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Retinopathy of Type 1 Diabetes in Arab Countries: Systematic Review and Meta-Analysis

Hatem Zayed[a] Ussama M. Abdel Motal[b] Akila Gopalakrishnan[a]
Chinnayan Ponnuraja[c] C. George Priya Doss[d] Nasser Rizk[a] Fatma M. Shebl[e]

[a]Department of Biomedical Sciences, College of Health Sciences, Qatar University, Doha, Qatar; [b]Sidra Medicine, Human Genetics, Translational Medicine, Qatar Foundation, Doha, Qatar; [c]National Institute for Research in Tuberculosis, Chennai, India; [d]VIT University, Vellore, India; [e]Yale School of Public Health, New Haven, CT, USA

Keywords
Diabetic retinopathy · Type 1 diabetes · Complications · North Africa · Arab countries · Prevalence

Abstract
Aims: To conduct a systematic review and meta-analysis of retinopathy prevalence in patients with type 1 diabetes (T1D) in 22 Arab countries. ***Methods:*** We systematically searched 4 different literature databases (PubMed, Science Direct, Web of Science and Embase), from the date of inception until December 2017, to collect all the information about patients with T1D who developed retinopathy complications; for statistical analysis, we used MetaXL to evaluate the pooled prevalence estimate and the subgroup prevalence estimates employing double arcsine transformation and inverse variance heterogeneity models. ***Results:*** Our search strategy returned 475 studies, of which 39 met our inclusion criteria; of those, 16 were eligible for meta-analysis that were captured only in 15 Arab countries, through 45 years (1969–2014). The number of retinopathy patients was 396 out of 1,931 patients with T1D. The prevalence of retinopathy was 19% (95% CI 10–28%). Substantial heterogeneity was observed (Q 240.78, $p < 0.0001$, I^2 93.77%, 95% CI 91.35–95.52%); however, no single study considerably affected the overall pooled prevalence estimate. ***Conclusion:*** Almost one fifth of T1D patients in 15 Arab countries have diabetic retinopathy, therefore it is important to improve the care of patients with T1D and in Arab countries to avoid the development of such a devastating complication.

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Introduction

It is estimated that more than 415 million people worldwide currently have diabetes and that number is predicted to rise to 642 million by 2040 [1]. It has become a chronic disease with several devastating complications. Diabetic retinopathy (DR) is a microvascular complication of diabetes and one of the leading causes of visual impairment worldwide, accounting for 93 million worldwide, with 28 million affected by vision-threatening DR [2]. With the expected global rise in the prevalence of diabetes [1, 3], the number of cases of DR and vision-threatening DR, which includes severe nonproliferative DR, proliferative DR, and diabetic macular edema, has been predicted to increase to 191.0 million and 56.3 million,

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E-Mail karger@karger.com
www.karger.com/ore

Hatem Zayed, PhD
Department of Biomedical Sciences, College of Health Sciences
Qatar University
Doha (Qatar)
E-Mail hatem.zayed@qu.edu.qa

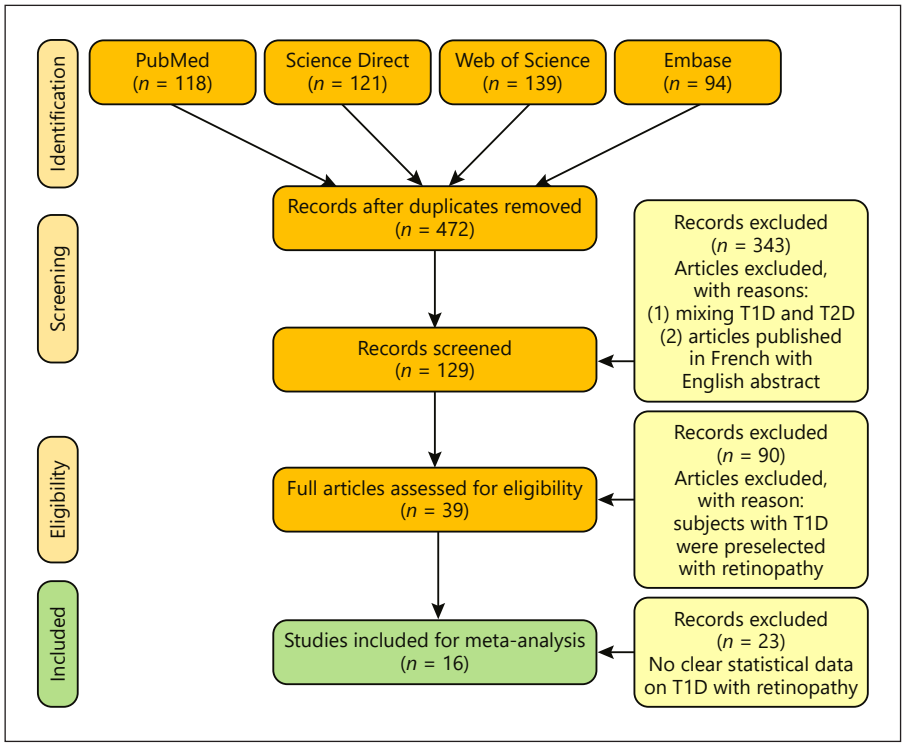

Fig. 1. Flow diagram of selected articles.

respectively, by 2030 [1]. Therefore, DR is declared as the priority disease in the VISION 2020 global elimination of blindness.

The Wisconsin Epidemiologic Study of Diabetic Retinopathy reported 3.6% of type 1 diabetes (T1D) and 1.6% of type 2 diabetes (T2D) patients as legally blind [4]. The prevalence of DR is higher in T1D compared to T2D, with sight-threatening retinopathy 2.5 times more common in T1D, independently of the duration of diabetes [4, 5]. The major risk factors for DR pathogenesis include diabetes duration, HbA_{1c}, high blood pressure, and dyslipidemia [2].

