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Prevalence and Outcomes of Retinopathy of Premature Neonates in Iran: A Systematic Review and Meta-Analysis

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Abstract

Background: Retinopathy of Prematurity (ROP) is a disease in the retina of premature infants, which is one of the preventable causes of blindness in children.

Methods: the present study is performed with the purpose of determining the prevalence and outcomes of ROP in Iran through a systematic review and meta-analysis.

Study design: All original published articles on the prevalence of ROP in premature infants in Iran were included in the study. On the other hand, intervention articles, meta-analysis, case reports, congress articles, medical dissertations, and articles with low quality were excluded from the study.

Results: 53 articles were included in the meta-analysis stage. Based on the results, the overall prevalence of ROP in Iran was 22.2% (95% CI: 18.5-26.5); the overall prevalence of the disease in ZONE I was 10.5% (95% CI: 3.0-30.6), the overall prevalence of the disease was 45.5% (95% CI: 33.8-57.8) in ZONE II, and 43.8% (95% CI: 25.1-64.4) in ZONE III. Regarding the stage of the disease, rate of 39.9% (95% CI: 29.2–51.7) was reported in STAGE I, rate of 30.3% (95% CI: 21.8–40.5) in STAGE II, and 14.9% (95% CI: 11.0 -19.9) in STAGE III.

Conclusion: Considering the high prevalence of ROP in premature infants in Iran, it is suggested to take necessary preventive measures in this field.

Key Words: Retinopathy, Retinopathy of prematurity, Neonatal diseases.

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1- INTRODUCTION

Women's health is very important, especially during pregnancy, when the mother and the child may be exposed to many physical and mental diseases (1-3). If the baby suffers from a disease for any reason, including premature birth or diseases during birth, it may cause irreparable complications for him; so that it can endanger the baby's health and also lead to hospitalization in the NICU department. Eye diseases are one of the most important diseases in infancy, which are very important due to the vulnerability of infants. One of these diseases is Retinopathy of Prematurity (ROP) (4-6).

ROP is a disease in the retina of premature infants, which is one of the preventable causes of blindness in children. In premature infants, the developmental process of the retinal vessels takes place in the extrauterine environment. In fact, ROP is a retinal vascular disease of premature infants that can lead to a wide range of vision disorders, and even retinal detachment and blindness (7). ROP is actually a multifactorial disease in which many factors are involved before and after its development. Various factors, such as premature birth are effective in causing this disease. These factors include phototherapy, respiratory distress syndrome, sepsis, mechanical ventilation, high oxygen saturation and anemia, premature birth, especially before the 31st week of pregnancy, and in birth weights less than 1500 grams (4, 8).

With the development of advanced methods for the survival of premature infants, the number of infants with the risk of ROP has increased. So, early diagnosis and treatment of these patients is a priority (9). Many investigations have been performed in the field of prevalence and factors affecting the development of ROP in the world and also in Iran (10-13). Among these studies, we can refer to the meta-analysis by Azami et al. (2018), in which 44 articles were reviewed and the prevalence of ROP was reported as 23.5% (13). With respect to the fact that the last article included in Azami et al.'s investigation was conducted in 2016 and many articles have been published in this field until 2023, the present Systematic review and meta-analysis was performed with the purpose of determining the prevalence and outcomes of ROP in Iran.

2- MATERIALS AND METHODS

2-1. Search strategy

The search was carried out in Iranian databases such as Magiran (https://www.magiran.com/), Scientific Information Database (https://www.sid.ir/) in Persian and English. The international databases, such as Medline, Scopus, and ISI Web of Sciences, PubMed, were also searched.

2-2. Inclusion and exclusion criteria

All original published articles on the prevalence of ROP in premature infants in Iran were included in the study. On the other hand, intervention articles, meta-analyses, case reports, congress articles, medical dissertations, and articles with low quality were excluded from the study.

2-3. Paper selection and data extraction

The search was started by two pediatricians (MA & BD) who had the necessary experience in this field. Then, the search results and the extracted data were reviewed by two quality supervisors: an ophthalmologist and a master of systematic reviewing and meta-analysis; and in case of any problem, they were referred to the research colleagues for a better search. After determining the final articles, data was extracted and entered into the checklist made by the researchers. This checklist included questions about the author's name, year of publication, sample size, gestational age, baby’s weight in grams, ZONE 1 to ZONE 3 and also stage 1 to stage 3.

