# COVID-19, new-onset alopecia, and gender distribution: a systematic review and meta-analysis

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Received: 25 February 2022 Accepted: 24 April 2022 **Background:** Among many coronavirus disease 2019 (COVID-19) integumentary system involvements, alopecia is one of the least investigated. This disorder has been reported in many individuals who have suffered from varying severities of COVID-19. We aimed to systematically review studies evaluating the onset of different types of alopecia following COVID-19.

**Methods:** The PubMed, Scopus, Web of Science, and Embase databases were searched with a specified string of relevant keywords. After quality assessments, the data of eligible studies were qualitatively and quantitatively synthesized.

**Results:** Sixteen studies were included in our review, six of which underwent meta-analysis for the differences in the risk of alopecia between males and females. Though the disorder was not differentiated in all the cases, we found that COVID-19 was associated with several different types of alopecia, including telogen effluvium, alopecia areata, alopecia parvimaculata, and lichen planopilaris. Moreover, although statistically insignificant, the odds of developing alopecia favored the female population.

**Conclusion:** Although many hypotheses have been suggested as to why an individual might be more predisposed to developing alopecia following COVID-19, the data obtained from the studies yielded results that could not lead to definite conclusions. Therefore, we recommend that further studies be conducted to evaluate the association between the two phenomena more confidently.

Keywords: COVID-19, alopecia, hair loss, systematic review, metaanalysis

Iran J Dermatol 2022; 25: 230-239

DOI: 10.22034/IJD.2022.331398.1518

# **INTRODUCTION**

Coronavirus disease 2019 (COVID-19) was declared a pandemic just a few months after its onset, substantially impacting both the daily lives of people worldwide and the approach to several medical diseases <sup>1-5</sup>. Since the onset, the infection has manifested with various pulmonary, gastrointestinal, neurologic, and dermatologic symptoms <sup>6</sup>.

Due to the disease's recency and its induced

limitations (e.g., exponential growth in the number of affected individuals and less-than-desirable access to them in the recovery phase), many have felt the urge to thoroughly investigate the short and long-term effects and adversities of the disease <sup>7</sup>. This issue is further amplified by suggestions that many factors (e.g., quarantine, hospitalization, decreased compliance with prescribed therapies, and psychological burdens) along with preexisting and underlying medical conditions are at play in the severity and persistence of COVID-19 manifestations <sup>8,9</sup>.

Among many COVID-19 integumentary system involvements, alopecia is one of the least investigated. Though aggravated by several stimuli, including stressful events, major surgeries, severe infections, febrile diseases, nutritional deficiencies, pregnancy, weight loss, and hospitalization, the disorder has been reported in many individuals who have suffered from varying severities COVID-19<sup>8,10</sup>. Furthermore, many suffer from its physical and psychological burdens, which persist over a prolonged period even though their initial manifestations are not left unattended in inpatient and outpatient settings <sup>11-13</sup>. Moreover, these symptoms might have much more aspects to them than first suspected, the investigation of which also aids immeasurably in understanding and attenuating the disease's severity and improving the prognosis <sup>14,15</sup>.

This study aimed to synthesize the literature on possible associations between COVID-19 and hair loss as a complication and investigate whether this manifestation significantly differs between males and females.

# PARTICIPANTS AND METHODS

We conducted our systematic review following the guidelines provided by the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) (http://www.prisma-statement.org/).

At the start of December 2021, the PubMed, Scopus, Web of Science, and Embase databases were systematically searched using a search string containing the keywords that follow: alopecia, hair loss, baldness, hypotrichosis, telogen effluvium, AND COVID, coronavirus, 2019nCOV, SARS-CoV-2, and severe acute respiratory syndrome. The exact search string is provided in Supplementary File S1.

