Review Article

Comparison of the outcomes of testicular torsion among children presenting during the Coronavirus Disease 2019 (COVID-19) pandemic versus the pre-pandemic period: A systematic review and meta-analysis

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Summary

Objective
To evaluate whether the Coronavirus Disease 2019 (COVID-19) pandemic resulted in a prolonged duration of symptoms, a delayed presentation to the medical facility, and consequently more orchiectomy procedures among children with testicular torsion compared to the pre-COVID-19 period.

Methods
Systematic search of four scientific databases was performed. The search terms used were (coronavirus OR novel coronavirus OR SARS-CoV-2 OR COVID-19) AND (testicular torsion OR orchidectomy OR orchiectomy OR orchidopexy OR orchiopexy). The inclusion criteria were all boys presenting with testicular torsion during the COVID-19 and pre-COVID-19 periods. A comparison of the average duration of symptoms, the proportion of children with delayed presentation (>24 h), and the proportion of children requiring orchiectomy was made among the two groups. The Downs and Black scale was used for methodological quality assessment.

Results
The present meta-analysis included six comparative studies (five retrospective studies). A total of 711 patients (473 during the COVID-19 period) were included. No significant differences in the average duration of symptoms (WMD: 2.6, 95% CI -6.78 to 11.99, P = 0.59), the proportion of children with delayed presentation (RR = 1.03, 95% CI 0.52—2.02, p = 0.94), and orchiectomy rate (RR = 1.23, 95% CI 0.82—1.84, p = 0.31) were observed among the two patient groups. All studies had a moderate risk of bias.

Conclusion
The duration of symptoms, the proportion of children with delayed presentation, and orchiectomy rate did not significantly differ among the children with testicular torsion presenting during the COVID-19 and pre-COVID-19 periods. However, due to the moderate risk of bias, the level of evidence of the available comparative studies is limited.
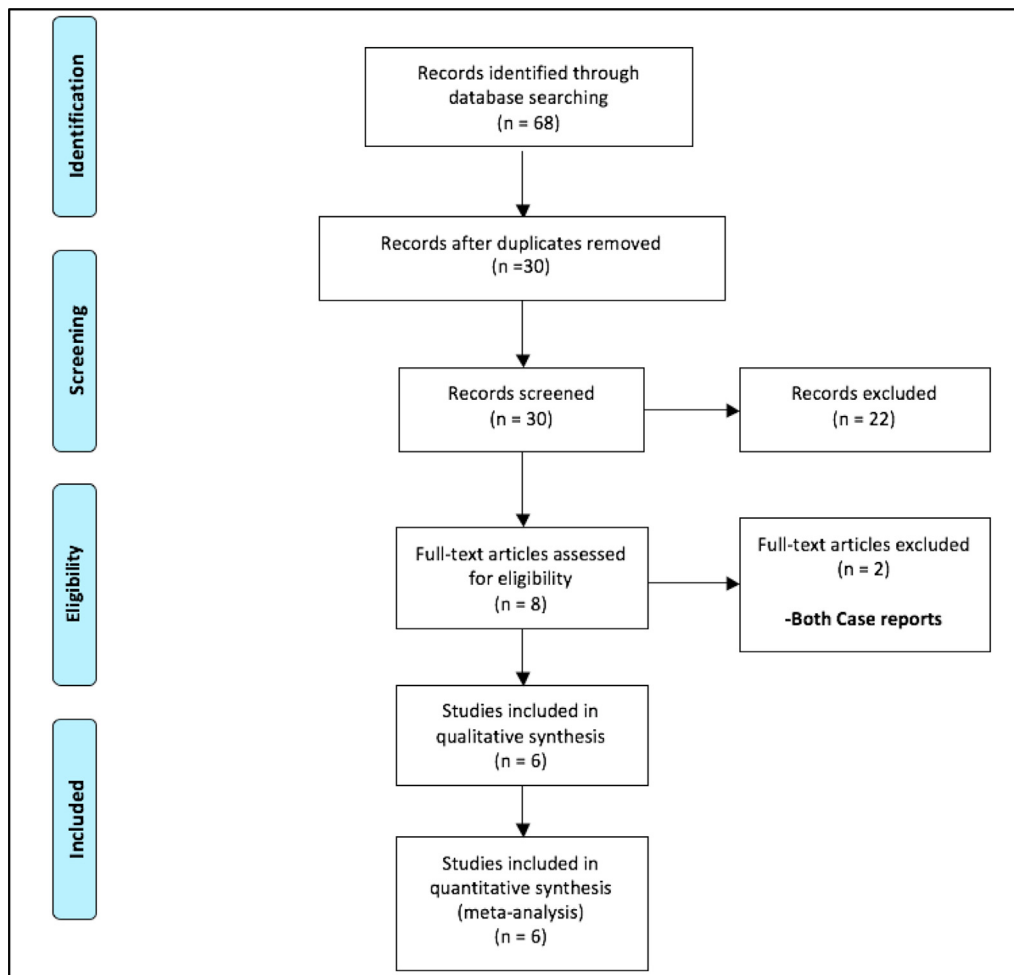
Summary Figure   Selection of the relevant studies using the Preferred Reporting Items for Systematic Review and Meta-Analysis (PRISMA) flow diagram