The Arab World is comprised of 22 Arab-speaking countries (http://www.arabbay.com/arabmap.htm). To date, the population of the Arab-speaking countries is approaching 0.5 billion [6]. In the Middle East and North Africa (mostly Arabs), 4 out of 10 adults with diabetes are undiagnosed [1]. Five Arab countries (United Arab Emirates, Bahrain, Kuwait, Qatar, and Saudi Arabia) rank within the top 15 nations in the world for highest rate of diabetes per capita (between 19.3 and 20%), whereas Egypt, Oman, and Lebanon rank within the top 40 nations. Although diabetes in the Arab countries is considered as a major public health problem, T1D and its complications are not well studied [7–9]. To date, there are no accurate reports about the estimated prevalence of DR among Arab patients with T1D [8, 9]. Therefore, in an effort to shed light onto such a serious complication of T1D among Arab patients, we performed a systematic review and meta-analysis on all reported literature from the time of inception until December 2017.

Methods

Search Strategy

We performed a systematic search using 4 different literature databases (PubMed, Science Direct, Web of Science, and Embase) (Fig. 1) from the time of inception until December 2017. The search terms used were: "Type 1 diabetes" and "Retinopathy" with the specific Arab country name, "microvascular complications" and "type 1 diabetes" and the name of each Arab country OR "IDDM" with "Diabetic Retinopathy" OR "T1D" OR "T1DM" with "Retinopathy" with the "name of each country" or "Middle East".

Study Selection

The inclusion criteria for our studies were: (1) only peer-reviewed research article, (2) the patients with T1D who presented with diabetic retinopathy, (3) only Arab patients residing in Arab countries. Our exclusion criteria were: (1) patients were a mix of T1D and T2D, with no clear distinction of retinopathy complication to either T1D or T2D, (2) retinopathy was only due to T2D, (3) no mention of the type of diabetes in the study.

Table 1. Epidemiology of retinopathy in the Arab countries among subjects with T1D

Country	Study period	T1D patients	DR patients	%	C/FH	M/F	Age, years	Study	Reference
Algeria	2008	138	44	0.32	NR	1.16/1	>15	clinical screening	Ayad et al. [48], 2010
	2009–2010	323	73	0.23	NR	NR	19–45	cross-sectional	Berkani et al. [13], 2013
	NR	41	16	0.39	NR	4.86/1	NR	follow-up	Vague et al. [12], 1988
Bahrain	2002	107	18	0.17	NR	1.02/1	NR	clinical	Al-Harbi et al. [45], 2004
	2000–2001	57	10	0.18	NR	1.02/1	NR	follow-up	Al-Hermi et al. [49], 2005
Egypt	2015	40	11	0.28	NR	F[a]	9–18	retrospective	Dayem et al. [14], 2015
	2010–2013	576	10	0.02	FH	1.3/1[b]	0.5–18	hospital registry	El Samahy et al. [19], 2015
	2011	75	9	0.12	NR	0.32/1	13–18	cohort	Elbarbary et al. [15], 2012
	2004–2006	55	5	0.09	NR	NR	NR	case control	El-Habashy et al. [20], 2010
	NR	150	15	0.10	NR	NR	16–22	cross-sectional	Gadallah et al. [16], 2010
	2012	30	8	0.27	NR	NR	NR	cross-sectional	Habeeb et al. [17], 2012
	2006–2007	416	17	0.04	C, FH	0.94/1	4–11	retrospective, descriptive	Ismail et al. [27], 2008
	2007–2008	354	81	0.23	NR	NR	NR	cross-sectional	Macky et al. [18], 2011
	2006–2008	60	18	0.30	NR	1/1	NR	cross-sectional	Salem et al. [44], 2011
Jordan	2003–2005	10	NR	NR	FH	NR	23–75	retrospective	Bahou et al. [50], 2007
	2003	66	29	0.44	NR	NR	NR	cross-sectional	Al-Till et al. [51], 2005
	1996–1998	140	59	0.42	NR	F[a]	NR	retrospective	Maayah et al. [52], 2001
Kuwait	2006	63	9	0.14	NR	NR	>18	cross sectional	Al-Sarraf et al. [47], 2010
Lebanon	2013	220	32	0.15	NR	0.88/1	12–46	clinical	Baz et al. [41], 2013
	2014	1	1	1.00	NR	NR	NR	case report	Sanyoura et al. [53], 2014
	1999	1	1	1.00	NR	NR	NR	case report	Simman et al. [54], 1999
Libya	2008	26	4	0.15	FH	2.25/1	5–90	cross-sectional	Elhwuegi et al. [40], 2012
	1969–1985	220	11	0.05	C	1.04/1	5–90	hospital registry	Kadiki et al. [34], 1987
Morocco	2002	20	18	0.90	NR	0.67/1	NR	retrospective	Khanfri et al. [55], 2005
	2006	72	50	0.69	FH	2.27/1	NR	prospective	Bentata et al. [56], 2013
	2000–2008	2	1	0.50	NR	NR	10–16	clinical report	Haddiya et al. [57], 2010
Oman	2001	207	41	0.20	NR	NR	40–70	cross-sectional	Khandekar et al. [43], 2003
	1996–1997	96	36	0.38	NR	NR	NR	clinical	El Haddad and Saad [42], 1998
Qatar	2011–2013	244	35	0.14	C, FH	NR	30–60	clinical	Bener et al. [58], 2014
Saudi Arabia	1993–2005	369	4	0.01	C, FH	0.95/1	5–14	retrospective	Al Rashed [21], 2011
	2013–2014	228	9	0.04	NR	0.62/1	1–18	cross-sectional	Al-Agha et al. [22], 2015
	1993–1998	174	74	0.43	NR	NR	NR	clinical	El-Asrar et al. [23], 1998–1999
	NR	210	90	0.43	NR	0.89/1	5–90	cross-sectional	El-Asrar et al. [24], 2001
	1998–2002	54	24	0.44	NR	NA	18–34	follow-up	Rahman et al. [25], 2007
Tunisia	2007–2011	255	NR	0.07	NR	NR	NR	cross-sectional	Kahloun et al. [59], 2014
UAE	2003–2004	47	18	0.38	NR	NR	NR	cross-sectional	Al-Maskari and El-Sadig [46], 2007
Yemen	2004	111	82	0.74	C	NR	NR	cross-sectional	Bamashmus et al. [26], 2009
Sudan	1977–1986	101	4	0.04	FH	0.91/1	NR	hospital registry	Elamin et al. [60], 1992
	1995	128	55	0.43	NR	1.08/1	15–75	NR	Elbagir et al. [28], 1995

T1D, type 1 diabetes; C/FH, consanguinity/family history; M/F, male/female ratio; NR, not reported; NA, not available. When the values could not be concluded due to the mix between T1D and T2D or not reported, the value is assigned "NR".