#### **Eligibility criteria**

All English prevalence and observational studies (case-control, cohorts, and cross-sectional studies) were of our interest. Studies with an interventional design, case reports, case series, reviews, editorials, letters to the editors, commentaries, and conference proceedings were excluded. The study's population comprised cases with a confirmed diagnosis of COVID-19 as the exposure, with no limitations on age, sex, race, and history of medical conditions. The existence of the comparator group (i.e., cases with a negative result of a valid diagnostic test) was not subject to limitations. In addition, the intended outcome was the new onset of alopecia, regardless of subtype.

#### **Study selection**

Duplicate studies were deleted using EndNote version 20 and manually. Two authors then independently screened the identified studies for title and abstract. Full texts of relevant studies were explored for their eligibility. Discrepancies between the reviewers at any stage were discussed and solved under the supervision of the senior author.

#### Data extraction and quality assessment

Two researchers independently extracted the data for the first author, country, year, and type of the study; COVID-19-positive and negative cases' gender, age, and total number; COVID-19 severity; past medical history (especially any prior history of alopecia); the time interval between COVID-19 diagnosis and hair loss initiation; and the type and number of each type of hair loss.

Quality assessment for the included studies was performed using the Joanna Briggs Institute critical appraisal tool (https://jbi.global/criticalappraisal-tools) with eight items for cross-sectional studies, eleven items for cohorts, and ten items for case-control studies.

#### Statistical analysis (meta-analysis)

As the number of studies with distinct reporting of alopecia distribution in both COVID-19-positive and COVID-19-negative individuals was scarce (i.e., only two studies, which themselves varied substantially regarding their characteristics of included samples), we performed an odds ratio meta-analysis based on the sex distribution of cases with alopecia and also pooled the mean interval between COVID-19 and alopecia onset using the 16<sup>th</sup> version of the STATA statistical software package. As the measures of alopecia screening and the COVID-19 severities notably varied from one study to another, we preferred the random-effects model over fixed-effects, as the dispersion between individual effect sizes most probably was not solely due to random sampling. Furthermore, this aim was achieved using the restricted maximumlikelihood method. We also set the confidence level at 95%, with P-values < 0.05 considered statistically significant. Moreover, the heterogeneity between the studies was also determined using I<sup>2</sup> and the chi-squared ( $\chi$ 2) test. We considered I<sup>2</sup> values greater than 75% and chi-squared P-values smaller than 0.05 as significant and proceeded to examine why such dispersions existed in the first place by methodological assessments and subgroup analyses. Ultimately, the assessment of publication bias was carried out using Egger's method.

# RESULTS

A total of 672 studies were systematically found through our search strategy. Following the omission of 320 duplicate studies, 352 studies were screened for relevancy based on title and abstract. Then, the full texts of 103 studies were evaluated. Ultimately, 16 studies met our criteria and were included in this systematic review (Figure 1).

This systematic review incorporated 16 observational studies, including 11 cohorts and 5 cross-sectional studies reporting any type of alopecia occurring after a confirmed COVID-19 diagnosis. A detailed summary is presented in Table 1. Most

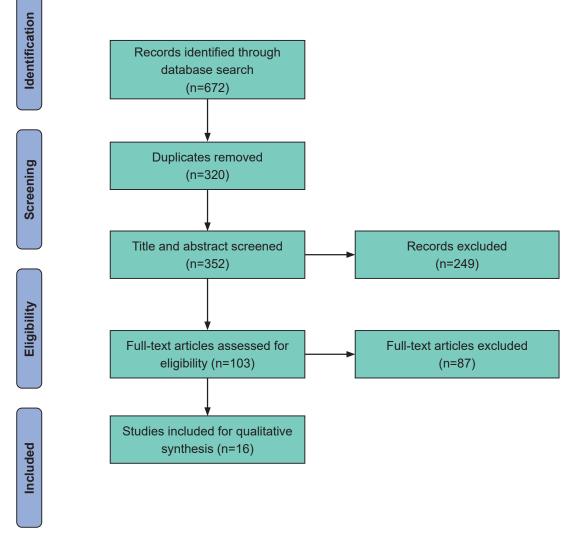


Figure 1. Systematic review flow diagram.