Introduction

Testicular torsion, defined as the twisting of the spermatic cord and its contents, is a true pediatric surgical emergency, with an annual incidence of 3.8 per 100,000 in the pediatric age group [1]. Testicular torsion is the cause of pediatric acute scrotum in 10—15% of cases, and in such cases, about 40% of surgical explorations result in an orchiectomy [1—3]. To avoid unfavorable outcomes and to ensure the viability of the testis, a diagnosis must be made promptly, ideally within 6 h [4,5]. It is therefore important to know the classic presentation of testicular torsion which consists of sudden onset unilateral testicular pain which may be accompanied by nausea and/or vomiting [6—8]. The affected testis is hard on palpation and is usually positioned at an unusual angle [3,9]. Apart from testicular torsion, there are multiple other causes of the acute scrotum, including torsion of testicular appendage, epididymo-orchitis, acute hydrocele, and idiopathic scrotal edema [1,3,10].

The current pandemic of coronavirus (COVID-19) has been hard on all aspects of life, but the medical system especially had to deal with a lot of challenges from the disease itself, and a multitude of other consequences on almost every aspect of medical care [11]. Lockdowns, social distancing, and some hospitals temporarily shutting down or operating at severely limited access have disrupted normal interactions and activities inside healthcare institutions [12]. The COVID-19 crisis has been linked to an increased patient avoidance of the Emergency Department for illnesses other than COVID-19 itself [11,13]. For example, hospitalizations for myocardial infarctions have halved in some countries during the pandemic when compared to the same period of the previous year [14]. Concerning pediatrics, the literature shows reduced Emergency Department visits across all diagnostic categories in multiple different countries since the onset of the COVID-19 pandemic [15,16]. There were also reduced patient visits for chronic complex conditions, which further suggests the Emergency Department avoidance behavior [15]. Pediatric patients uncommonly present with high mortality conditions, but prolonged time to diagnosis can nevertheless lead to increased morbidity, prolonged hospital stay, and increased financial burden [15].

Delaying the hospital visit in acute testicular torsion can lead to non-viability of the testis because of the aforementioned 6-h timeframe. Recent studies have

compared the characteristics and outcomes of children with testicular torsion presenting during the pandemic and pre-pandemic periods [17—22]. However, due to the conflicting findings, there is no consensus statement regarding the delayed healthcare presentation and high orchiectomy rates among the patients presenting during the pandemic. Considering all this, we conducted a meta-analysis of the available comparative studies focusing on the impact of the COVID-19 pandemic on pediatric testicular torsion in terms of the duration of symptoms, the proportion of children with delayed presentation, and orchiectomy rate. We hypothesize that no significant difference in the abovementioned outcomes exists between the two patient groups.