[a] All patients were females. [b] 24 patients of the enrolled 600 patients were T2D cases.

Table 2. The prevalence of retinopathy complication among Arab subjects with T1D in the included studies

Study	Prevalence	95% CI		Weight, %
		lower	higher	
Ayad et al. [48], 2010	0.32	0.24	0.40	7.14
Vague et al. [12], 1988	0.39	0.25	0.55	2.14
Al-Harbi et al. [45], 2004	0.17	0.10	0.25	5.54
Dayem et al. [14], 2015	0.28	0.15	0.43	2.09
El-Habashy et al. [20], 2010	0.09	0.03	0.18	2.86
Gadallah et al. [16], 2010	0.10	0.06	0.15	7.76
Ismail et al. [27], 2008	0.04	0.02	0.06	21.48
Salem et al. [44], 2011	0.30	0.19	0.42	3.12
Al-Sarraf el al. [47], 2010	0.14	0.07	0.24	3.27
Baz et al. [41], 2013 (French)	0.15	0.10	0.20	11.37
Elhwuegi et al. [40], 2012	0.15	0.04	0.32	1.37
Khandekar et al. [43], 2003	0.20	0.15	0.26	10.70
El Haddad and Saad [42], 1998	0.38	0.28	0.47	4.98
El-Asrar et al. [23], 1998–1999	0.43	0.35	0.50	9.00
Elbagir et al. [28], 1995	0.42	0.32	0.52	4.72
Al-Maskari and El-Sadig [46], 2007	0.38	0.25	0.53	2.45
Pooled	0.19	0.10	0.28	100.00
Statistics				
I^2	93.77	91.35	95.52	
Cochran's Q	240.80			
χ^2 (p value)	0.00			

Due to the dearth of the studies found, we decided to capture all the studies which met the inclusion criteria without age limits; the citations were transferred to Endnote X7.1, then duplicates were removed, yielding 472 studies that were assessed for inclusion or exclusion as explained above and shown in the flow diagram (Fig. 1).

Data Extraction

To ensure that the data were captured correctly, 3 scientists (H.Z., U.M.A.M., and F.M.S.) independently reviewed the data. All the retrieved titles and abstracts identified were reviewed individually by each investigator. The screening of the research papers was performed using keywords such as: "retinopathy" OR "T1DM" OR "T1DM" OR "IDDM" OR "male" OR "female" OR "age" OR "family" OR "history" OR "relative" OR "cousin" OR "consang" OR "duration" OR "HbA_{1c}" OR "pressure". The captured data were tabulated after reaching a consensus among the authors.

Data Synthesis and Statistical Analysis

We used the double arcsine transformation to overcome the issue of the prevalence proportion close to extremities (0 and 1), the resultant confidence limits outside the 0 and 1 range, and also the variance instability [10]. The presence of heterogeneity in the meta-analysis presents a challenge in estimating a pooled estimate due to the multiple sources of heterogeneity. Random effect models have been proposed; however, studies have shown that random effect models usually underestimate the statistical error and lead to spuriously overprecise estimates [11]. Two new alternatives have been proposed, including quality models and an inverse variance heterogeneity model. Because the information on the quality of some of the captured studies was not available, we used an inverse variance heterogeneity model, which is a fixed effect model with a quasi-likelihood-based variance structure. The effect size presented the prevalence of the retinopathy. For assessment of heterogeneity to determine whether the variation is above and beyond simple sampling error, we used the Q value and I^2 (Table 2). To assess the source of heterogeneity, subgroup analyses were conducted by sample size, period, and region. In addition, we conducted meta-regression to evaluate the difference between subgroups. Funnel plot and Doi plot were generated to assess publication bias. The Luis Furuya-Kanamori (LFK) index was used as a quantitative measure of Doi plot asymmetry such that no asymmetry, minor asymmetry, and major asymmetry were defined as LFK index $\leq \pm 1$, $\pm 1 <$ LFK index $\leq \pm 2$, and LFK index $> \pm 2$, respectively. Sensitivity analysis was conducted to assess the impact of excluding a study on the prevalence estimates as well as heterogeneity. We considered the excluded study as influential on the pooled prevalence estimate if the overall pooled prevalence estimate 95% confidence limits of the 16 studies (full-set) did not include the pooled prevalence estimate without the excluded study (i.e., reduced set of the remaining 15 studies). The MetaXL© 2010–2016 program (version 5.3) was used for all the listed analyses.

Results

Search Results

Our search strategy captured 472 articles, of which 129 remained after removal of duplicates; of these, 39 were eligible for full article review (Table 1; Fig. 1). Of the 39 articles, 16 articles were included in the meta-analysis, which reported 396 T1D patients who developed DR out of 1,931 T1D patients who were the basis of the meta-analysis (Table 2). These patients were a mix of different ages, ranging from less than 1 year to 90 years (Table 1); in some studies the age specifications were not reported or it was not possible for us to determine the exact age range in the mix of diabetic patients, where the diabetes type was not clearly mentioned (Table 1).

Diabetic Retinopathy in the Arab Countries

We reviewed the full articles of the extracted 39 different studies across 15 Arab countries that were captured through our search strategy. In the other 7 Arab countries (Iraq, Palestine, Syria, Comoros, Djibouti, Mauritania, and Somalia), no data could be captured using our search strategy, even after using additional search through Google scholars and Google using the same search techniques mentioned in the Methods section.

