Sleeping Behavior and Keratoconus: A Scoping Review

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SUMMARY

Aims: This scoping review was conducted to investigate whether nocturnal eye compression from inappropriate sleeping postures may contribute to the development or asymmetry of keratoconus (KC), by examining the association between sleeping positions and KC.

Material and Methods: A systematic search of CENTRAL, MEDLINE, EMBASE, LILACS, ClinicalTrials.gov, gray literature, and selected journals from inception to January 18, 2023, was undertaken.

Results: Ten studies involving 2 322 participants met inclusion criteria. These studies were categorized into analytical and non-analytical designs to evaluate the relationship between prone, lateral, or supine sleeping positions and KC presence or asymmetry. Among the included studies, 50% were non-analytical, all indicating a correlation between KC parameters and nocturnal eye compression. In contrast, a statistically significant association between sleeping positions and KC risk was reported in 3 out of 5 analytical studies (60%).

Conclusion: Findings suggest a possible link between prone or lateral sleeping positions and KC development or asymmetry, implying that these positions may increase corneal biomechanical stress during sleep. However, the association was confirmed in only 60% of analytical studies. The review highlights the necessity for additional research to validate these findings and to explore potential causal mechanisms between sleeping positions and KC.

Key words: cornea, keratoconus, sleep, asymmetric keratoconus, sleeping behavior

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INTRODUCTION

Keratoconus (KC) is considered a bilateral but predominantly asymmetric condition, usually presenting between the second and fourth decades of life, characterized by progressive corneal steepening with associated thinning and protrusion, causing irregular astigmatism. In advanced cases, this condition may result in apical corneal scarring [1–4]. All these corneal alterations can ultimately lead to visual impairment and even require corneal transplantation [4–6].

Prevalence of KC has been estimated to be between 0.2 and 4 790 per 100 000 persons, [4,7,8] while incidence is reported to range from 1.5 to 25 per 100 000 persons/year [9–12]. These significant disparities between rates reported in diverse epidemiological studies reflect the wide global variation, attributed to differences in geographic location and ethnicity, definition of KC, diagnostic criteria, study design, age, and cohort of subjects assessed, among other factors [1,4].

KC etiology and pathogenesis is still a matter of study, and certain theories have been gaining importance over time. Traditionally, KC had been described as a noninflammatory disease, but recent studies have reported associations with significant alterations in inflammatory mediators [4,13,14]. Both genetic and environmental factors are generally considered to influence its occurrence. One of the most widely recognized environmental risk factors is eye rubbing [4,15–18]. The repeated mechanical pressure on the cornea has been associated with the release of proinflammatory mediators, which, among other potential mechanisms, ultimately may contribute to structural modifications in the collagen lamellae, and the development of corneal ectasia [1,4,13–15,17–20]. Indeed, it has recently been suggested that discontinuing eye rubbing could halt the progression of KC, without requiring any additional procedures [21].

Over the last few decades, nocturnal eyeball compression has increasingly emerged as another potentially significant environmental factor in the onset and progression of KC [4,16,18,22–28]. Several studies have specifically identified its impact in cases of asymmetric KC, demonstrating that the eye subjected to nighttime pressure, whether from the hand or pillow, exhibits significantly more pronounced corneal steepness and thinner thickness [4,16,18,22,25–28]. An illustrative example was observed in the case of a pair of monozygotic twins with discordant corneal findings: while one twin exhibited advanced asymmetric KC, the other showed no signs of the condition [29]. The only differences between them were the persistent eye rubbing and the predilection of side sleeping in the twin with the asymmetric KC. The authors suggested that these external factors, related to persistent mechanical compression of the eye, played a significant role in determining the differing corneal findings observed in this pair of identical twins [29]. It has been suggested that environmental factors could be 'a second hit' necessary to trigger a condition in a patient who is genetically predisposed [4]. Alternatively, a hypothesis posits that genetics may not play a crucial role; instead, it suggests that behaviors causing corneal compression serve as the primary, indispensable factor for the onset and progression of KC [15,30].

Given the context mentioned above, this scoping review aims to systematically map the research conducted on the association between KC and sleeping position. A scoping review, rather than a meta-analysis, was chosen due to the limited number of studies available in this field. The purpose is to identify research gaps and provide an overview of this topic using the available evidence. However, the evidence is too scarce to conduct a meta-analysis that could provide statistical summaries of effects.

MATERIAL AND METHODS

We conducted this study in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) extension for scoping reviews (PRISMA-ScR). The protocol is available for reference on the Open Science Framework webpage (osf.io/xw85p). In brief, all clinical studies – both observational and experimental – involving patients of any sex and age with KC, were included. To be eligible for the review, studies must describe and/or analyze the sleeping position and, optionally, the nighttime position of the hand with respect to the face. No restrictions on language or publication status were imposed.