Materials and methods

Systematic search

The present review was not registered in any prospective register or database. The literature search for this review was performed as per the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines [23]. Two authors (ZP and SA) independently conducted a preliminary literature search in the PubMed database on August 30, 2021. After confirming the absence of any published meta-analysis on this subject, both the authors explored the PubMed, Web of Science, Scopus, and EMBASE databases (Annexure A) on the same day. The search keywords used were: (coronavirus OR novel coronavirus OR SARS-CoV-2 OR COVID-19) **AND** (testicular torsion OR orchidectomy OR orchiectomy OR orchidopexy OR orchiopexy). Once the total articles were identified, the duplications were removed. The remaining records were screened as per the eligibility criteria to select the relevant articles for meta-analysis.

Eligibility criteria

The inclusion criteria were: *Participants*-All patients, aged <18 years, presenting during the COVID-19 pandemic and diagnosed with testicular torsion as per the clinicoradiologic criteria; *Intervention*-detorsion followed by orchiopexy or orchiectomy; *Comparison*-children with testicular torsion presenting during the pre-pandemic period and were offered similar treatment; *Outcomes*-the average duration of symptoms (i.e. from the onset till presentation to the emergency room), the proportion of children with delayed presentation (>24 h), and the proportion of children requiring orchiectomy were the outcomes studied in this review.

All comparative studies where the orchiectomy rates were reported were eligible for inclusion. Also, no specific eligibility criteria related to the laterality of torsion (left/right) or operative approach (scrotal/inguinal) were followed in this review. Case series, review articles, expert opinions, editorials, letters to the editor, and commentaries were excluded. In addition, the studies with unavailable full-texts were also excluded.

Data synthesis

Two authors, SA and NK, independently utilized Microsoft Excel spreadsheets (Version 15.24) for data extraction. For each study, the data including the total sample size, the number of subjects in each patient group, the average age at presentation, the incidence of torsion (per week or per month) in each group, the average duration of symptoms, the proportion of children with delayed presentation, and the proportion of children requiring orchiectomy were extracted. Additionally, the information about the name of the first author, year of publication, and type of the study design were also noted. Any disagreements among the authors were resolved by discussion with the third author (ZP).

Methodological quality assessment

The quality assessment was independently performed by two investigators (SA and NK) utilizing the Downs and Black scale [24]. The scale has twenty-seven items of assessment, yielding total scores ranging from 0 to 32. On the basis of these scores, the risk of bias in each study was declared as low (score >23), moderate (score = 16—23), or high (score 0—15). Subsequently, the kappa statistics were used to adjudge the inter-observer agreement regarding the Downs and Black scores [25]. The level of agreement was classified as slight (0.00—0.20), fair (0.21—0.40), moderate (0.41—0.60), substantial (0.61—0.80), or almost perfect (0.81—1.00).

Data analysis

The baseline data were expressed as numbers, proportions, averages (mean or median), and ranges. RevMan 5.4 (Cochrane Collaboration, London, UK) was used to perform the meta-analysis. For each study, the risk ratio (with 95% CI) and mean difference (with 95% CI) were calculated for dichotomous and continuous outcomes respectively. Subsequently, the pooled risk ratio and weighted mean difference were estimated utilizing the Mantel-Haenszel and the inverse variance methods respectively. I^2 statistics were used to estimate the level of heterogeneity among the included studies. A random-effects model was selected if the heterogeneity was substantial ($I^2 > 50\%$). A p-value of <0.05 was considered statistically significant. For the purpose of analysis, groups A and B included children presenting during the COVID-19 pandemic and pre-pandemic periods respectively.