We were able to extract the data from 37 full articles and 2 abstracts. Data were extracted from the abstracts because for the first study we could not get the complete

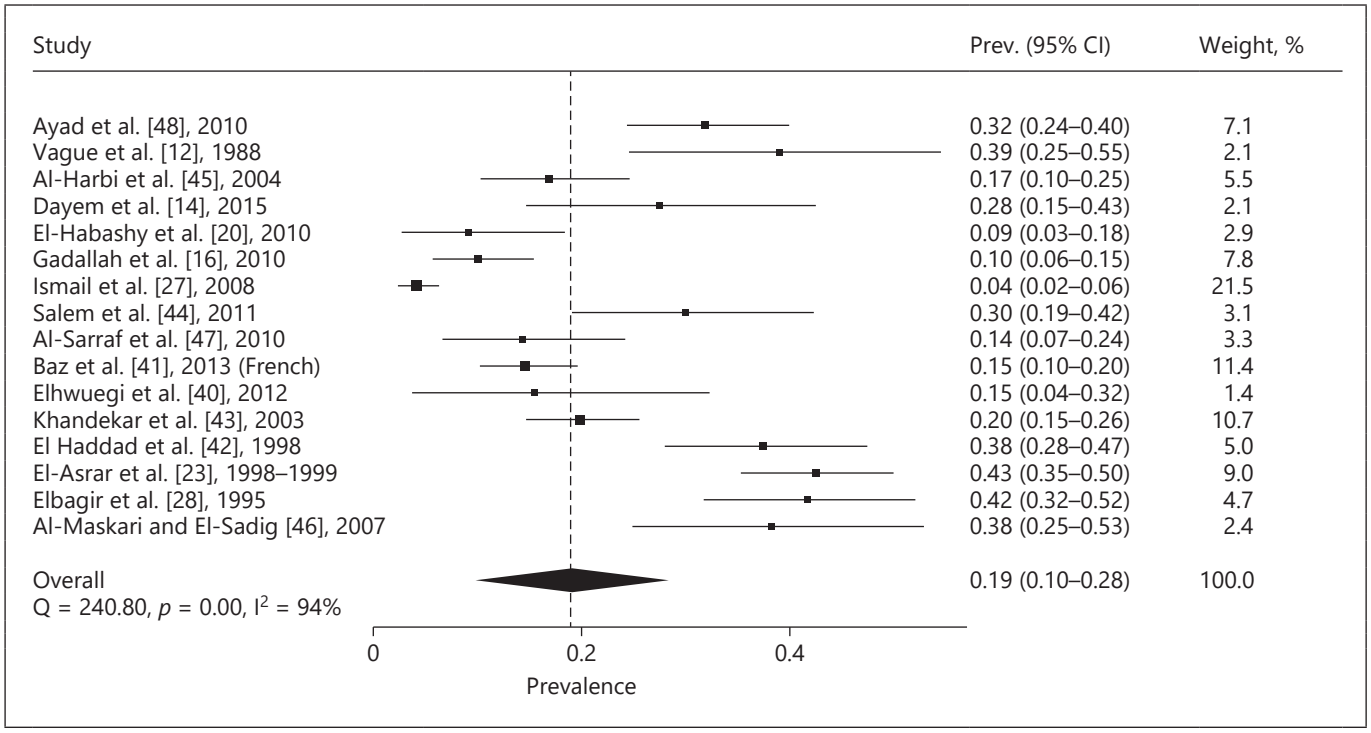

Fig. 2. Forest plot for the prevalence of retinopathy in subjects with type 1 diabetes. Forest plot of the 16 studies that investigated the association between retinopathy and T1D among Arab subjects using an inverse variance fixed-effects heterogeneity model. The effect size chosen is the prevalence. The midpoint of each segment is the estimate of prevalence. The size of the midpoint is proportional to the population of each study. The segment length shows the 95% confidence intervals (CI) for each study. The center of the diamond mark shows the prevalence in all the studies, and the edges show the 95% confidence intervals. Note that the prevalence is 19% (95% CI 10–28).

article [12], and for the second study, the article was in the French language but the abstract was in English [13]. Through 45 years (1969–2014), most of the studies reported were carried out in Egypt, with 9 studies [14–20], followed by Saudi Arabia with 5 studies [21–25] (Table 1). The rates of retinopathy among Arab patients with T1D ranged from low in Saudi Arabia [21] to high in Yemen [26] (Table 1).

Meta-Analysis Results

We captured 39 studies through our systematic search (Table 1). Of the 39 studies, 16 belong to only 10 Arab countries and were eligible for meta-analysis (Table 2). The earliest study was reported from Algeria in 1988 and presented one of the highest prevalence rates (39%) [12]. The prevalence of retinopathy ranged between 4 and 43%, the lowest rates were reported from studies conducted in Egypt [16, 20, 27], with the smallest prevalence proportion reported in a study conducted among 4- to 11-year-old children [27]. The highest prevalence was reported in studies from Saudi Arabia (43%) [23] and Sudan (42%) [28].

To investigate the association between diabetic retinopathy and Arab patients with T1D, we performed a meta-analysis using a fixed-effects, inverse variance heterogeneity model. Figure 2 shows the forest plot of the meta-analysis of the 16 studies. For each study, the midpoint of the segment is the estimate of prevalence, and the size of the midpoint is proportional to the population size while the segment length shows the 95% confidence intervals (CI). The pooled prevalence is indicated by the center of the diamond mark, and the edges of the diamond show the 95% CI. The pooled estimate of the prevalence is 0.19, which means 19% with a 95% CI of 10–28% (Table 2; Fig. 2).

To evaluate the heterogeneity among the 16 different studies and to determine whether the variation results from sampling error or true variation in the effect size, we performed the Q test and I^2 (Table 2). Q was found to be 240.80 ($p < 0.0001$) which is much greater than the degree

Table 3. Meta-regression of the association between period and sample size predictors and the prevalence of retinopathy complication among Arab subjects with T1D

	β	SE	*t*	*p* value	95% CI	
					lower limit	upper limit
Period				0.274		
2001–2008	–0.37	0.22	–1.72	0.129	–0.89	0.14
2009+	–0.44	0.27	–1.62	0.150	–1.08	0.20
<2001	ref.					
Sample size				0.102		
51–100	–0.20	0.25	–0.79	0.457	–0.79	0.40
101–150	–0.20	0.26	–0.75	0.476	–0.81	0.42
150+	–0.53	0.21	–2.48	0.042	–1.04	–0.02
<50	ref.					
Region				0.113		
Africa	–0.27	0.15	–1.81	0.113	–0.63	0.08
Asia	ref.					
Constant	1.69	0.34	4.99	0.002	0.89	2.50

of freedom (df). Accordingly, this result suggests that there is an evidence of variation in the true effects (prevalence). Therefore, we investigated further, how much of the variance we observed was true variance using the I^2 test. I^2 was 93.77% (95% CI 91.35–95.52%) (Table 2), indicating that there is substantial heterogeneity, and about 94% of the observed variance in the effects is true.