The PICO criteria in this study includes:

P: Premature Neonates with ROP diagnosis;

I: Amount of ROP in premature neonates;

C: Comparison of premature and healthy neonates in ROP;

O: Report of ROP prevalence;

2-4. Statistical analysis

Data analysis was done by CMA 3 software, using the random model.

3- RESULTS

In the initial search, 1125 articles were found, and after the final screening, 53 articles entered the meta-analysis stage (**Fig. 1**).

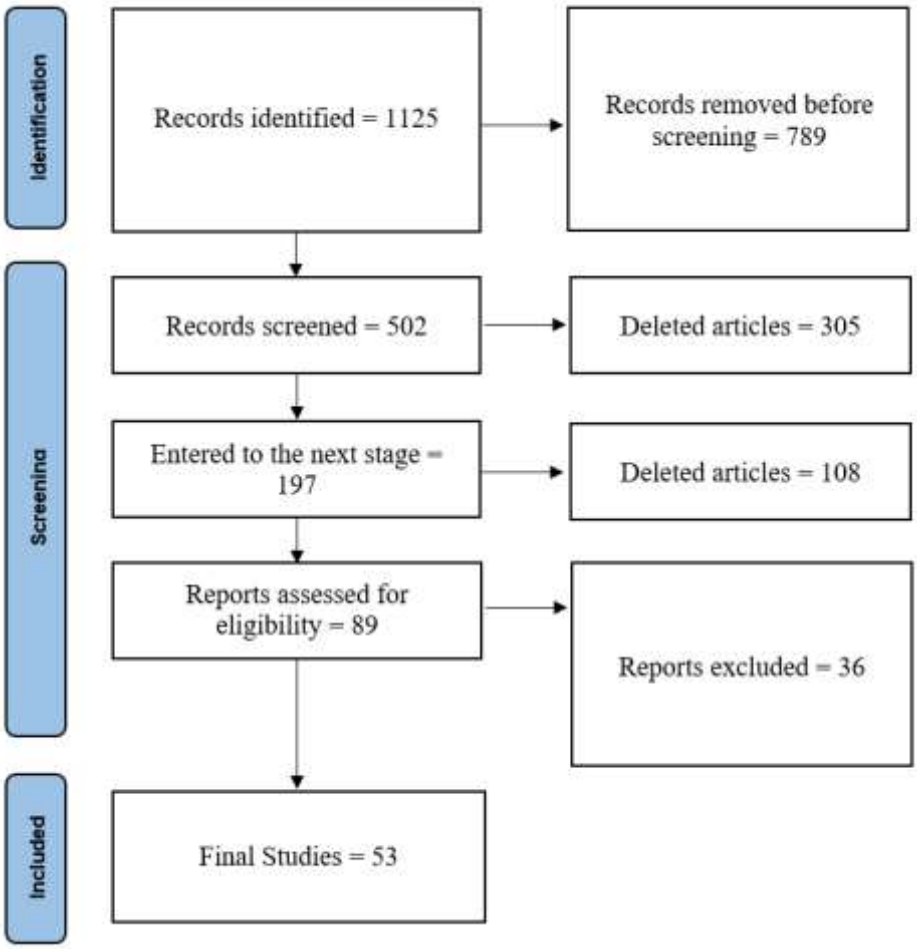

Fig. 1: Flowcharts for systematic review

Based on the results, the overall prevalence of ROP in Iran was 22.2% (95% CI: 18.5-26.5) (**Fig. 2**), the overall prevalence of the disease in ZONE I was 10.5% (95% CI: 3.0-30.6), the overall prevalence of the disease was 45.5% (95% CI: 33.8-57.8) in ZONE II and 43.8% (95% CI: 25.1-64.4) in ZONE III (**Fig. 3-5**). Regarding the stage of the disease, rate of 39.9% (95% CI: 29.2–51.7) was reported in STAGE I, rate of 30.3% (95% CI: 21.8–40.5) in STAGE II, and rate of 14.9% (95% CI: 11.0 -19.9) in STAGE III (**Fig. 6-8**). The graph of publication bias, the meta-regression of the prevalence of ROP, and the articles' years of publication are shown in **Fig. 9** and **10**.