The information specialist (P.A.N) designed search strategies for the main bibliographic databases, selected those with the highest potential to obtain the best available evidence, conducted searches, saved and organized search results, and shared them with the reviewers (A.P.C, S.J.V, and A.T) in appropriate formats. The reviewers assessed the search terms and results for each database, providing feedback.

The comprehensive electronic search included the Cochrane Central Register of Controlled Trials (CENTRAL; searched January 18, 2023) via Ovid, MEDLINE via Ovid (searched January 18, 2023), EMBASE via Elsevier (searched January 18, 2023), and LILACS via BIREME (searched January 18, 2023), using the following MeSH search terms: Cornea, Keratoconus, Ectasia, Keratoconic Cornea, Sleep, Sleeping Behavior, Unilateral Keratoconus, Asymmetric Keratoconus, and Very Asymmetric Keratoconus with database-specific syntax. We also searched additional sources: (I) clinical trial registries for ongoing or recently completed trials on ClinicalTrials.gov (searched January 18, 2023]; (II) reference lists of papers reporting studies selected for inclusion in this review; (III) gray literature in the following electronic resources: GreySource, Health Management Information Consortium (HMIC), and The US National Technical Information Service (NTIS); and (III) in the following full text and high-quality journals available electronically: Graefe's Archive for Clinical and Experimental Ophthalmology, Ophthalmology, JAMA Ophthalmology, American Journal of Ophthalmology, Eye, British Journal of Ophthalmology, Investigative Ophthalmology and Visual Science, Cornea, Journal of Cataract and Refractive Surgery, and Acta Ophthalmologica. Search strategies for bibliographic databases are detailed in supplementary Table 1.

We incorporated all types of publications including observational, experimental studies, systematic review or meta-analysis and conference abstracts published between inception to January 18, 2023, regardless of language or publication status (published, unpublished, or in press), that evaluated the relation of sleeping behavior with KC. Our inclusion criteria encompassed studies with either a comparator or no control group, involving patients (both men and women) diagnosed with KC. There were no age restrictions. The studies assessed the exposure to sleeping positions, including prone or lateral decubitus, as well as the position of the hand close to the face when sleeping. We only excluded narrative reviews. Articles written in languages other than English and Spanish were translated.

Two independent reviewers (A.P.C and S.J.V) screened the titles and abstracts to identify potentially pertinent publications, and those deemed relevant had their full text obtained. The two reviewers, working independently, made the final eligibility decision. Agreement between the reviewers resulted in the study being included.

Discrepancies were solved with a third reviewer (A.T., and P.A.N.). The article authors were contacted if any additional information or clarification was required. The selection process was performed using the Rayyan web tool [31].

Two paired reviewers (A.P.C and S.J.V.) independently extracted data using a specific Excel form (Microsoft Corp., Redmond, WA, USA) for this review. The following main variables were extracted: author name, year of publication, journal name, corresponding author information, location where the study was conducted, study design, inclusion and exclusion criteria, study population, number of participants, characteristics of the population, history of previous treatments for KC, reported sleeping positions, hand position when sleeping, KC involvement (unilateral or bilateral), KC grade, visual acuity, refraction, and corneal parameters.

In this review, the included studies were categorized as either non-analytical or analytical. Studies focused solely on describing characteristics or patterns without comparing groups were labeled as non-analytical; these included case reports, case series, and descriptive cross-sectional studies. In contrast, studies were considered analytical if they were designed to examine associations or differences, such as case-control studies. Cross-sectional studies that used statistical tests to compare two or more groups of patients to assess associations or differences were also classified as analytical.

This scoping review did not involve the collection of new primary data from human subjects. Instead, it involved summarizing and analyzing existing literature and research findings. As such, it did not require Ethics Committee approval.

RESULTS

Search results

Initially, we identified 469 records in electronic databases and registers. We also found 19 additional references