Subgroup Analyses and Meta-Regression

Because of the heterogeneity in the results, we examined the effects by subgroups of the period of the data collection, sample size, and region. Studies conducted prior to 2001 reported the highest prevalence (41%, 95% CI 36–46%) and showed the least heterogeneity (Q = 0.71, I^2 = 0%) and was different from studies conducted later (Table 3; Fig. 3). There were no marked differences by sample size. The lowest heterogeneity was observed in the subgroup with less than 50 subjects (Q = 9.66, I^2 = 59%), whereas the prevalence (37%, 95% CI 27–48%) was the highest among the different sample sizes (Table 3; Fig. 4).

Studies were divided by region into African and Asian Arab countries. The pooled prevalence from studies conducted in Africa of 14% (2–30%) was lower than the pooled prevalence from studies from Asia of 25% (15–35%). However, the difference was not statistically significant (Table 3; Fig. 5).

Sensitivity Analysis

We also examined the effect of excluding one study at a time from the analysis. The study by Ismail et al. [27] had the biggest impact on prevalence, Q, and I^2 estimates. However, none of the prevalence estimates from the reduced-set estimates were outside the 95% CI of the pooled prevalence estimate obtained from the full set (Table 4). Therefore, we concluded that no single study markedly affected the overall pooled prevalence estimate.

Publication Bias

The funnel and Doi plot indicated the presence of some bias. The LFK index was 1.86, therefore we concluded that there was minor asymmetry (Fig. 6a, b).

Discussion

To our knowledge, this is the first systematic review and meta-analysis that scrupulously analyzed all the published data on the 22 Arab nations of Arab patients with T1D who had DR; our research strategy returned data on only 15 out of 22 Arab countries, from the time of inception to December 2017, through 45 years (1969–2014). In these patients, the rates of retinopathy ranged from low in Saudi Arabia [21] to high in Yemen [26] (Table 1). Among the 39 studies, we carefully selected 16 studies that met the eligible criteria for meta-analysis where they clearly stated the total sample size, the type of diabetes, and the characteristics of the subjects. Our meta-analysis pointed to a pooled prevalence estimate of 19%. Interestingly, we observed that articles published before 2001 reported higher prevalence rates of DR among the Arab population than the rates reported in recent studies. This can be due to the increase in the level of higher education among Arabs and the spread of awareness about diabetes and its complications; another reason could be that the overall consanguinity rates among Arabs decrease, which has led to a decrease in the genetically transmitted diseases, including T1D and its complications.

In these 16 studies, the total number of subjects with T1D is 1,931, of whom 396 had retinopathy (Table 2); however, the heterogeneity measure (Q test of 240.80, *p* value of 0.00) was highly significant. We estimated that I^2 was 93.77% of the variation observed in the pooled estimate and was due to heterogeneity between studies, suggesting that there were variations across the studies. This relatively high heterogeneity could be attributed to several reasons, such as the extremes in prevalence rate between studies, the wide range of age groups, and the in-

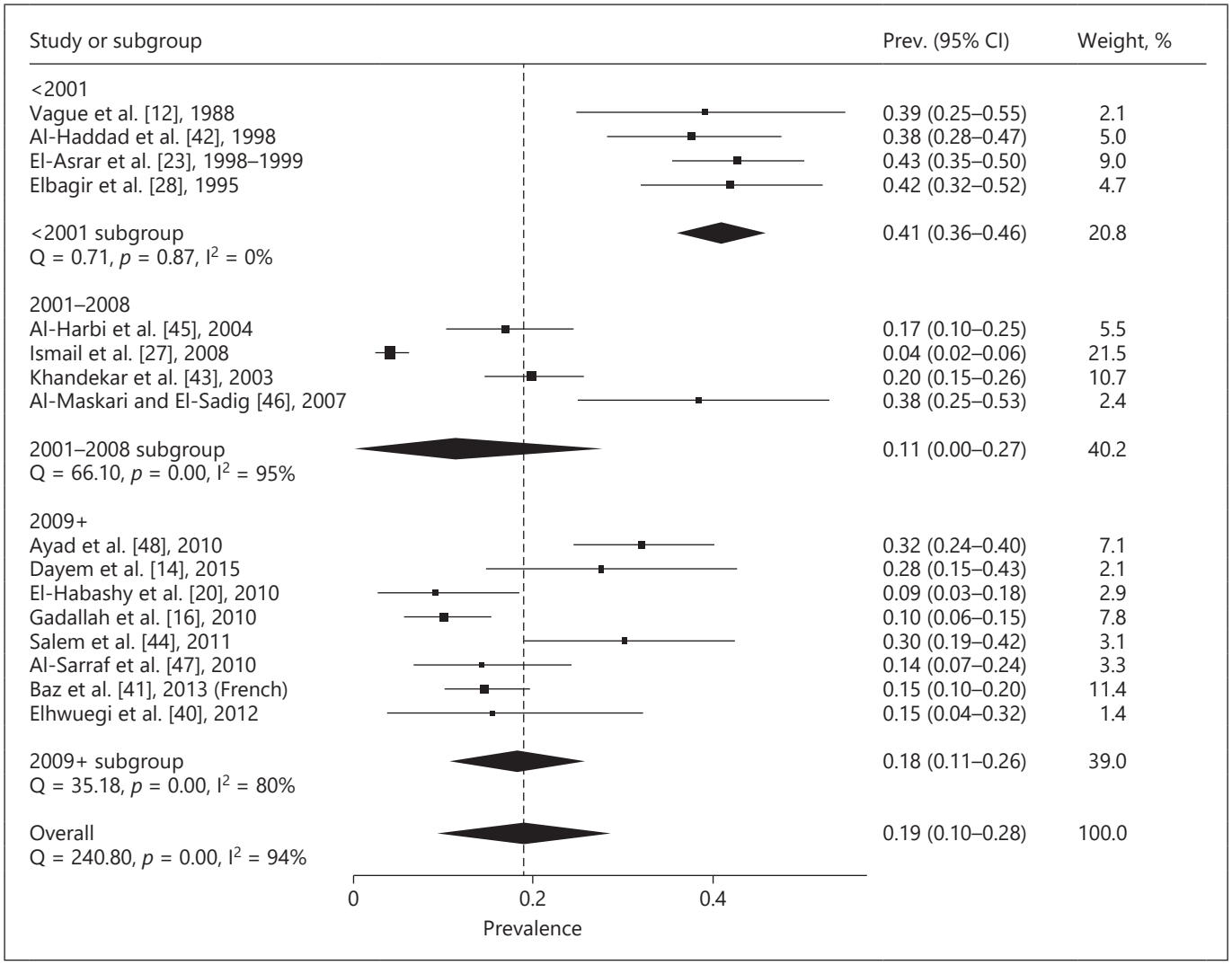

Fig. 3. Forest plot for the prevalence of retinopathy in subjects with type 1 diabetes by period of the study. Forest plot of the 16 studies that investigated the association between retinopathy and T1D among Arab subjects, stratified by 3 study periods. before 2001, 2001–2008, and 2009 and after.

ability to retrieve information by age category from some studies, the span of the studies' duration, and the regional variation. Our subgroup and meta-regression analysis did not indicate any significant difference by period, region, or sample size; however, heterogeneity was still observed within subgroups.

