389/fcell.2020.00410
4. Karia R, Gupta I, Khandait H, Yadav A, Yadav A. COVID-19 and its modes of transmission. SN comprehensive clinical medicine. 2020 Oct;2(10):1798-801.doi:10.1007/s42399-020-00498-4
5. Siordia Jr JA. Epidemiology and clinical features of COVID-19: A review of current literature. Journal of Clinical Virology. 2020 Jun 1;127:104357. doi:10.1016/j.jcv.2020.104357
6. Pessolani TG, de Legaria MM, Apellániz ME, Moreno SS, Cortés MD, Sánchez SG. Multi-organ pathological findings associated with COVID-19 in postmortem needle core biopsies in four patients and a review of the current literature. Revista Española de Patología. 2021 Oct 1;54(4):275-80.doi:10.1016/j.patol.2020.09.003
7. Hariri LP, North CM, Shih AR, Israel RA, Maley JH, Villalba JA, Vinarsky V, Rubin J, Okin DA, Sclafani A, Alladina JW. Lung histopathology in coronavirus disease 2019 as compared with severe acute respiratory sydrome and H1N1 influenza: a systematic review. Chest. 2021 Jan 1;159(1):73-84.doi:10.1016/j.chest.2020.09.259
8. Pandey P, Agarwal S. Lung pathology in COVID-19: A systematic review. International Journal of Applied and Basic Medical Research. 2020 Oct 1;10(4):226-33.doi:10.4103/ijabmr.IJABMR
9. Pannone G, Caponio VC, De Stefano IS, Ramunno MA, Meccariello M, Agostinone A, Pedicillo MC, Troiano G,

Zhurakivska K, Cassano T, Bizzoca ME. Lung histopathological findings in COVID-19 disease–a systematic review. Infectious Agents and Cancer. 2021 May 17;16(1):34.

10. Satturwar S, Fowkes M, Farver C, Wilson AM, Eccher A, Girolami I, Pujadas E, Bryce C, Salem F, El Jamal SM, Paniz-Mondolfi A. Postmortem findings associated with SARS-CoV-2: systematic review and meta-analysis. The American journal of surgical pathology. 2021 May 1;45(5):587-603.doi:10.1097/PAS.0000000000001650
11. Idalsoaga F, Ayares G, Arab JP, Díaz LA. COVID-19 and indirect liver injury: a narrative synthesis of the evidence. Journal of Clinical and Translational Hepatology. 2021 Oct 10;9(5):760.doi:10.14218/JCTH.2020.00140
12. Díaz LA, Idalsoaga F, Cannistra M, Candia R, Cabrera D, Barrera F, Soza A, Graham R, Riquelme A, Arrese M, Leise MD. High prevalence of hepatic steatosis and vascular thrombosis in COVID-19: A systematic review and meta-analysis of autopsy data. World journal of gastroenterology. 2020 Dec 12;26(48):7693.doi:10.3748/wjg.v26.i48.7693
13. Rehman A, Iqbal MA, Xing H, COVID IA. detection empowered with machine learning and deep learning techniques: A systematic review., 2021, 11, 3414. DOI: https://doi. org/10.3390/app11083414. 19.
14. Shao M, Li X, Liu F, Tian T, Luo J, Yang Y. Acute kidney injury is associated with severe infection and fatality in patients with COVID-19: A systematic review and meta-analysis of 40 studies and 24,527 patients. Pharmacological research. 2020 Nov 1;161:105107. doi:10.1016/j.phrs.2020.105107
15. Yang X, Tian S, Guo H. Acute kidney injury and renal replacement therapy in COVID-19 patients: a systematic review and meta-analysis. International immunopharmacology. 2021 Jan 1;90:107159.doi:10.1016/j.intimp.2020.107159
16. Silver SA, Beaubien-Souligny W, Shah PS, Harel S, Blum D, Kishibe T, Meraz-Munoz A, Wald R, Harel Z. The prevalence of acute kidney injury in patients hospitalized with COVID-19 infection: a systematic review and meta-analysis. Kidney medicine. 2021 Jan 1;3(1):83-98.doi:10.1016/j.xkme.2020.11.008
17. Oliveira CB, Lima CA, Vajgel G, Coelho AV, Sandrin-Garcia P. High burden of acute kidney injury in COVID-19 pandemic: systematic review and meta-analysis. Journal of Clinical Pathology. 2021 Dec 1;74(12):796-803.doi:10.1136/jclinpath-2020-207023
18. Kanczkowski W, Gaba WH, Krone N, Varga Z, Beuschlein F, Hantel C, Andoniadou C, Bornstein SR. Adrenal gland function and dysfunction during COVID-19. Hormone and Metabolic Research. 2022 Aug;54(08):532-9.doi:10.1055/a-1873-2150
19. Pajo AT, Espiritu AI, Apor AD, Jamora RD. Neuropathologic findings of patients with COVID-19: a systematic review. Neurological Sciences. 2021 Apr;42:1255-66.doi:10.1007/s10072-021-05068-7
20. Almamlouk R, Kashour T, Obeidat S, Bois MC, Maleszewski JJ, Omrani OA, Tleyjeh R, Berbari E, Chakhachiro Z, Zein-Sabatto B, Gerberi D. COVID-19–Associated cardiac pathology at the postmortem evaluation: a collaborative

systematic review. Clinical Microbiology and Infection. 2022 Aug 1;28(8):1066-75.doi:10.1016/j.cmi.2022.03.021