Results

Study characteristics

A total of 68 articles were identified during the database search. Out of these, 38 were duplicate records. The abstracts of the remaining 30 articles were screened for eligibility (Fig. 1). Of these, 22 records were excluded and only 8 articles were eligible for full-text review. Two of
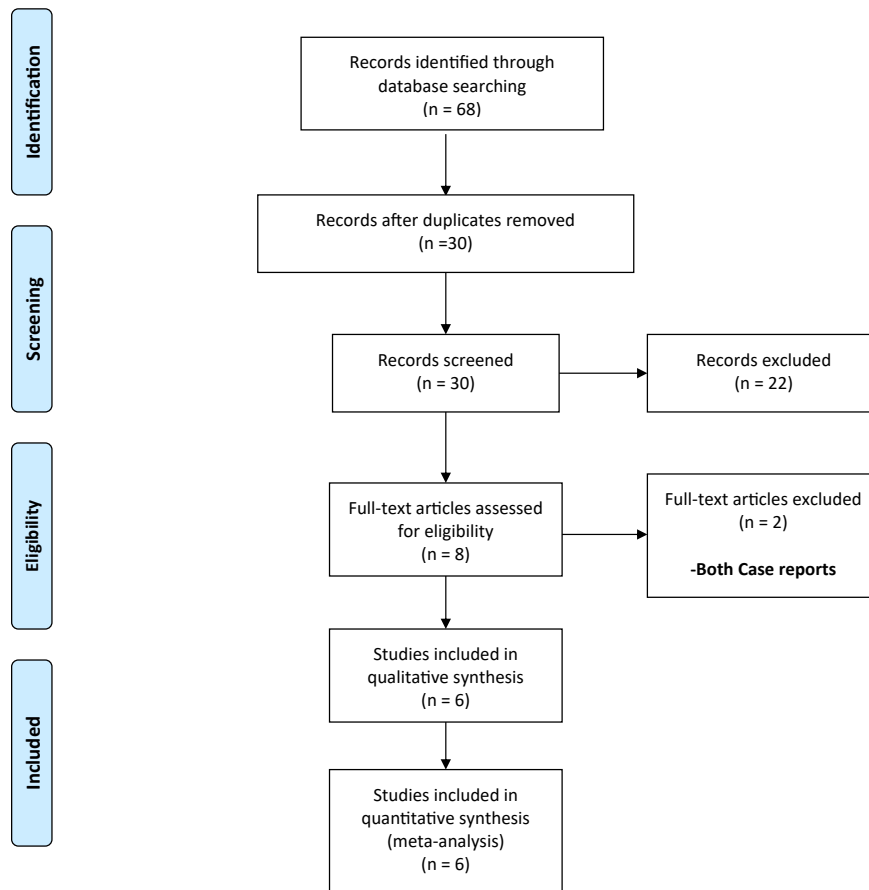
Fig. 1 Selection of the relevant studies using the Preferred Reporting Items for Systematic Review and Meta-Analysis (PRISMA) flow diagram.

these were further excluded as both were case reports [26,27]. Therefore, only six studies were included in the final meta-analysis [17–22]. Five of them had a retrospective study design [18–22]. The remaining study was a prospective cohort with a retrospective comparison (pre-pandemic) group [17]. A total of 711 patients, 238 and 473 in groups A and B respectively, were included in the meta-analysis.

The baseline characteristics of the included studies are depicted in Table 1. In all studies, no significant difference in the age of presentation was observed among the two patient groups. Except for one study [18], all reported a comparatively higher incidence of testicular torsion during the pandemic. Four studies also reported the proportion of children who were referred from other centers/hospitals [17–20]. No significant difference was observed among the two groups in terms of the proportion of referred patients. The side of the torsed testicle and the degrees of torsion were only reported by two included studies [21,22]. The summary of findings of the included studies are depicted in Table 2.

Methodological quality assessment

The independent quality assessment by both the observers is depicted in Supplementary table 1. The average Downs

and black scores assigned to the included studies ranged from 18 to 20; with all the studies having a moderate risk of bias. The studies by Holzman et al. [17] and Shields et al. [22] had the lowest and highest risk of bias respectively. The inter-observer agreement for Downs and Black scoring was almost perfect (Kappa = 0.957; p < 0.001).

Outcome analysis

Duration of symptoms
The average duration of symptoms (in hours) was reported by all six studies [17–22]. Pooling the data (Fig. 2) showed no significant difference in the average duration of symptoms among the patients belonging to group A compared to group B (WMD: 2.6, 95% CI −6.78 to 11.99, $P = 0.59$). For this outcome, the estimated heterogeneity among the included studies was statistically significant ($I^2 = 78\%$, $P = 0.0004$).