Consanguinity is part of the endogenous Arab culture, with a significant high prevalence of first-cousin marriage [29], which is still rising in some Arab countries [30], which is found to be responsible for the high prevalence of genetic diseases in the Arab countries [8, 9, 31–33]. Few studies ($n = 5$) reported the consanguinity [21, 26, 27, 30, 34] (Table 1). The highest rate of DR was reported in a highly consanguineous cohort of patients from Yemen [26]; in the other studies, we were not able to capture the T1D or DR patients who belong to consanguineous families (Table 1), therefore we could not correlate consanguinity with the level of T1D or DR. However, consanguinity should be investigated further for their correlation with diabetic complications as it simplifies the mode of inheritance by reducing the complexity of multifactorial diseases including T1D [8], which may pave the way towards deciphering the genetic etiology of T1D and DR [8]. Moreover, the genomic revolution which is currently witnessed in the Arab world, with launching the Arab genome project [35, 36], is expected to contribute to our

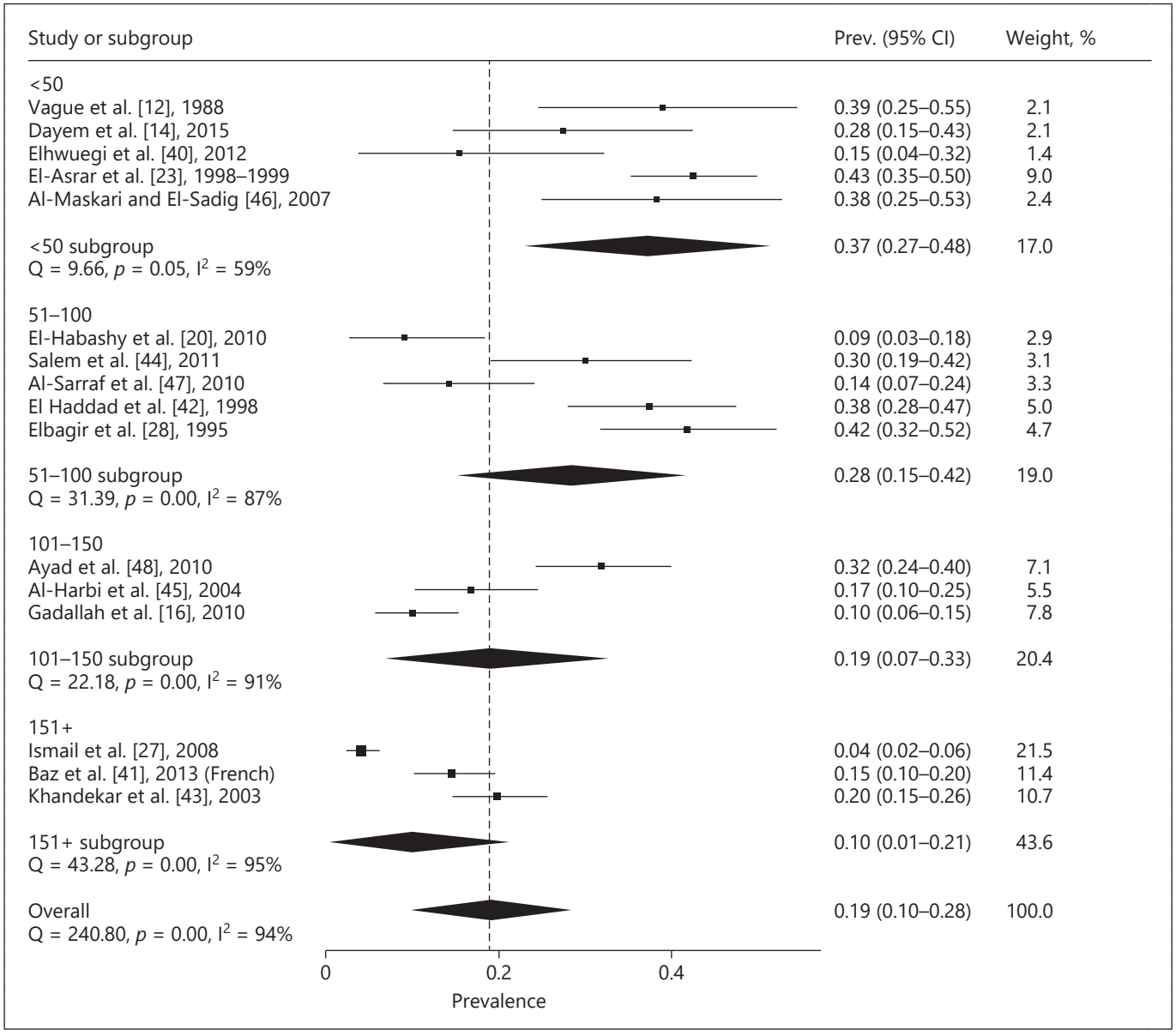

Fig. 4. Forest plot for the prevalence of retinopathy in subjects with type 1 diabetes by sample size of the study. Forest plot of the 16 studies that investigated the association between retinopathy and T1D among Arab subjects, stratified by 4 sample sizes: <50, 51–100, 101–150, and ≥151.

understanding of the genetics of the diabetic complications.