Study (Year)	Country	Study type	COVID-19 cases (No.	cases (No.)	COI	COVID-19 cases (Age)	(age) st	Alopecia	COVID-19 alopec	COVID-19 cases with alopecia (No.)	COVID-19 cases with alopecia (age)	COVID-19 severity in cases with alopecia (No.)	erity in cas (No.)	ses with alo		Interval between COVID-19 and alopecia
			Total	Sex	Mean ± SD	Median	Range	type (No.)	Total	Sex	Mean±SD Range Asymptomatic Mild	Asymptomatic	•	Moderate S	Severe	(Mean ± SD)
Xiong <i>et al.</i> (2020) <sup>25</sup>	China	Cohort	COVID (+) = 538/ COVID (-) = 154	COVID (+) =245 M, 293 F/ COVID (-) =96 M, 88 F		COVID (+) = 52 / COVID (-) = 50	COVID (+) = 22-79/ COVID (-) =20-71		COVID-19 (+) =154/ COVID-19 (-) =0	COVID-19 (+) =12 M, 142 F		103	103 "general"		5	Of these, 112 patients reported alopecia starting after discharge from the hospital, and 42 cases appeared during hospitalization
Thuangtong <i>et al.</i> (2021) <sup>24</sup>	Thailand	Retrospective cohort	93	54 M, 39 F	40.8 ± 15.1		21-83		22	8 M/ 14 F	43.4 ± 16.8	7		7	~~ <u>~</u>	19 patients after hospital discharge [median= 42 days, range=6-105 days]. 3 patients during admission [median= 12 days, range, 3-16 days].
Recalcati <i>et al.</i> (2021) <sup>23</sup>	Italy	Retrospective cohort	345		54.6		7-94	Telogen effluvium (n=5); lichen planopilaris (n=1)	ω	3 M/ 3 F	51.1 ± 8.8	0	-	-	m	70.3 ± 27.96
Kim <i>et al.</i> (2021) <sup>21</sup>	Korea	Cohort	COVID (+) =7958/ COVID (-) =222,257	COVID (+) = 3236 M, 4834 F / 4834 F / 106,082 M 116,175 F			0-9 (81) 10-19 (276) 20-29 (2,057) 30-39 832 40-49 1,036 50-59 1,567 60-69 1,199 60-69 1,199 70-79 617 ≥80 465	Alopecia areata	COVID-19 (+) =18/ COVID-19 (-) =195							
Otsuka <i>et al.</i> (2021) <sup>22</sup>	Japan	Cross- sectional	87	41 M, 46 F		40	0-19 (9) 20-29 (20) 30- 39 (14) 40-49 (15) 50-59 (20) 60-69 (5) ≥70 (4)		30							
Almeida <i>et al.</i> (2021) <sup>18</sup>	Brazil/USA	Cohort	45	25 M, 20 F	37.2 ± 19		1-68	Telogen effluvium (n=10)	10	7 M/ 3 F	31.3 ± 11.98	a	2	0	0	
Amin <i>et al.</i> (2021) <sup>19</sup>	Bangladesh	Cross- sectional	439	303 M, 136 F			16-60		222	159 M/ 63 F						
Cheng <i>et al.</i> (2021) <sup>20</sup>	¥	Retrospective cohort	113						2							
Mohta <i>et al.</i> (2021) <sup>27</sup>	India	Prospective cohort	118					Alopecia parvimaculata (n=3)	m							
Olds <i>et al.</i> (2021) <sup>28</sup>	NSA	Cross- sectional	552	198 M, 354 F				Telogen effluvium (n=10)	10	1 M/ 9 F	48.5 ± 11.58	e		2		50.1 ± 25.69
Miyazato <i>et al.</i> (2020) <sup>9</sup>	Japan	Prospective cohort	58						4	9 M/ 5 F						58.6±37.2
Hennig <i>et al.</i> (2021) <sup>26</sup>	Germany	Prospective cohort	122						22							
Tawfik <i>et al.</i> (2021) <sup>30</sup>	Egypt	Retrospective cohort	120	50 M, 70 F	33.7 ± 7.29		23–62		4							
Shang <i>et al.</i> (2021) <sup>29</sup>	China	Prospective cohort	796	404 M, 392 F		62	20–97		4	2 M/ 2 F		0	0	0	4	
Sharquie and Jabbar (2021) <sup>17</sup>	Ireland	Cross- sectional	30	3 M, 36 F	41.3 ± 11.6		22–67	Telogen effluvium (n=39)	30	3 M/ 36 F	41.3 22–67	0	15	24	0	2–3 months
Babaei <i>et al.</i> (2021) <sup>16</sup>	Iran	Cross- sectional	526	116 M, 410 F	30.97 ± 9.59		8-62	Telogen effluvium	526	116 M/ 410 F	30.97 ± 9.59	0	250	193	83	7.65 ± 1.74 weeks