Proportion of children with delayed presentation (> 24 h)
Four out of six studies [17–19,21] compared this outcome among the two patient groups. A delayed presentation was seen in 65/183 and 94/317 patients belonging to groups A and B respectively. The pooled risk ratio (Fig. 3) for the delayed presentation among the patients belonging to

Table 1 Baseline characteristics of the included studies.

Author	Study design	No of patients		% of patients referred		Median (IQR) age at presentation; in years		Monthly incidence of torsion	
		A	B	A	B	A	B	A	B
Nelson et al., 2020	Retro	17	77	47	49	15.2 (14.2—16)	14.2 (12.6—15.8)	1.3[b]	0.7[b]
Holzman et al., 2021	Pro	84	137	43	45	13.1 (10.7—14.7)	13.7 (11.6—15.2)	16.5	10.5
Lee et al., 2021	Retro	27	55	44	55	14 (13—15)	14 (12—15)	3.86	3.93
Littman et al., 2021	Retro	21	57	62	71	12.9 (2.1)[a]	12.9 (2.6)[a]	3[b]	1.6[b]
Pogorelić et al., 2021	Retro	51	68	—	—	15 (14—16)	14 (13—16)	5.6	4.8
Shields et al., 2021	Retro	38	79	—	—	13 (12—14)	14 (12—15)	38[c]	10.8[c]

Abbreviations: Retro, retrospective study. Pro, prospective cohort. A and B, groups A (pandemic) and B (pre-pandemic) patient groups.
[a] Mean (range).
[b] Incidence per week.
[c] Incidence over a 10-months period.

Table 2 Summary of findings of the included studies.

Author	Period of observation		Average (SD) duration of symptoms; in hours		Orchiectomy rate (percentage)	
	A	B	A	B	A	B
Nelson et al., 2020	March—May, 2020	Jan, 2018—Feb, 2020	14.1 (30.6)	8.0 (11.6)	29.4%	16.9%
Holzman et al., 2021	March—July, 2020	Jan, 2019—Feb, 2020	23.8 (32.1)	13.2 (18.0)	40.5%	29.2%
Lee et al., 2021	March 11, 2020- Oct 1, 2020	March 11- Oct 1, 2018 & 2019	8.8 (7.6)	23.2 (32.0)	33.3%	50.9%
Littman et al., 2021	March 15-May 4, 2020	Same months of 2015—2019	21.3 (29.7)	23.2 (35.0)	25%	44.7%
Pogorelić et al., 2021	March 11-Dec 31, 2020	Jan 1, 2019—March 10, 2020	22.3 (32.8)	10.3 (14.4)	43.1%	16.2%
Shields et al., 2021	March—Dec, 2020	Same months of 2015—2019	23.0 (33.1)	20.3 (32.5)	50%	38%

Abbreviations: A and B, patient groups A (pandemic) and B (pre-pandemic). Jan, January. Feb, February. Oct, October. Dec, December. SD, standard deviation.

group A versus group B demonstrated no significant difference (RR = 1.03, 95% CI 0.52—2.02, p = 0.94). For this outcome, the estimated heterogeneity among the included studies was statistically significant (p = 0.004; I^2 = 78%).

Proportion of children requiring orchiectomy
All included studies [17—22] compared this outcome among the two patient groups. A total of 94/237 and 143/463 children, belonging to groups A and B respectively, required orchiectomy. Pooling the data (Fig. 4) demonstrated no significant difference in the requirement for orchiectomy among the two patient groups (RR = 1.23, 95% CI 0.82—1.84, p = 0.31). The estimated heterogeneity among the included studies was statistically significant (p = 0.01; I^2 = 66%) for this outcome.