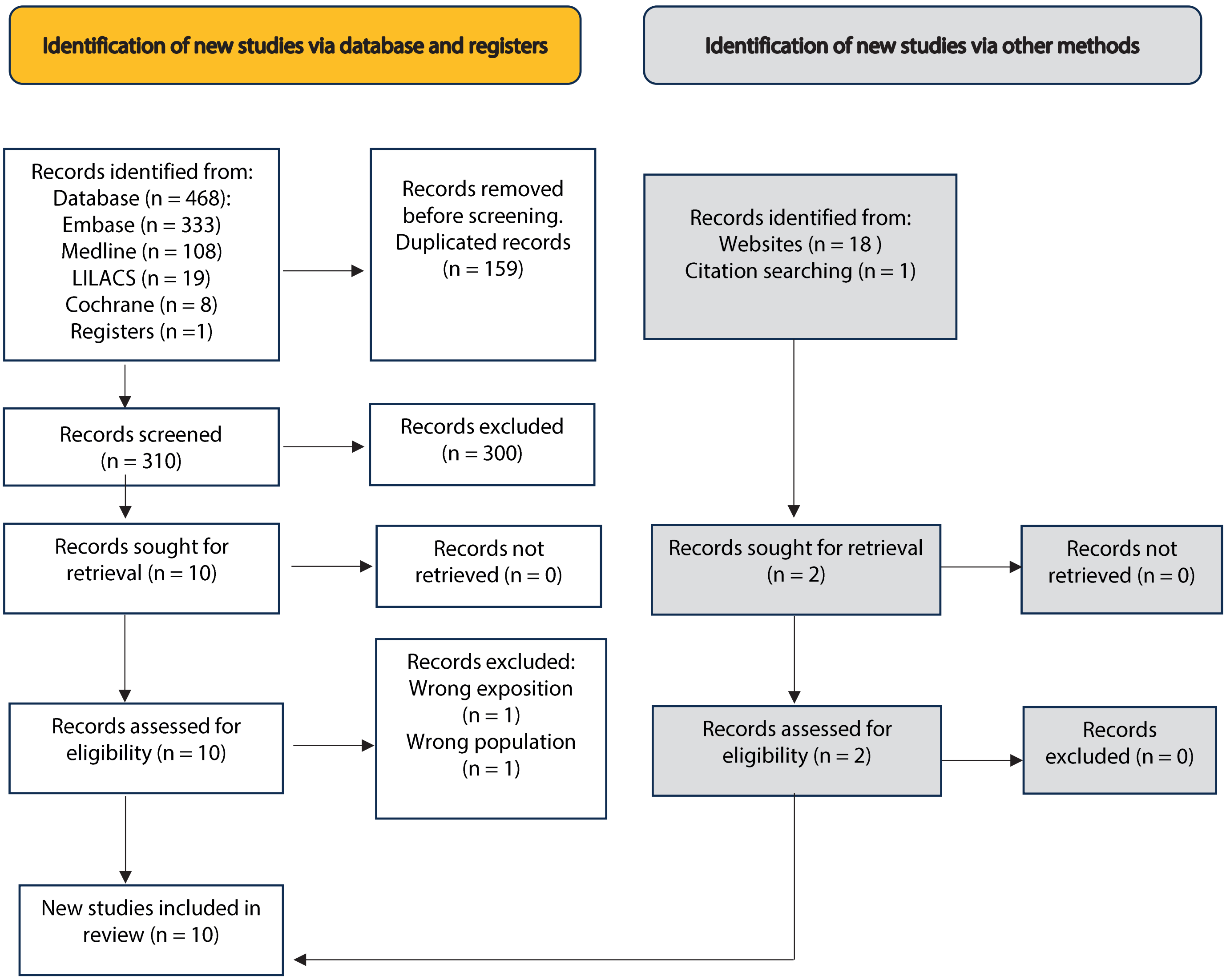

Figure 1. The PRISMA flowchart of systematic review of primary studies in CENTRAL, MEDLINE, EMBASE, LILACS, ClinicalTrials.gov, reference lists, gray literature, and selected reputable journals

using other methods: 16 in the full text and selected journals, 2 in gray literature, and 1 in citation searching. Based on titles and abstracts, 12 studies were selected by the two reviewers (A.P.C and S.J.V). The agreement between the reviewers was perfect (Kappa = 1.0, P < 0.001), indicating very high reliability in their decisions. After full-text evaluation, studies reported in 10 records met our inclusion criteria. The PRISMA flowchart is shown in Figure 1.

Demographics and Clinical Characteristics

Table 1 provides a summary of the main characteristics of each of the 10 studies, which collectively involved 2 322 participants. Five of these studies (50%) were analytical, comprising analytical cross-sectional (n = 2) [32,33] and case-control studies (n = 3) [16,18,25]. The other five (50 %) were non-analytical, including case series (n = 2) [22,26], non-analytical cross-sectional studies (n = 2) [27,28], and a case report (n = 1) [29].

All studies included both males (n = 1 265, 54.5%) and females (n = 1 057, 45.5%). The mean age of participants across the studies was 35.7 ±12.9 years. The research projects were conducted in five countries: France (n = 4, 40%) [16,18,25,29], the USA (n = 2, 20%) [22,28], Turkey (n = 1, 10%) [33], Japan (n = 1, 10%) [32], and Brazil (n = 2, 20%) [26,27]. To facilitate a visual representation of the studies categorized by study