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of the studies (n = 14) were conducted in 2021. The locations of studies in order of frequency were Asia (n = 9), Europe (n = 4), Americas (n = 2), and Africa (n = 1).

#### Quality assessment

A detailed assessment of the quality of the included studies is provided in Supplementary File S2. Most studies had relatively high quality in reporting their evidence, while a few had moderate quality.

Among these sixteen studies, two included cases with telogen effluvium after COVID-19 and reported their characteristics as well as the association with COVID-19 severity <sup>16,17</sup>, while the primary aim of others was to evaluate general manifestations of COVID-19 cases, among which was hair loss <sup>9,18-30</sup>. In these fourteen studies, among 11,384 included cases with prior confirmed severe acute respiratory syndrome coronavirus 2 (SARS-COV-2) infection, 526 (4.62%) suffered from hair loss. Four studies reported a mean interval between COVID-19 and the onset of alopecia, the pooled mean of which was approximately 53.5 days <sup>9,16,23,28</sup> (Figure 2). Five of these studies specified the type of hair loss, namely alopecia areata, telogen effluvium, lichen planopilaris, and alopecia parvimaculata <sup>18,21,23,27,28</sup>.

COVID-19 severity was reported in eight studies. Among eight studies with 617 cases of alopecia, 326 experienced at least moderate infection (52.83%), while 291 were mild at worst <sup>16-18,23,24,28,29</sup>. Furthermore, Xiong *et al.* <sup>25</sup> reported that out of 154 cases with alopecia, 51 had severe or critical conditions in the acute phase of COVID-19, while the other 103 cases had "general" conditions.

## **Telogen effluvium (TE)**

Three studies specifically reported TE as a complication of COVID-19<sup>18,23,28</sup>. Out of 942 cases of COVID-19, 25 developed TE (11 men, 14 women).

Almeida et al. <sup>18</sup> investigated the cutaneous manifestations of 45 COVID-19-positive patients. They diagnosed ten patients with TE. The interval between systemic symptom onset was a few days with concurrent COVID-19-related cutaneous manifestations, including erythematous and vascular rashes and blanching and nonblanching urticarial rashes. Half of these cases had asymptomatic COVID-19, while the other half had mild COVID-19. 7 out of these 10 cases were male. All the TE-involved cases had a past medical history of atopic dermatitis, and one man had a benign vascular brain tumor. Regarding the prior history of alopecia, four cases had androgenic alopecia (3 male, 1 female), and a male suffered from alopecia areata. Two out of ten cases had TE of the hair and beard.

Recalcati *et al.* <sup>23</sup> observed 345 confirmed COVID-19-positive patients, of which 52 cases had dermatological manifestations, including hair loss. They diagnosed 5 cases with TE (3 males, 2 females), with a mean interval of 70.3 days between the COVID-19 diagnosis and the onset of this complication. Three cases experienced severe