The estimated prevalence rates of DR among the Arab population differ from those reported from different parts of the world; for example in the USA, the rates are estimated to be 74.9 and 82.3% in black and white individuals, respectively, and of vision-threatening retinopathy they were 30.0 and 32.2%, respectively [5]. However, among Asian Indians, the DR rate was estimated as 53.3% [37]. In European patients of Western Norway, the DR prevalence was estimated to be 61% [38], and in T1D patients from Thailand, the DR prevalence was found to be 21.6% [39]. These reports indicated that the prevalence rates of DR are higher than the rate observed in this study (19%). However, given the limitations of our studies that an appreciable number of studies was excluded and that

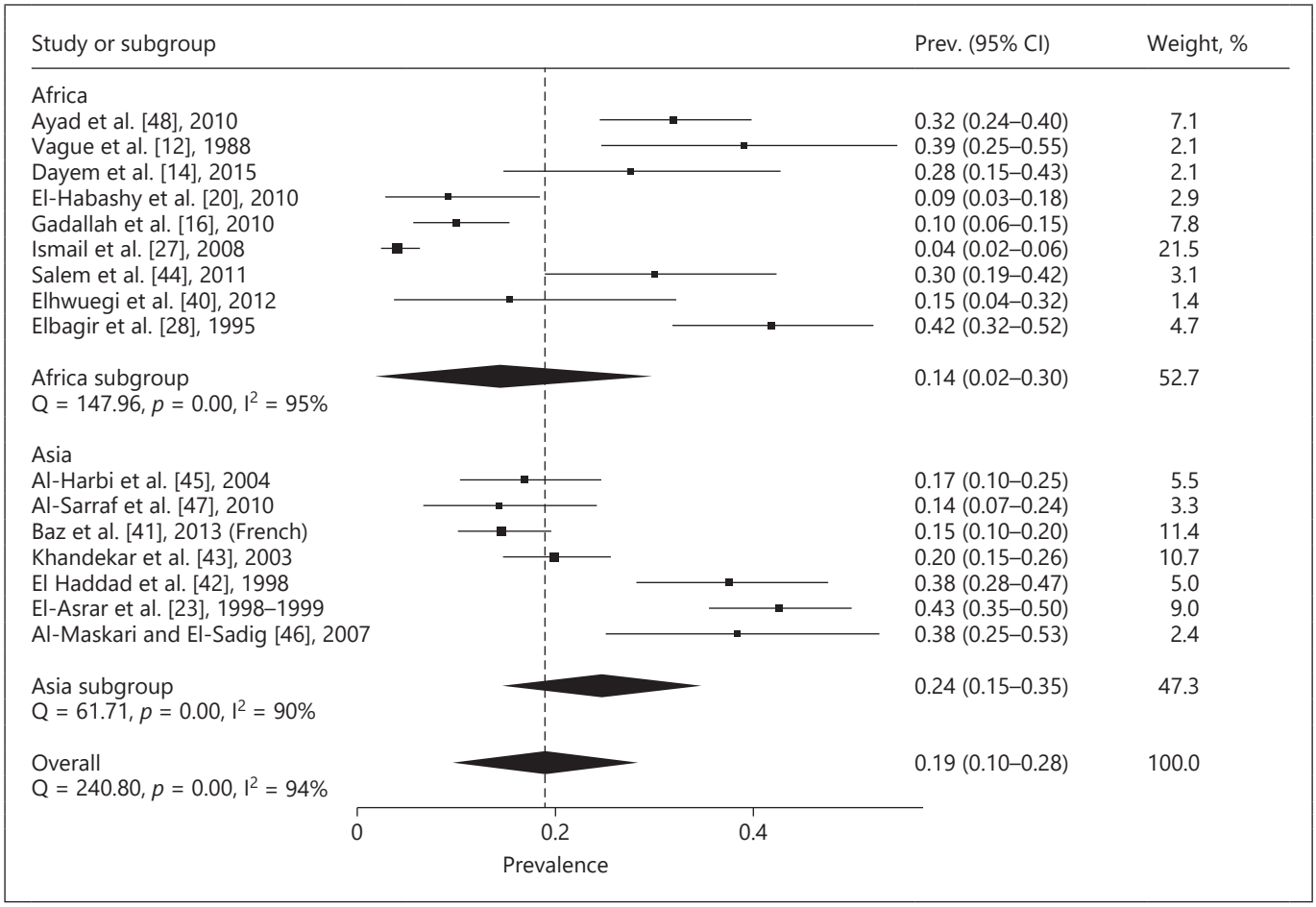

Fig. 5. Forest plot for the prevalence of retinopathy in subjects with type 1 diabetes by region of the study. Forest plot of the 16 studies that investigated the association between retinopathy and T1D among Arab subjects, stratified by 2 regions, Africa and Asia.

the published literature does not reflect the real image of DR among patients with T1D in Arab countries due to the poor publishing culture among Arab countries, we believe that the estimated prevalence here is underrated.

The strength of our study is that this is the first systematic review and meta-analysis to comprehensively study the retinopathy prevalence among Arab patients with T1D, providing a platform for improving the health care of Arab patients with diabetic complications and further epidemiological studies. However, we faced several limitations, including the small sample size in several studies (n = 4) [12, 14, 23, 40]; in addition, the age distribution varied considerably between studies (n = 11) [14, 16, 20, 23, 27, 28, 40–44] and was not reported in some of them [12, 23, 45–48], which might contribute to the observed variation in the prevalence and also hindered our ability to conduct subgroup analysis by age or to adjust for age in the meta-regression. More specifically, studies of younger age groups (n = 1) (age 4–11 years) reported a low prevalence (10%) [27], but studies which included older subjects (n = 2) reported a higher prevalence [23, 28]. Our search strategy yielded studies in only 15 Arab countries out of 22, which limits the full benefit of this study, and this emphasizes the need for more comprehensive studies, which cover countries like Iraq, Palestine, Syria, Comoros, Djibouti, Mauritania, and Somalia. We understand that the DR risk is highly dependent upon diabetes duration and HbA_{1c}; however, these data were not available in the literature obtained to make sense of their association with DR. Finally, we had to exclude many articles where the distinction between T1D and T2D was not possible.