Table 1. Characteristics of included studies

Authors. Year	Type of study	Study period	Country	Sample (N)	Population definition	Age in yrs. (mean ±SD)	Sex (M:F)	Was sleeping behavior a risk factor for KC or AKC?	Observations
Non-analytical									
Bitton et al. 2022 [29]	Case report	NR	France	2	MZ twins, one with AKC	29 ±0.0	2:0	Yes	The sleeping position was suggested to play a role in the development of KC in one of two MZ twins, who obviously shared identical genetic inheritance.
Donnenfeld, et al. 1991 [22]	Case series	NR	USA	5	Patients with KC and concomitant Floppy Eyelid syndrome	32.8 ±10.6	2:3	Yes	Both KC and the Floppy Eyelid syndrome was worse on the side on which the patients slept.
Lima et al. 2016 [27]	Cross-sectional	January to December 2014	Brazil	60	Patients with KC	NR	25:35	Yes	The eye that was positioned inferiorly during sleep had greater topographic changes.
Nayak et al. 2014 [28]*	Cross-sectional	NR	USA	21	Patients with KC	33.4 ±11.1	16:5	Yes	Right-face down sleepers had higher flat K and thinner corneas.
Santos et al. 2021 [26]	Case series	May 2015 to July 2016	Brazil	34	Patients with KC who were candidates for intrastromal corneal ring segments surgery	26.5 ±7.5	20:14	Yes	Keratometric values were worse in the eye corresponding to the preferred side for sleeping.
Analytical									
Dourdeau et al. 2022 [25]	Case-Control	June 2019 to February 2021	France	Cases: 195	Cases: Patients with KC	Cases: 32 ±12.3	Cases: 130:65	Yes	The contact of the hand or forearm with the eyes during sleep was associated with KC. In KC cases, the worse eye was linked to more rubbing and potential pressure during the night based on sleeping position.
				Controls: 195	Controls: patients consulting an ophthalmologist without KC	Controls: 32 ±12.3	Controls: 130:65		

Mazhar-ian et al. 2020 [16]	Case--Control	January 2017 to April 2018	France	Cases: 33	Cases: Patients with KC	Cases: 29.12 ±7.4	Cases: 26:7	Yes	Sleeping on the sides and prone position showed a significant association with KC. Additionally, the worse eye among KC cases was significantly associated with the preferred side for sleeping.
				Con-trols: 64	Controls: Refractive surgery patients without KC	Con-trols: 28.1 ±6.3	Con-trols: 50:14		
Moran et al. 2020 [18]	Case--Control	May 2014 to Novem-ber 2017	France	Cases: 202	Cases: KC patients attending initial or follow-up consultation	Cases: 32.5 ±6.1	Cases: 149:53	Yes	Prone and side sleep positions were sig-nificantly associated with KC.
				Con-trols: 355	Controls: Patients who attended refractive consultation without KC	Con-trols: 30.7 ±6.2	Con-trols: 149:207		
Nakao et al. 2021 [32]	Cross--sectio-nal	April 2017 to June 2020	Japan	Group 1: 505	Group 1: Patients with KC	Group 1: 45.0 ±14.6	Group 1: 324:181	No	No significant dif-ferences in sleeping behavior were found between the AKC and KC patients.
				Group 2: 66	Group 2. Patients with AKC	Group 2: 43.8 ±12.5	Group 2: 42:24		
Özalp et al. 2021 [33]	Cross--sectio-nal	March 2019 to March 2020	Turkey	Group 1:23	Students and faculty members with KC or subclinical KC	Group 1: 23.6 ±3.0	Group 1: 8:15	No	Prone sleep position was not statistically significant as a risk factor.
				Group 2: 562	Students and faculty members without KC or subclinical KC	Group 2: 21.5 ±2.6	Group 2: 192:370		

**This study was reported in a conference abstract.*
M – Male, F – Female, NR – No reported, KC – Keratoconus, USA – United States of America, UHAKC – Unilateral or Highly Asymmetric Keratoconus, AKC – Asymmetric Keratoconus, MZ – monozygotic

type and country of origin, we developed an interactive geographic map using the open-source tool Eviatlas (Figure 2) [34].

The included populations varied across studies, with different definitions used: patients with KC [18,25,27,28], patients with asymmetric KC [16,32], individuals with KC eligible for intrastromal corneal ring segments surgery [26], patients with concomitant KC and Floppy Eyelid Syndrome [22] and students and faculty members at a university health center with KC or subclinical KC [33]. One study reported discordant KC in monozygotic twins: one had bilateral and asymmetrical KC, while the other had normal corneas without evidence of KC [29].

Nine studies [16,18,22,25,26,28,29,32,33] evaluated also eye rubbing and allergies as potential risk factors for KC. Among the patients with KC 62.3% (n = 714), had a history of eye rubbing, and 68.8% (n = 788) had a history of allergy. However, only four (44.4%) of the nine studies showed a statistically significant difference in proportions between cases and controls for the history of eye rubbing [25,16,18,33] and three (33.3%) studies showed a significant difference for the history of allergy [16,31,32]. Among the five studies that assessed familial history of KC, only one (20%) reported a statistically significant difference between patients with KC (n = 39, 20%) and those without KC (n = 2, 1%). (see Table 2) [25].