Study		Mean Interval with 95% Cl	Weight (%)
Recalcati et al.		- 70.33 [ 47.97, 92.69]	0.21
Olds et al.	<b>.</b>	50.10 [ 34.19, 66.01]	0.42
Miyazato et al.		58.60 [ 39.12, 78.08]	0.28
Babaei et al.		53.55 [ 52.51, 54.59]	99.08
Overall	•	53.59 [ 52.55, 54.62]	
Heterogeneity: $\tau^2 = 0.00$ , $I^2 = 0.00\%$ , $H^2 = 1.1$	00		
Test of $\theta_i = \theta_j$ : Q(3) = 2.60, p = 0.46			
Test of θ = 0: z = 101.57, p = 0.00			
	40 60 80	100	
Figure 2 Pooled mean interval between COVID-19	and alonecia onset		

Figure 2. Pooled mean interval between COVID-19 and alopecia onset

COVID-19 during admission, and four also had trichodynia.

A study by Olds *et al.* <sup>28</sup> reviewed medical records of 552 confirmed COVID-19 patients. 10 TE cases (9 women and 1 male) with a mean age of 48.5 years were diagnosed. They also reported a mean interval of 50 days between COVID-19 and TE. 7 out of these cases had at least moderate COVID-19 severity. Two studies included COVID-19-related TE cases and evaluated their manifestations, revealing that out of 565 total cases (females = 446), 256, 217, and 83 cases experienced mild, moderate, and severe COVID-19, respectively <sup>16,17</sup>. Hair loss initiation was reported 7.65 and 8–12 weeks after COVID-19 diagnosis in the studies by Babaei *et al.* <sup>16</sup> and Sharquie and Jabbar <sup>17</sup>.

Babaei *et al.* <sup>16</sup> evaluated the association between COVID-19 and its recovery period and the onset of telogen effluvium. They demonstrated that the more severe the COVID-19, the shorter it took for alopecia to manifest itself. Furthermore, the mentioned interval was significantly shorter in females and younger cases.

#### Alopecia areata (AA)

Kim *et al.*<sup>21</sup> investigated the risk of new-onset AA between COVID-19-positive and COVID-19negative participants. With a total of 226,737 included participants, 18 out of 7,958 cases with a prior history of COVID-19 and 195 out of 218,584 cases without prior COVID-19 history had new-onset AA, revealing that the ratio of new-onset AA was twice in COVID-19-positive cases (0.2% vs. 0.1%). This difference was statistically significant (P < 0.001).

#### Alopecia parvimaculata

Mohta *et al.* <sup>27</sup> found that in a sample of 118 patients recovering from COVID-19, three developed alopecia parvimaculata, whereas in a sample of 163 cases with ongoing COVID-19, none suffered from the complication. Their investigations revealed that these cases were probably more susceptible to the disease due to seborrheic folliculitis flare-ups, which healed with spotted scarring.

#### Lichen planopilaris

Recalcati et al. 23 reported a 38-year-old female

with new-onset lichen planopilaris, resulting in cicatricial alopecia, with a 15-day interval between COVID-19 and the onset of this complication. Moreover, a histopathological examination revealed an ulcerated epidermis, diffusely fibrotic dermis, and lymphocytic infiltrations adjacent to hair follicles. Furthermore, several vessels at the hair bulge experienced thrombosis leading to poor perfusion.

#### **Unspecified studies**

Nine studies did not report the specific type of alopecia <sup>9,19,20,22,24-26,29,30</sup>. A total of 2,366 cases with confirmed COVID-19 were evaluated in these studies, with 479 reported cases of hair loss.

In a study by Amin *et al.* <sup>19</sup> with snowball sampling, more than half of the cases reported alopecia (222 out of 429), with a male majority with no significance (P = 0.233). Patients less than 40 years old were more predisposed to COVID-19-associated hair loss (P < 0.001), and cases with prior chronic comorbidities were significantly less affected (P < 0.001).

Cheng *et al.* <sup>20</sup> noted that 6% (n = 7) of the cases (n = 113) that attended their follow-up sessions complained of hair loss symptoms. Otsuka *et al.* <sup>22</sup> reported that among 87 followed cases, 16 (18.4%) primarily had hair loss complaints. They noted that this complication seems to appear more commonly in the chronic phase of COVID-19.