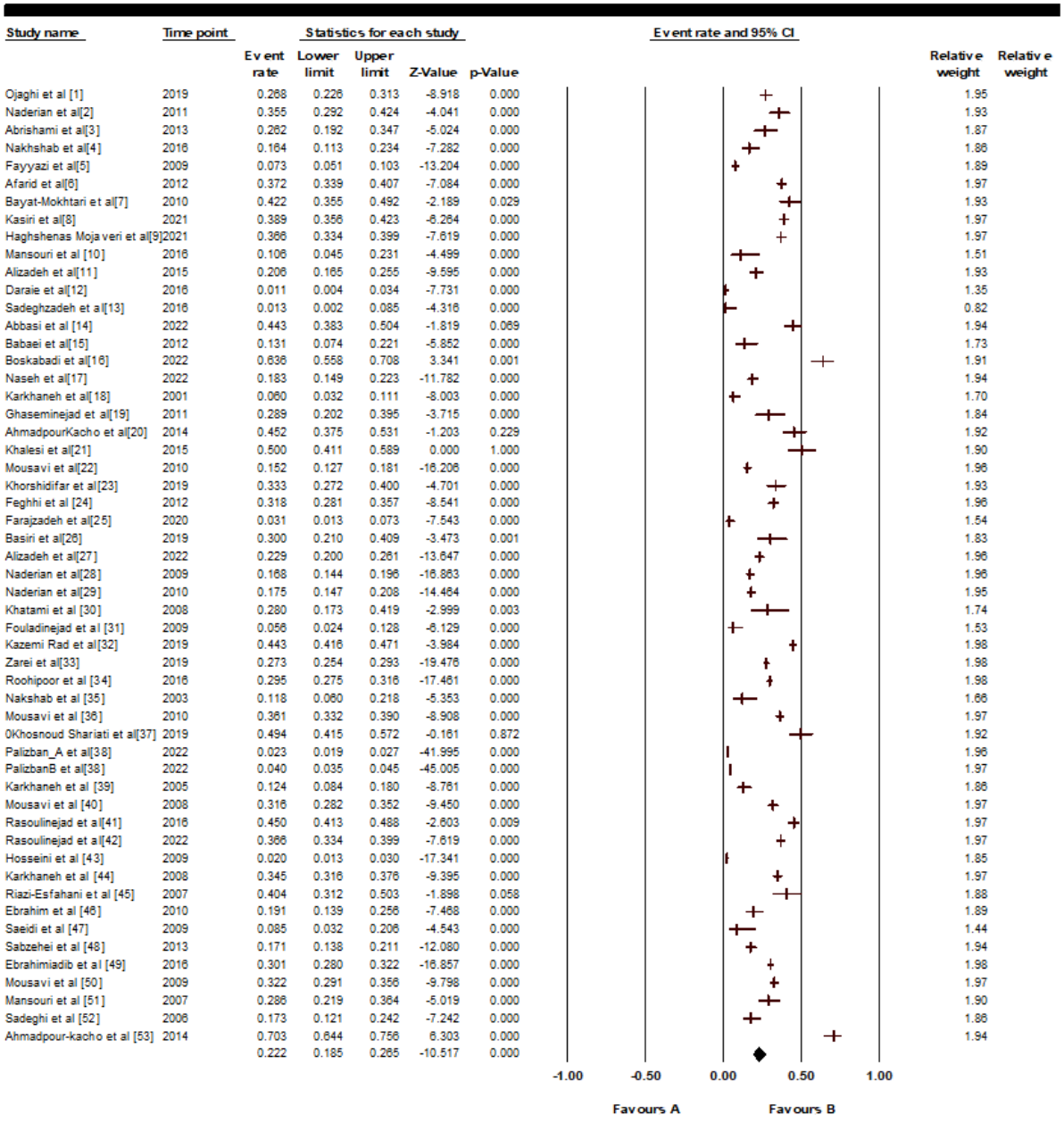

Fig. 2: The prevalence of ROP in Iran

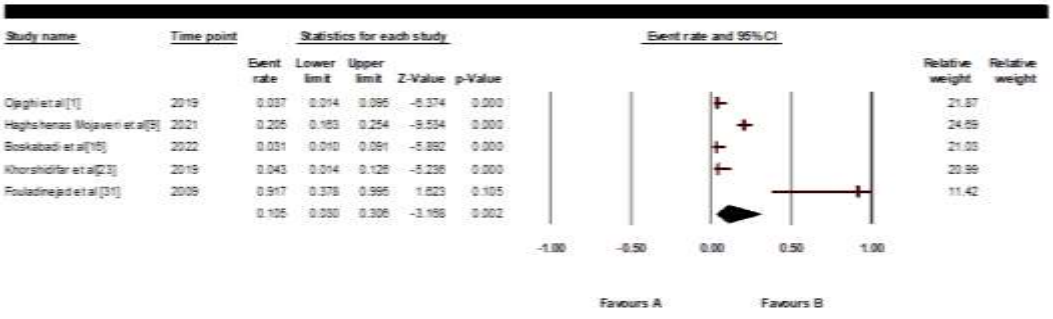

Fig. 3: The prevalence of Zone I of prematurity with ROP in Iran

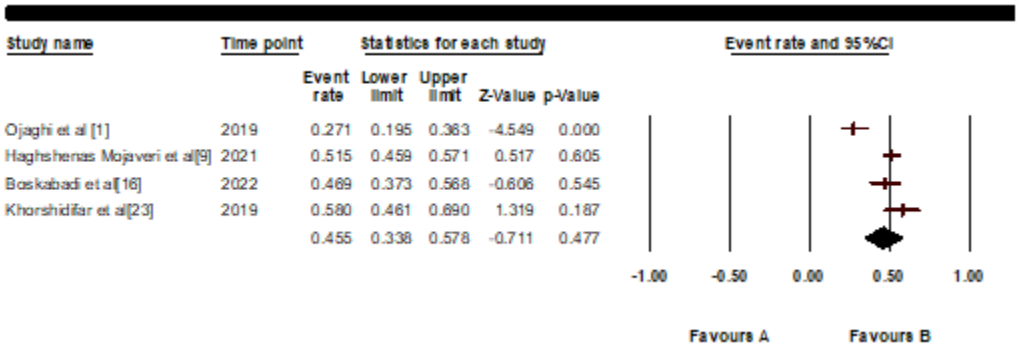