Sleeping behavior and KC

As expected, and in accordance with the inclusion criteria, all the 10 studies assessed sleeping behavior as a potential risk factor for developing or increasing the severity of KC. The five non-analytical studies [22,26–29] collectively reported that out of 122 KC patients, 36.1% (n = 44) adopted a right-sided sleeping position, 27.0% (n = 33) favored a left-sided position, 15.6% (n = 19) preferred a prone sleep position, 5.7% (n = 7) assumed any lateral decubitus position, and 4.9% (n = 6) maintained a supine position. 10.7% (n = 13) assumed an unspecified sleeping posture (see Table 2). Donnenfeld et al. (1991) reported five cases of bilateral Floppy Eyelid syndrome with concomitant KC. In four cases with asymmetric KC and Floppy Eyelid syndrome, patients reported predominantly sleeping on the most involved side [22]. Nayak et al. (2014) conducted a cross-sectional study to explore the link between sleep position and KC, revealing statistically significant associations: (1) subjects who slept on their sides exhibited a higher level of inter-ocular differences in spherical equivalent refraction; (2) those who favored a right-side face-down sleeping position demonstrated an increased value of flat keratometry and thinner corneas in the right eye (OD); and (3) patients who believed they applied pressure on their OD while sleeping displayed notably greater inter-ocular differences in maximum keratometry (Kmax) and posterior elevation at the thinnest point, compared to those who denied exerting pressure on either eye [28].

Santos et al. (2021) analyzed the relation between the laterality and severity of KC and individuals' preferred sleeping positions. They demonstrated that the Kmax measurements of both the right and left eyes aligned with the respective sleeping sides. Specifically, for participants who favored sleeping on their right side, the Kmax was 63.6 ±5.6 Diopters (D) for the OD and 57.7 ±7.7 D for the left eye (OS). Similarly, for those who preferred a left-sided sleeping position, the OD Kmax measured 58.6 ±7.7 D, while the OS Kmax was 61.2 ±5.8 D [26].

Lima et al. (2016) examined the relationship between asymmetry in KC and participants' preferred sleeping positions. Out of their total sample of 60 participants, 93.3% (n = 56) exhibited topographic asymmetries between their eyes. A significant association was observed between the lateral decubitus sleeping position and the eye with the most significant KC involvement (p = 0.014). Specifically, 63.6% (n = 14) of individuals with asymmetric KC who slept on their right side and 76.5% (n = 13) who preferred their left side, exhibited the greatest KC severity in the corresponding eye on the same side of their preferred sleeping position [27].

In relation to the five analytical studies [16,18,25,32,33], out of 1 024 KC patients, 27.2% (n = 279) preferred