In a study by Thuangtong et al. <sup>24</sup> evaluating the dermatological manifestations after COVID-19, 93 cases were included. The researchers reported that out of 22 cases with hair loss (mean age of 43.4), 10 did not have any prior history of hair shedding. 19 patients started losing their hair after hospital discharge (median time = 42, range = 6-105 days), while 3 experienced it during admission (median time of 12 days after the diagnosis of COVID-19, range = 3-16 days). They also found statistical significance between COVID-19 severity and alopecia, revealing that cases with asymptomatic to mild COVID-19 had less hair shedding than moderate to critical COVID-19 (16.4% vs. 42.3%; P = 0.008). Females were more susceptible to hair loss than males (35.9% vs. 14.8%, *P* = 0.018)

Xiong *et al.* <sup>25</sup> successfully followed 538 cases of COVID-19 and 184 cases with negative COVID-19 tests, comparing their demographic and clinical features. They, by telephoning, found that among COVID-19 survivors, 154 had significant residual or new hair loss three months after hospital discharge, while in the comparison group, none had alopecia  $(P \le 0.01)$ . Alopecia was significantly more common in females (92% of cases with alopecia; P < 0.01), also showing that 48% of females had alopecia while only 4% of males had this complication. Differences in the age distribution of alopecia were statistically significant (P = 0.01). Middle-aged patients were more at risk of alopecia, showing that 53% of cases were 41-60 years old. Comparing cases with and without alopecia showed no significance in the duration of viral shedding (P = 0.19), disease severity (P = 0.13), and hospital length of stay (P = 0.27).

In the study by Miyazato *et al.* <sup>9</sup>, 58 out of 63 cases completed the telephone follow-up interviews. 14 cases revealed alopecia as a late-onset symptom. With a male majority (n = 9), this symptom emerged 58.6  $\pm$  37.2 days after COVID-19 onset. In 5 cases, alopecia resolved within 76.4  $\pm$  40.5 days, while the other 9 cases with a mean duration of 47.8  $\pm$  32.2 days still had alopecia at the interview time.

Hennig *et al.* <sup>26</sup> included 122 COVID-19-positive cases, of which 14 had a prior history of hypohidrotic ectodermal dysplasia (HED), and compared the risk of hair loss in cases with and without HED. They reported that 22 cases had noticeable hair loss (8 cases had HED). The interval between COVID-19 diagnosis and hair loss in these cases was about two months, and the hair loss lasted

for about six months.

In Shang *et al.*'s study <sup>29</sup>, out of 796 individuals, 2 men and 2 women had hair loss; all 4 experienced severe COVID-19 and were aged below 65. No statistical significance was found regarding age (above or below 65), sex, and COVID-19 severity (severe or critical), with P-values of 0.155, 0.999, and 0.999, respectively. Out of 120 cases with a positive COVID-19 history in Tawfik's study <sup>30</sup>, four showed hair loss at the first-month follow-up that persisted till the third-month follow-up.

## Meta-analysis results

A total of six studies were included in our quantitative synthesis of the risk of alopecia based on sex (Figure 3). Based on the pooled estimates of effect sizes, the incidence odds favored females as much as 56%. However, the heterogeneity between the studies' estimates was substantial ( $I^2 = 93.31$ ,  $\chi 2$  P-value < 0.01), and the overall effect size was not statistically significant (P = 0.28), with four studies suggesting a female predominance and two reporting a male predominance. Nonetheless, Egger's test for publication bias yielded results indicating statistical insignificance (Prob > |z| = 0.7865).