21. Maiese A, Frati P, Del Duca F, Santoro P, Manetti AC, La Russa R, Di Paolo M, Turillazzi E, Fineschi V. Myocardial pathology in COVID-19-associated cardiac injury: a systematic review. Diagnostics. 2021 Sep 8;11(9):1647.doi:10.3390/DIAGNOSTICS11091647
22. Roshdy A, Zaher S, Fayed H, Coghlan JG. COVID-19 and the Heart: A Systematic Review of Cardiac Autopsies. Front Cardiovasc Med. 2021;7(January). doi:10.3389/fcvm.2020.626975
23. Singh A, Zaheer S, Kumar N, Singla T, Ranga S. Pathology - Research and Practice Covid19 , beyond just the lungs : A review of multisystemic involvement by Covid19. Pathol - Res Pract. 2021;224(January):153384. doi:10.1016/j.prp.2021.153384
24. Deshmukh V, Motwani R, Kumar A, Kumari C, Raza K. Histopathological observations in COVID-19 : a systematic review. Published online 2021:76-83. doi:10.1136/jclinpath-2020-206995
25. *Gesaka SR, Obimbo MM, Wanyoro A. Coronavirus disease 2019 and the placenta: A literature review. Placenta. 2022;126(December 2021):209-223. doi:10.1016/j.placenta.2022.07.007*
26. Sharps MC, Hayes DJL, Lee S, et al. A structured review of placental morphology and histopathological lesions associated with SARS-CoV-2 infection. *Placenta*. 2020;101(June):13-29. doi:10.1016/j.placenta.2020.08.018
27. Almohammadi NH. A review of the main placenta histopathological findings reported in coronavirus disease 2019. Journal of Taibah University Medical Sciences. 2022 Apr 1;17(2):165-73.doi:10.1016/j.jtumed.2022.02.009
28. Ghazi HA, Burhan MM, Mekkey SM, Kazem HW. Histopathological changes in the placenta of women with COVID-19 infection: A review article. Jour Med Resh and Health Sci. 2022 Sep 28;5(9):2264-9.
29. Kloping YP, Hidayatullah F, Rahman ZA, Chung E, Hakim L. Male Reproductive Tract Involvement and Sperm Parameters in SARS-CoV-2 Patients: A Systematic Review and Meta-Analysis. The World Journal of Men's Health. 2023 Jul;41(3):538.
30. Sengupta P, Leisegang K, Agarwal A. The impact of COVID-19 on the male reproductive tract and fertility: A systematic review. Arab Journal of Urology. 2021 Jul 3;19(3):423-36.doi:10.1080/2090598X.2021.1955554
31. Najar Nobari N, Seirafianpour F, Dodangeh M, Sadeghzadeh-Bazargan A, Behrangi E, Mozafarpoor S, Goodarzi A. A systematic review of the histopathologic survey on skin biopsies in patients with Corona Virus Disease 2019 (COVID-19) who developed virus or drug-related mucocutaneous manifestations. Experimental dermatology. 2021 Sep;30(9):1233-53.doi:10.1111/exd.14384
32. Rongioletti F, Ferreli C, Sena P, Caputo V, Atzori L. Clinicopathologic correlations of COVID-19–related cutaneous manifestations with special emphasis on histopathologic patterns. Clinics in Dermatology. 2021 Jan 1;39(1):149-62.doi:10.1016/j.clindermatol.2020.12.004
33. Hammoud H, Bendari A, Bendari T, Bougmiza I. Post mortem pathological

findings in COVID-19 cases: A Systematic Review. medRxiv. 2020 Oct 14:2020-10.

34. Malik P, Patel K, Akrmah M, Donthi D, Patel U, Khader SN, Asiry S. COVID-19: a Disease with a Potpourri of Histopathologic Findings—a Literature Review and Comparison to the Closely Related SARS and MERS. SN comprehensive clinical medicine. 2021 Dec;3(12):2407-34.
35. Octavius GS, Wijaya JH, Tan AO, Muljono MP, Chandra S, Juliansen A. Autopsy findings of pediatric COVID-19: a systematic review. Egyptian Journal of Forensic Sciences. 2022 Jul 14;12(1):32.doi:10.1186/s41935-022-00288-0
36. Vasquez-Bonilla WO, Orozco R, Argueta V, Sierra M, Zambrano LI, Muñoz-Lara F, López-Molina DS, Arteaga-Livias K, Grimes Z, Bryce C, Paniz-Mondolfi A. A review of the main histopathological findings in coronavirus disease 2019. Human pathology. 2020 Nov 1;105:74-83.2020;105:74-83. doi:10.1016/j.humpath.2020.07.023
37. Menezes RG, Rizwan T, Ali SS, Hassan W, Khetpal A, Aqil M, Madadin M, Siddiqi TJ, Usman MS. Postmortem findings in COVID-19 fatalities: A systematic review of current evidence. Legal Medicine. 2022 Feb 1;54:102001.102001. doi:10.1016/j.legalmed.2021.102001