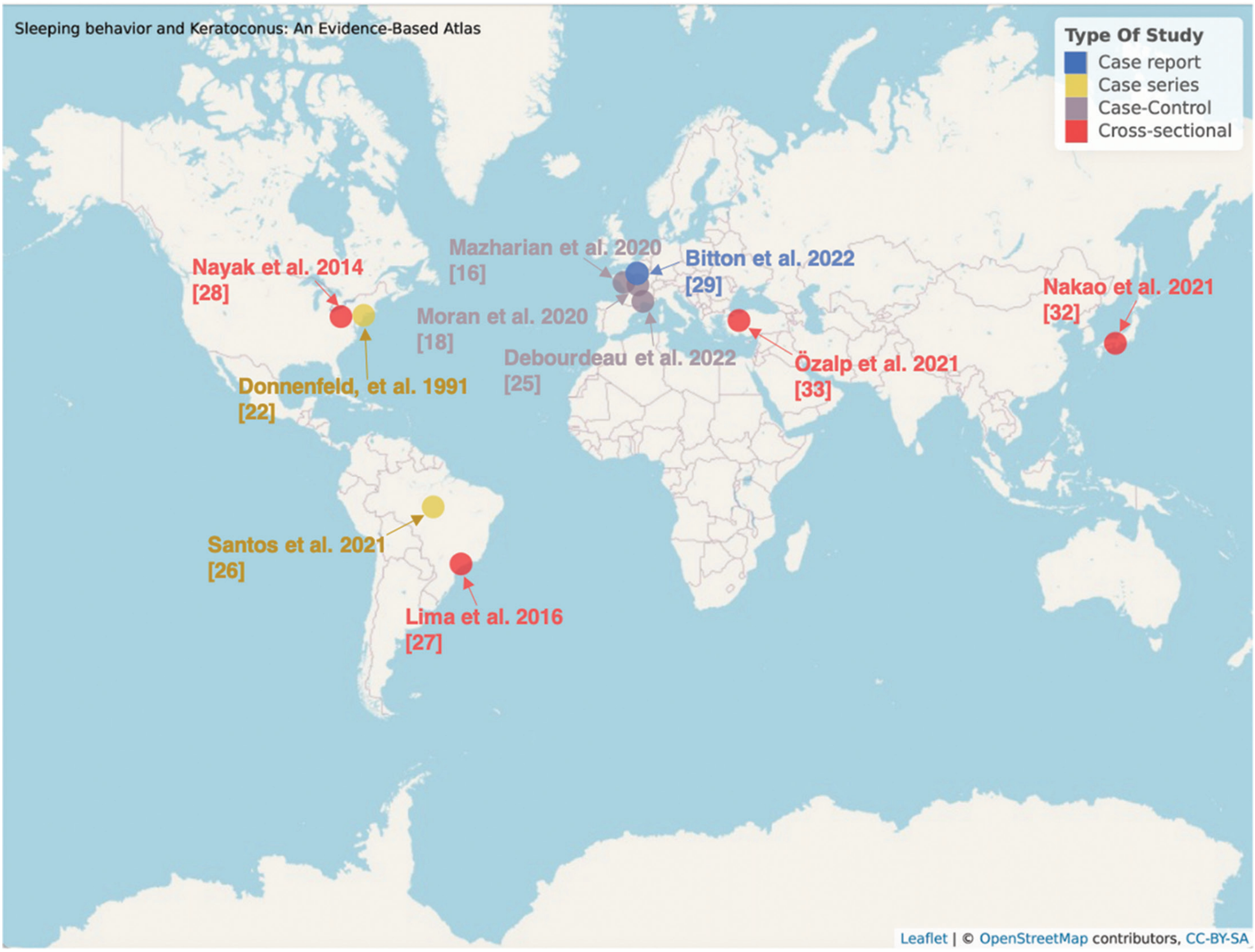

Figure 2. Map with the geographical origin of the 10 studies included in this scoping review. First author's last name, year of publication, and reference number are shown. The type of study is indicated by a color code (top right corner)

sleeping on either side and 21.6% (n = 221) of cases chose a prone sleep position (see Table 2). Moran et al. (2020) conducted a case-control study to evaluate the risk factors associated with KC, demonstrating through a model of multivariate regression analysis, adjusted for age, that the prone sleep position (OR = 11.63; 95% CI: 3.88–38.16) and side sleep position (OR = 10.17; 95% CI: 3.84–33.73) significantly correlated with KC, indicating their importance as risk factor for development [18]. Similarly, Mazharian et al. (2020) conducted a case-control study to investigate the association between sleeping positions and patients with Unilateral or Highly Asymmetric Keratoconus (UHAKC). In the univariate analysis of the UHAKC group, comparing the worse and the better eye, it was observed that a sleeping position on either side was associated with the more advanced KC presentation in the eye on the corresponding side (OR = 94.72, 95% CI: 19.24–466.43). In the multivariate analysis, statistical significance was confirmed for prone or lateral decubitus sleeping positions (OR = 65.02, 95% CI: 5.05–573.91) and sleeping on the side of the most affected eye (OR = 144.02, 95% CI: 7.37–2815.88) [16]. Likewise, in a case-control study by Debourdeau et al. (2022), the researchers observed that when analyzing asymmetry in KC cases, the worse eye was associated with the potentially more compressed eye during the night, based on sleeping position (p = 0.041) [25].

Contrastingly, Nakao et al. (2021) found no significant differences in sleeping behavior between patients with very asymmetric keratoconus (i.e. one eye without clinical or topographic signs of keratoconus) and non-asymmetric keratoconus patients (p = 1.0) [32].

Debourdeau et al. (2022), reported no statistically significant difference regarding the supine or lateral decubitus position between patients with KC and healthy controls (p = 0.73 and p = 0.34, respectively). Nevertheless, they did find an association between the contact of the hand or forearm with the eyes during sleep and the presence of KC (p = 0.01) [25].

On another note, in a cross-sectional population-based study, Özalp et al. (2021) concluded, in contrast to the findings of Moran et al. [18], that the prone sleep position was not a statistically significant risk factor for keratoconus (p = 0.70) [33].

DISCUSION

In this scoping review, our findings suggest that the study of sleeping positions in patients with KC is not common in current ophthalmology. However, there has been a rapid increase in the number of studies investigating these habits as a potential risk factor for KC over the past few years [4,16,18,22–29,32,33]. We identified 10 primary studies including 2 322 subjects, which addressed the role of sleeping behavior in KC, published between 1991 and 2022. The authors of these studies hailed from diverse regions across four continents worldwide, encompassing South America [26,27], North America [22,28], Europe [16,18,25,29,33] and Asia [32] (see Figure 2).