We then assessed the underlying factors leading to this heterogeneity by evaluating the suspecting factors at play. Initially, as the results of the publication bias analysis demonstrated statistical insignificance, we opted to analyze each study's methodology and results. One of the suspected

	Male A	lopecia	Female Alopecia		Odds Ratio	Weight
Study	Yes	No	Yes	No	with 95% Cl	(%)
Xiong et al.	12	233	142	151	0.05 [ 0.03, 0.10]	19.73
Thuangtong et al.	8	46	14	25	0.31 [ 0.11, 0.84]	18.20
Almeida et al	7	18	3	17	2.20 [ 0.49, 9.94]	15.64
Amin et al.	159	144	63	73		20.36
Olds et al.	1	197	9	345	0.19 [ 0.02, 1.55]	12.77
Shang et. al.	2	402	2	390	0.97 [ 0.14, 6.92]	13.30
<b>Overall</b> Heterogeneity: $\tau^2 =$ Test of $\theta_i = \theta_j$ : Q(5) Test of $\theta = 0$ : z = -1	= 74.74,	p = 0.00	, H <sup>2</sup> = 9.63		0.44 [ 0.13, 1.44]	

Figure 3. Meta-analysis of sex distribution of COVID-19-related alopecia.

influential factors might be the inconsistency between the studies' outcome measures, as four studies collected their data through patient selfreporting of the outcome in a specific setting (i.e., those who were priorly admitted due to dermatological diagnoses), while two proceeded to examine the hair loss objectively via the pull test from a sample of recovering COVID-19 cases.

Therefore, we performed a subgroup analysis, dividing the studies based on their methodology and measures, which led to relative mitigation of heterogeneity in the group of studies with objective hair loss assessment ( $I^2 = 70.98\%$ ,  $\chi 2 P = 0.06$ ), while the heterogeneity in the other group persisted ( $I^2 = 95.73\%$ ,  $\chi 2 P < 0.01$ ). Moreover, the differences between the two groups in effect estimates did not show statistical significance (P = 0.65) (Figure 4).

## DISCUSSION

The early detection and prompt management of

dermatologic manifestations related to COVID-19 have been expressed as areas of significant concern by those in the field <sup>7</sup>. In our systematic review, alopecia was investigated as one of the mentioned manifestations.

We found that more than 500 cases were subject to various hair loss complaints following COVID-19, amounting to an approximate rate of 4.2%, manifesting approximately 53 days after the infection. This interval was hypothesized to be associated with the slowing of the follicle anagen phase following the high levels of proinflammatory cytokines in the acute phase of infection <sup>16,22,26</sup>. Even though most of the studies did not have the alopecia subtype differentiated, of those whose disorder type was specified, the most prevalent subtypes were, in order, TE, AA, alopecia parvimaculata, and lichen planopilaris. We found a relative predominance of alopecia (subtype not specified) existed in cases with more severe preceding infection as evident, for example,

	М	ale	Fer	nale						Odds Ra	tio	Weight
Study	Yes	No	Yes	No						with 95%	CI	(%)
Interview												
Xiong et al.	12	233	142	151	_	_				0.05 [ 0.03,	0.10]	19.73
Thuangtong et al.	8	46	14	25						0.31 [ 0.11,	0.84]	18.20
Amin et al.	159	144	63	73						1.28 [ 0.85,	1.92]	20.36
Shang et. al.	2	402	2	390		_				0.97 [ 0.14,	6.92]	13.30
Heterogeneity: $\tau^2$ =	2.01,	$ ^2 = 9$	93.29%	6, H <sup>2</sup> = 1	4.91					0.36 [ 0.08,	1.58]	
Test of $\theta_i = \theta_j$ : Q(3)	) = 70.	19, p	= 0.00	)								
Examination												
Almeida et al	7	18	3	17						2.20 [ 0.49,	9.94]	15.64
Olds et al.		197	-	345		_				0.19 [ 0.02,	1.55]	12.77
Heterogeneity: $\tau^2$ =	= 2.09,	$ ^{2} = 7$	70.98%	%, H <sup>2</sup> = 3	45					0.73[ 0.07,	7.80]	
Test of $\theta_i = \theta_j$ : Q(1)	) = 3.4	5, p =	0.06									
Overall						-				0.44 [ 0.13,	1.44]	
Heterogeneity: $\tau^2$ =	= 1.77,	$ ^{2} = 8$	39.629	6, H <sup>2</sup> = 9	63					•		
Test of $\theta_i = \theta_i$ : Q(5)	) = 74.	74. p	= 0.00	)								
Test of group differ					62							
rest of group differ	CHUCS	о. «b(	·) - 0.	20, p = 0	-		4.10					
Pondom offorte DE		adal			1/32	2 1/8	1/2	2	8			
Random-effects REI		Juei										

Figure 4. Subgroup analysis based on outcome measures.

in the studies by Thuangtong *et al.*, Sharquie and Jabbar, and Babaei *et al* <sup>16,17,24</sup>.