Discussion

The quick and accurate diagnosis of testicular torsion is of utmost importance, with a delay in diagnosis (and subsequent surgery) putting the testicular viability at risk,
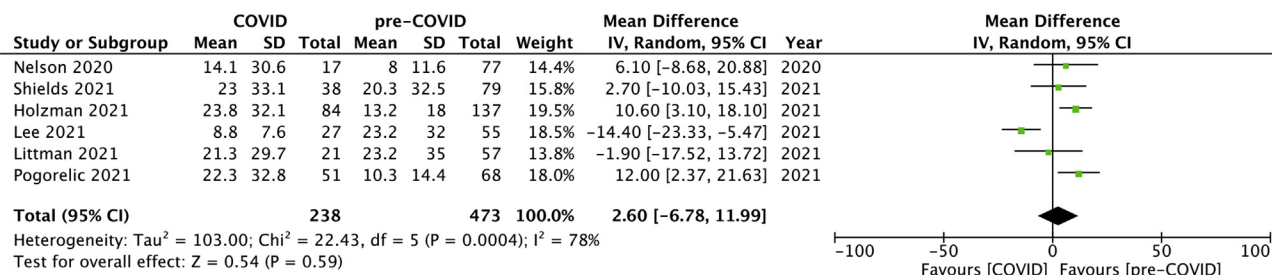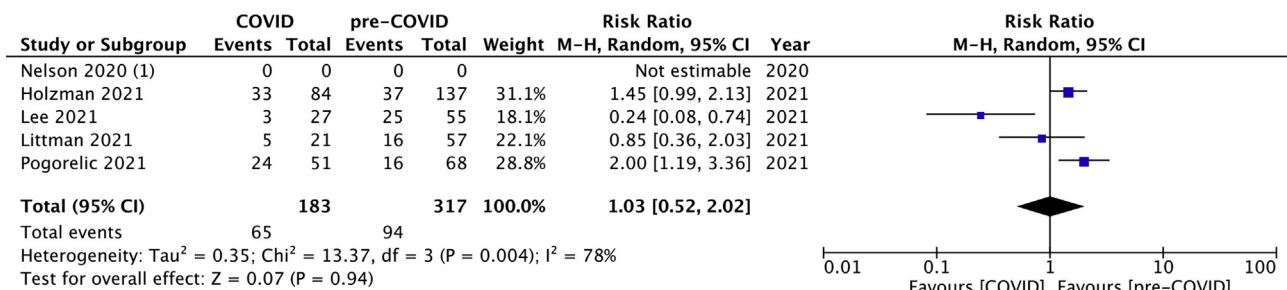

Fig. 2 Forest plot comparison between the two groups, COVID versus pre-COVID, in terms of the average duration of symptoms (hours). COVID, Coronavirus Disease 2019. IV, inverse variance method. CI, confidence interval.

Study or Subgroup	COVID Events	Total	pre-COVID Events	Total	Weight	Risk Ratio M-H, Random, 95% CI	Year	Risk Ratio M-H, Random, 95% CI
Nelson 2020 (1)	0	0	0	0		Not estimable	2020	
Holzman 2021	33	84	37	137	31.1%	1.45 [0.99, 2.13]	2021	
Lee 2021	3	27	25	55	18.1%	0.24 [0.08, 0.74]	2021	
Littman 2021	5	21	16	57	22.1%	0.85 [0.36, 2.03]	2021	
Pogorelic 2021	24	51	16	68	28.8%	2.00 [1.19, 3.36]	2021	
Total (95% CI)		**183**		**317**	**100.0%**	**1.03 [0.52, 2.02]**		
Total events	65		94					

Heterogeneity: Tau^2 = 0.35; Chi^2 = 13.37, df = 3 (P = 0.004); I^2 = 78%
Test for overall effect: Z = 0.07 (P = 0.94)

Favours [COVID] Favours [pre-COVID]

Footnotes
(1) Data not available. However, no intergroup difference in the proportion of children with > 12 hours time of presentation was observed.