Our findings suggest a plausible association between prone and side sleep positions and the presence or asymmetry of KC. In the five non-analytical studies [22, 26–29],

Table 2. Description of potential risk factors associated with keratoconus, including sleeping position

Authors. Year	Eye rubbing		Family history of KC		Allergy		Lateral decubitus sleep position		Prone sleep position	
	Cases N, (%)	Controls N, (%)	Cases N, (%)	Controls N, (%)	Cases N, (%)	Controls N, (%)	Cases N, (%)	Controls N, (%)	Cases N, (%)	Controls N, (%)
Non-analytical										
Bitton et al. 2022 [29]	1, (50.0)	NA	0, (0.0)	NA	1, (50.0)	NA	1, (50.0)	NA	0, (0.0)	NA
Donnenfeld et al. 1991 [22]	2, (40.0)	NA	1, (20.0)	NA	2, (40.0)	NA	4, (80.0)	NA	1, (20.0)	NA
Lima et al. 2016 [27]	NR	NA	NR	NA	NR	NA	46, (76.7)	NA	13, (21.7)	NA
Nayak et al. 2014 [28][α]	19, (90.5)	NA	NR	NA	14, (66.7)	NA	12, (57.1)	NA	5, (23.8)	NA
Santos et al. 2021 [26]	16, (47.1)	NA	NR	NA	26, (76.5)	NA	21, (61.8)	NA	NR	NA
Analytical										
Debourdeau et al. 2022 [25]	164, (84.1)*	66, (33.9)	39, (20.0)*	2, (1.0)	124, (63.6)	78, (40.0)	131, (67.2)	122, (62.6)	NR	NR
Mazharian et al. 2020 [16]	32, (97.0)*	10, (15.6)	1, (3.0)	1, (1.6)	25, (75.8)*	33, (51.6)	31, (93.9)[β]*	9, (14.1)[β]*	28, (84.8)**	18, (28.1)**
Moran et al. 2020[18]***	201, (99.5)*	181, (51.0)	14, (6.9)	4, (1.1)	122, (60.4)	129, (36.3)	117, (57.9)*	195, (54.9)	76, (37.6)*	82, (23.1)
Nakao et al. 2021 [32]	270, (53)	37, (56)	20, (4)	2, (3.0)	464, (92)*	61, (92)	NR	NR	112, (22)	12, (19)
Özalp et al. 2021 [33]	9, (39.1)*	121, (21.5)	1, (4.3)	3, (0.5)	10, (43.5)*	100, (17.8)	NR	NR	5, (21.7)	154, (27.4)

NA – Not applicable, NR – No Reported
** There was a significant statistical difference between cases and controls.*
*** The authors evaluated the prone position as: "sleeping on stomach or sides".*
**** The authors adjusted the raw data for age in preparation for multivariate analysis. This table displays the data before the adjustment.*
[α]This study was reported in a conference abstract.
[β]Sleeping on the same side as the eye with the steepest keratometry.

the most prevalent sleeping position among KC patients was right-sided (n = 44; 36.1%), followed by left-sided (n = 33; 27.0%), and prone position (n = 19; 15.6%). All of these studies indicated a correlation between parameters of KC progression (such as steepening of keratometry values and Kmax, and corneal thickness thinning) and potential nocturnal eye compression related to lateral or prone decubitus sleeping positions. On the other hand, only in 60% (n = 3) [16,18,25] of analytical studies, the authors found a statistically significant association for sleeping position such a risk factor for KC, with 27.2% (n = 279) of participants preferring to sleep on either side and 21.6% (n = 221) choosing the prone sleeping position.

In the study conducted by Moran et al. [18], the variables 'side sleep position' and 'prone sleep position' were adjusted for age in both crude and multivariate analyses. The results demonstrated that both sleeping positions acted as risk factors for KC. However, to gain a deeper understanding of the impact of these variables without adjusting for age, we asked the authors to provide access to the database in the context of this scoping review. Our data analysis revealed that sleeping in a prone position increases the risk of KC (OR = 2.63, 95% CI: 1.64–4.20), while sleeping in a supine position decreases the probability of developing KC (OR = 0.21, 95% CI: 0.10–0.47). On the other hand, sleeping in a side position did not show statistical significance (OR = 0.78, 95% CI: 0.51–1.18).

In a meta-analysis conducted by Song et al. [35], which focused on non-genetic risk factors for KC, only two of the studies included in the present review were also analyzed by them for sleep position [16,18]. The outcomes suggested a potential increase in the likelihood of KC associated with side-sleep position (OR: 3.8, 95% CI: 0.31–46.23) and prone position (OR: 12.76, 95% CI: 0.27–598). Nevertheless, these results should be interpreted cautiously due to significant heterogeneity ($I^2 = 95\%$, $P < 0.00001$), a small sample size, lack of statistical significance for the overall effect ($p = 0.29$ for side sleep position, and $p = 0.19$ for prone sleep position), and wide confidence intervals extending beyond the non-effect limit.