In this study, we found that the pathophysiology of the mentioned post-COVID-19 alopecia subtypes was not investigated in the majority of studies. However, in TE, for instance, while the specific etiology is yet to be thoroughly evaluated, hypoxia and localized follicular vasoconstriction may contribute, as reported in one study <sup>18</sup>. One other study suggested the activation of the coagulation cascade in response to the infection and subsequent inflammation, microthrombi formation, and perfusion disruption to be the possible cause of TE <sup>28</sup>. However, Sharquie et al. demonstrated the effects of psychological burdens following the infiltration of the skin cells via their ACE-2 receptors by the virus as the possible underlying mechanism for increased risk of TE in COVID-19<sup>17</sup>.

The predisposition to alopecia parvimaculata, according to Mohta *et al.*, was due to the flare-up of seborrheic folliculitis in cases who were recovering with spotted scarring <sup>27</sup>. Furthermore, the onset of lichen planopilaris was reportedly due to inadequate perfusion following lymphocytic infiltration and thrombosis in the study by Recalcati *et al* <sup>23</sup>.

We also sought to analyze the odds of developing alopecia by comparing COVID-19 cases with otherwise healthy subjects. However, we found only two studies with the desired characteristics, in one of which all alopecia types were studied, while in the other, the focus was solely on AA. Therefore, an analysis could not be performed due to the inconsistency between the studies' population and methodologies.

In this study, we also found that even though females were subjects to more incidents of alopecia, this finding needs to be considered with a grain of salt, as some studies reported opposite findings, leading to substantial heterogeneity. Furthermore, we also found that studies that objectively examined alopecia reported less heterogeneous data. Therefore, we hypothesize that the heterogeneity in the group whose hair loss was subjectively evaluated might be due to their methodological nature, as the overall effects of the pandemic and the fact that its psychological burdens can induce adversities in the affected populations regardless of their demographic differences, but rather rooted in their levels of resilience. Ultimately, one of the constraints that must be considered in this literature review is that since research related to dermatologic manifestations of COVID-19 is still in its early stages and is constantly changing, the data may not be conclusive and applicable to the whole population. Moreover, some of the included studies did not identify the comorbidities that can affect an individual's predisposition to alopecia. Furthermore, the precise mechanism by which this virus causes alopecia is still unknown. Therefore, we believe that with the conduction of further large-scale studies designed consistent with the mentioned desired methodology, the assessment of alopecia risk would finally become possible.

# FUNDING

No funding or sponsorship was received for the conduction of this study.

# AUTHORSHIP

All named authors meet the International Committee of Medical Journal Editors (ICMJE) criteria for authorship for this article, take responsibility for the integrity of the work as a whole, and have given their approval for this version to be published.

# **AUTHORS' CONTRIBUTIONS**

All authors participated in designing the protocol. ZA and NS performed the literature search. ZA, MA, HR, and NS selected the studies and extracted the relevant information, which were assessed and confirmed by the senior author. All authors then participated in synthesizing the data. NS, MS, and NA wrote the first draft of the paper. NA provided critical guidance on the analysis and overall direction of the study. MS performed the meta-analysis. All authors critically revised successive drafts of the paper and approved the final version.

## **Ethics approval**

No ethical approval was required as this manuscript is a review article with no original research data.

#### Availability of data and materials

The dataset supporting the conclusions of this article (i.e., data extracted from included studies) is available upon reasonable request to the corresponding author, Najmeh Ahramiyanpour.

## Conflict of interests: None declared.

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