Table 4. Sensitivity analysis of the effect of removing each study on the pooled prevalence, and heterogeneity

Excluded study	Pooled prevalence	95% CI		Cochran's Q	*p* value	I^2	I^2 95% CI	
		lower	higher				lower	higher
Ayad et al. [48], 2010	0.18	0.09	0.28	226.96	0.00	93.83	91.34	95.60
Vague et al. [12], 1988	0.18	0.10	0.28	231.96	0.00	93.96	91.55	95.69
Al-Harbi et al. [45], 2004	0.19	0.10	0.29	240.57	0.00	94.18	91.88	95.83
Dayem et al. [14], 2015	0.19	0.10	0.28	238.84	0.00	94.14	91.82	95.80
El-Habashy et al. [20], 2010	0.19	0.10	0.29	236.89	0.00	94.09	91.74	95.77
Gadallah et al. [16], 2010	0.20	0.10	0.30	230.92	0.00	93.94	91.51	95.67
Ismail et al. [27], 2008	0.24	0.17	0.32	115.67	0.00	87.90	81.70	91.99
Salem et al. [44], 2011	0.18	0.10	0.28	236.31	0.00	94.08	91.72	95.76
Al-Sarraf el al. [47], 2010	0.19	0.10	0.29	240.04	0.00	94.17	91.86	95.82
Baz et al. [41], 2013 (French)	0.19	0.10	0.30	237.72	0.00	94.11	91.77	95.78
Elhwuegi et al. [40], 2012	0.19	0.10	0.29	240.71	0.00	94.18	91.89	95.83
Khandekar et al. [43], 2003	0.19	0.09	0.29	240.62	0.00	94.18	91.88	95.83
El Haddad and Saad [42], 1998	0.18	0.09	0.28	222.67	0.00	93.71	91.16	95.53
El-Asrar et al. [23], 1998–1999	0.17	0.09	0.26	188.27	0.00	92.56	89.36	94.80
Elbagir et al. [28], 1995	0.18	0.09	0.27	215.94	0.00	93.52	90.85	95.40
Al-Maskari and El-Sadig [46], 2007	0.18	0.10	0.28	231.32	0.00	93.95	91.52	95.68

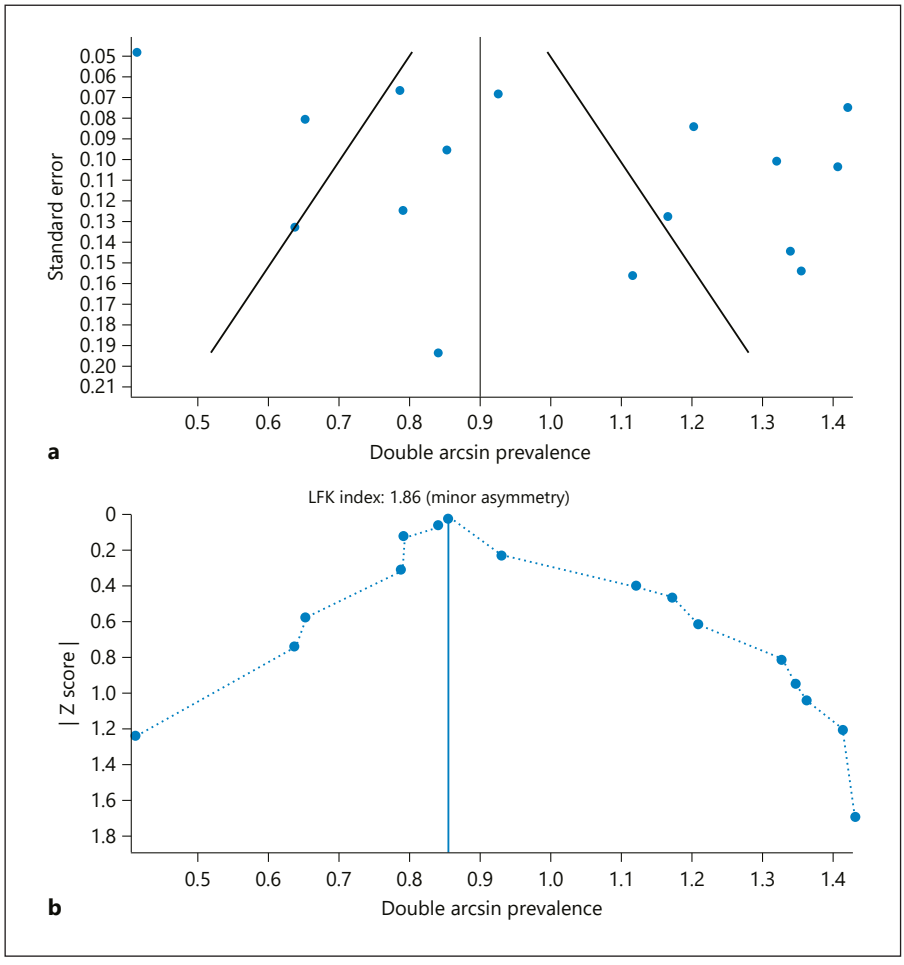

Fig. 6. Publication bias: funnel plot (**a**) and Doi plot (**b**) for the prevalence of retinopathy in subjects with type 1 diabetes. Publication bias is said to be present if asymmetry in the plots is observed. The two plots revealed mild asymmetry. In addition, the LFK index was 1.86 denoting minor asymmetry.

In conclusion, we present the first systematic review and meta-analysis of DR among Arab patients with T1D in 15 different Arab countries. Although our search strategy was broad, we were only able to find few reports compared to the scale of the problem in the Arab countries; our meta-analysis revealed that the prevalence is high (19%) with significant variations among different Arab countries, even within the same country. Our findings will help to guide clinicians and scientists to individualize their efforts to protect patients from the devastating complication of T1D and increase the awareness of the high prevalence of retinopathy and the need to screen patients for retinopathy. The high degree of heterogeneity observed in our study indicates that there is a need for well-controlled studies to obtain an accurate estimation of the problem in the Arab countries. We believe that the actual prevalence in the Arab world is underestimated and rigorous controlled epidemiological studies should be undertaken in order to save a life now and in the future.

Statement of Ethics

Human and Animal Rights and Informed Consent: This article does not contain any studies with human or animal subjects performed by any of the authors.

Disclosure Statement

The authors have no conflict of interest to declare.

Author Contributions

H.Z. originated the study, acquired the data, analyzed, interpreted the data, and drafted the manuscript. F.M.S. analyzed and interpreted the data, and drafted the manuscript. U.M.A.M. and C.P. analyzed, interpreted, and critically reviewed the data. A.G. collected the data. C.G.P.D. collected the data and drafted the manuscript. N.R. drafted part of the manuscript.

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