This scoping review holds several strengths. Firstly, it represents the first comprehensive evidence-based analysis of studies examining sleep behavior in patients with KC. Secondly, we utilized structured Cochrane methods for the systematic search, data extraction, and result synthesis [36]. Lastly, our review mapped the research landscape in this area, defining its scope and identifying research gaps related to the potential causality of nocturnal eyeball compression due to sleep position and KC.

However, there are potential limitations to this study. The review did not represent wide geographic and ethnic groups. We encountered methodological heterogeneity due to variability in study designs and diverse outcome measurement tools. Notably, the absence of a validated questionnaire to assess sleep behavior in patients with KC resulted in heterogeneous reporting of different sleep positions across studies. Additionally, information bias may arise during retrospective evaluation of sleeping behavior using a questionnaire [37]. The inherent variability in sleep positions throughout the night raises the possibility that individuals may not consistently maintain the reported sleeping position, and, in reality, they might adopt different positions during most of the night.

Our findings underscore a knowledge gap in the field of nighttime postures and the absence of an objective measurement tool to assess both sleep position and nocturnal eyeball compression. Developing such a tool would not only characterize them, but also deepen our understanding of the relationship between sleep habits and KC. This, in turn, could contribute to the development of more effective preventive measures, including nocturnal eye protection devices, to forestall the onset and/or progression of KC. We have been working for some time on developing an all-night continuous recording instrument to obtain more reliable data, and we expect to have the prototype ready soon.

CONCLUSION

This scoping review marks the inaugural systematic mapping of research on the relationship between sleeping behavior and KC. Our findings suggest a feasible association between prone and side sleep positions, possibly through ocular compression, with KC development and progression. However, a significant limitation is the lack of an instrument that enables the objective measurement of sleeping position and potential nocturnal compression of the eyeball. Further studies are necessary to increase the certainty of evidence. We emphasize the importance of employing study designs, such as experimental research involving animal models or *ex vivo* approaches, as potential avenues to explore the causality between sleeping position and KC.

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Supplementary Table 1. Detailed account of the literature search

Search strategy for MEDLINE (OVID) and CENTRAL (OVID)		
Population	1	exp Cornea/
	2	exp Keratoconus/
	3	Cornea*.tw.
	4	Keratoconu*.tw.
	5	(Unilateral adj3 keratoconu*).tw.
	6	(Asymmetric adj3 keratoconu*).tw.
	7	(Very adj3 asymmetric adj3 keratoconu*).tw.
	8	Ectasia*.tw.
	9	(Keratoconic adj3 cornea*).tw.
	10	1 or 2 or 3 or 4 or 5 or 6 or 7 or 8 or 9 or 10
Exposition	11	exp Sleep/
	12	(Sleep* adj3 position*).tw.
	13	(sleep* adj3 behavior).tw.
	14	11 or 12 or 13
Population AND inter-vention	15	10 and 14

Search strategy for LILACS (BIREME)		
Population	1	(mh:(„Cornea“))
	2	(mh:(„Keratoconus“))
	3	((mh:(„Cornea“))) OR ((mh:(„Keratoconus“)))
Exposition	4	(mh:(„Sleep“))
	5	(mh:(„Risk Factors“))
	6	((mh:(„Sleep“))) OR ((mh:(„Risk Factors“)))
Population AND inter-vention	8	(((mh:(„Cornea“))) OR ((mh:(„Kerato-conus“)))) AND (((mh:(„Sleep“))) OR ((mh:(„Risk Factors“)))) AND (db:(„LILACS“))

Search strategy for EMBASE (ELSEVIER)		
Population	1	'Cornea'/exp
	2	'Keratoconus'/exp
	3	Cornea*:ab,ti,kw
	4	Keratoconu*:ab,ti,kw
	5	(Unilateral NEAR/3 keratoconu*):ab,ti,kw
	6	(Asymmetric NEAR/3 keratoconu*):ab,ti,kw
	7	(Very NEAR/3 asymmetric NEAR/3 kerato-conu*):ab,ti,kw
	8	Ectasia*:ab,ti,kw
	9	(Keratoconic NEAR/3 cornea*):ab,ti,kw
	10	#1 OR #2 OR #3 OR #4 OR #5 OR #6 OR #7 OR #8 OR #9
Exposition	11	'Sleep'/exp
	12	(Sleep* NEAR/3 position*):ab,ti,kw
	13	(sleep* NEAR/3 behavior):ab,ti,kw
	14	#11 OR #12 OR #13
Population AND inter-vention	15	#10 AND #14

Search strategy for ClinicalTrials.gov		
Population	1	"Cornea"
	2	"Keratoconus„
	3	1 OR 2
Exposicion	4	"Sleep"
	5	"Risk Factors"
	6	4 OR 5
Population AND inter-vention	14	#3 and 6

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