Fig. 3   Forest plot comparison between the two groups, COVID versus pre-COVID, in terms of the proportion of children with delayed presentation (>24 h) to the healthcare facility. COVID, Coronavirus Disease 2019. M−H, Mantel-Haenszel method. CI, confidence interval.
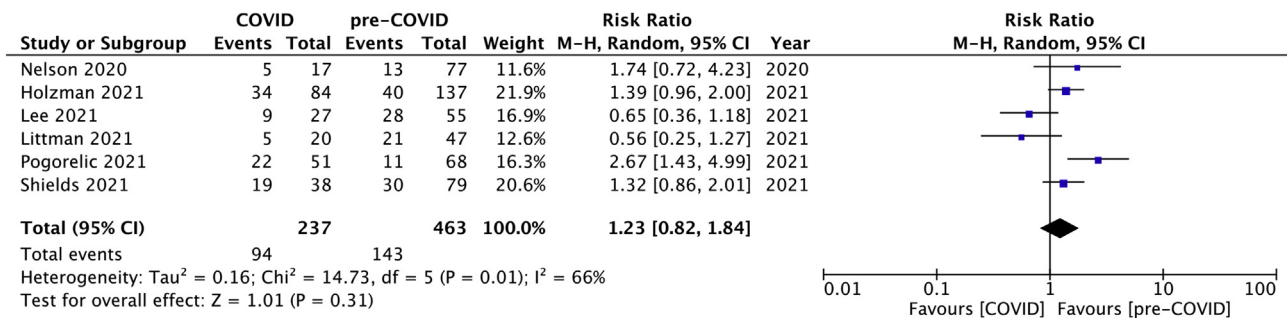
Study or Subgroup	COVID Events	Total	pre-COVID Events	Total	Weight	Risk Ratio M-H, Random, 95% CI	Year	Risk Ratio M-H, Random, 95% CI
Nelson 2020	5	17	13	77	11.6%	1.74 [0.72, 4.23]	2020	
Holzman 2021	34	84	40	137	21.9%	1.39 [0.96, 2.00]	2021	
Lee 2021	9	27	28	55	16.9%	0.65 [0.36, 1.18]	2021	
Littman 2021	5	20	21	47	12.6%	0.56 [0.25, 1.27]	2021	
Pogorelic 2021	22	51	11	68	16.3%	2.67 [1.43, 4.99]	2021	
Shields 2021	19	38	30	79	20.6%	1.32 [0.86, 2.01]	2021	
Total (95% CI)		**237**		**463**	**100.0%**	**1.23 [0.82, 1.84]**		
Total events	94		143					

Heterogeneity: Tau^2 = 0.16; Chi^2 = 14.73, df = 5 (P = 0.01); I^2 = 66%
Test for overall effect: Z = 1.01 (P = 0.31)

Favours [COVID] Favours [pre-COVID]

Fig. 4   Forest plot comparison between the two groups, COVID versus pre-COVID, in terms of the orchiectomy rate. COVID, Coronavirus Disease 2019. M−H, Mantel-Haenszel method. CI, confidence interval.

whereas over diagnosing results in patients undergoing unnecessary surgery. A systematic review compiling 30 studies with 2166 cases specifically focused on investigating the correlation between the duration of torsion and testicular survival [28]. When operated within the "golden" 6 h since the onset of torsion, 97.2% of testes survived. On the other hand, the survivability of the affected testicle dropped to only 24.4% after 24—48 h of torsion [28,29]. The typical age distribution where testicular torsion can be expected to be the cause of acute scrotum is bimodal, with the first peak in the neonatal period, and the second happening around puberty [30,31].

The COVID-19 pandemic is causing a significant burden on the healthcare system, dramatically overturning routine activities inside hospitals. A recent systematic review demonstrated that access to the operating theatre is almost exclusively restricted to emergencies and oncological procedures [32]. Further research into COVID-19 effects on urologic emergencies was conducted, with one study demonstrating that urgent care visits from patients directly to the emergency department decreased (from 219 to 107) while those urgent care visits who were referred by their general practitioners remained unchanged (74—72) when comparing the same periods (from March 9th to April 14th) in 2020 (during the time of COVID-19 pandemic) and 2019 (before the pandemic) [33]. The same study highlighted that the rate of visits for each of the emergencies including the acute scrotum, acute urinary retention, hematuria, cystitis, prostatitis, sepsis, and genito-urinary

trauma from the emergency department and general practitioners remained unchanged when comparing the two time periods [33].

Out of all emergency surgeries being affected by COVID-19 in some way or the other, the studies included in the present meta-analysis aimed their interest at testicular torsion, comparing the outcomes of such cases during the pandemic period compared to the pre-pandemic period. Three outcomes were investigated: the average duration of symptoms, the proportion of children with delayed presentation (>24 h), and the proportion of children requiring orchiectomy. First, there was no significant difference in the average duration of symptoms among the patients presenting with testicular torsion during the pandemic compared to the pre-pandemic period. Second, the proportion of children with delayed presentation showed no difference among the two groups. Finally, the comparison of orchiectomy rates also showed no significant difference among the two patient groups.

Although the exact reason behind the outcome variations among the included studies is not known. One of the possible explanations for these can be the differences in their study designs and sample sizes. Single-center studies with smaller samples [18—20,22] did not show significant differences in investigated parameters, while these differences were significant in multi-center studies with larger sample sizes [17,21]. Other non-modifiable variables affecting the findings of the individual studies can be the distance of healthcare facility from the patient's

residence, the number of centers providing surgical care during the pandemic, availability of the surgeon, etc. Although of significant importance, the hospital transfer rates show minor differences during the pandemic and pre-pandemic periods [17]. Parental unawareness and embarrassment among young boys in some regions might also contribute to delays in treatment-seeking. In addition, the total ischemia time also takes into account the time spent between the diagnosis and reaching the operation room. The delays in COVID-testing prior to the surgery might also result in higher orchiectomy rates during the pandemic. However, despite these reasons, the present meta-analysis revealed no differences in the pooled estimates of the outcomes among the two patient groups. Hence, it is believed that the variations in the individual studies may be geographic and seasonal, and the nature of the disease and the severity of the symptoms associated with this pediatric surgical emergency ultimately take precedence over all these subtle variations.

The results of this review must be interpreted within the context of few limitations. First, all the included comparative studies had a moderate risk of bias. The sample sizes of these studies were also limited. Second, the retrospective nature of all except one study can be a source of bias due to variable reporting. A non-uniform reporting of one of the study outcomes (the proportion of children with delayed presentation) was observed among these studies. Only four out of six studies had reported this outcome. A similar variable reporting was observed in the baseline characteristics (percentage of referred patients). Third, this meta-analysis involves the pooling of heterogeneous data ($I^2 >50\%$ for all outcomes). Not only the study subjects in these included studies were from different geographical locations, but they were recruited in different months. In fact, the patients and controls of the same study were treated in different months of the year [17,20,21]. This can cause outcome variations as previously published studies have highlighted the seasonal differences in the occurrence of testicular torsion [3]. Fourth, the COVID-19 pandemic is not over yet and various centers will share their experiences on this subject in the coming months. It is quite possible that the studies conducted in the future will provide additional insights on the studied outcomes. Finally, these patients were operated upon by different surgeons. This can also affect the outcomes as there is a lack of universal criteria for orchiectomy, and the decision of orchiectomy is mainly subjective, especially in cases of equivocal vascularity after detorsion.

To our best knowledge, the present review is the first to compare the outcomes of children with acute testicular torsion presenting during the pandemic and pre-pandemic periods. However, due to the moderate risk of bias, the level of evidence of the included studies is limited. The strengths of this review include reporting and external validity while the weaknesses lie in internal validity and power.

Conclusion

To conclude, this meta-analysis is likely to be the largest such study that will be performed, and provides a definitive answer as we are likely to get regarding the impact of COVID-19 pandemic on testicular torsion. The results of this meta-analysis depict no significant differences in the duration of symptoms, the proportion of children with delayed presentation, and orchiectomy rate among the children with acute testicular torsion presenting during the pandemic and pre-pandemic periods. However, the moderate risk of bias of the included studies prevents us to derive an appropriate estimate of the overall effect.

Conflict of interests

None.

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Previous publication

None.

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Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.jpurol.2022.01.005.