Fig. 4: The prevalence of Zone II of prematurity with ROP in Iran

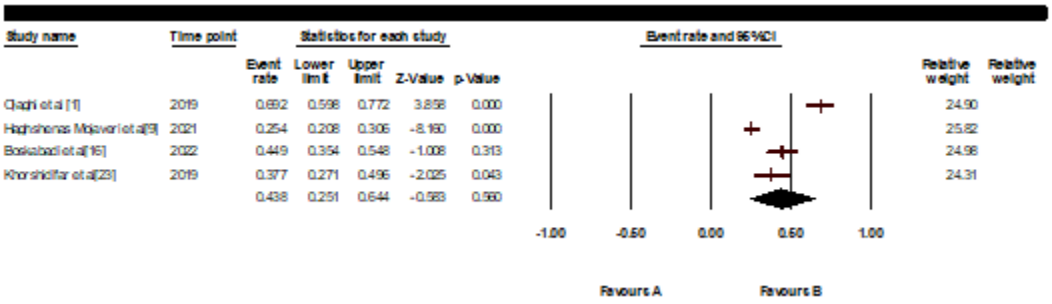

Fig. 5: The prevalence of Zone III of prematurity with ROP in Iran

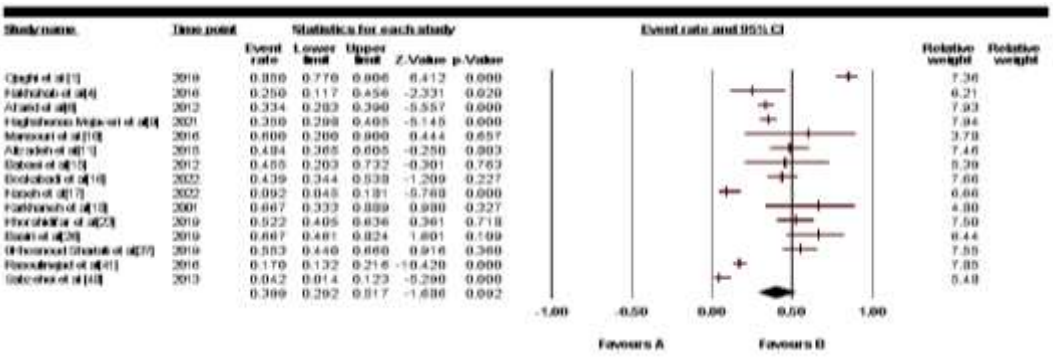

Fig. 6: The prevalence of Sage I of prematurity with ROP in Iran

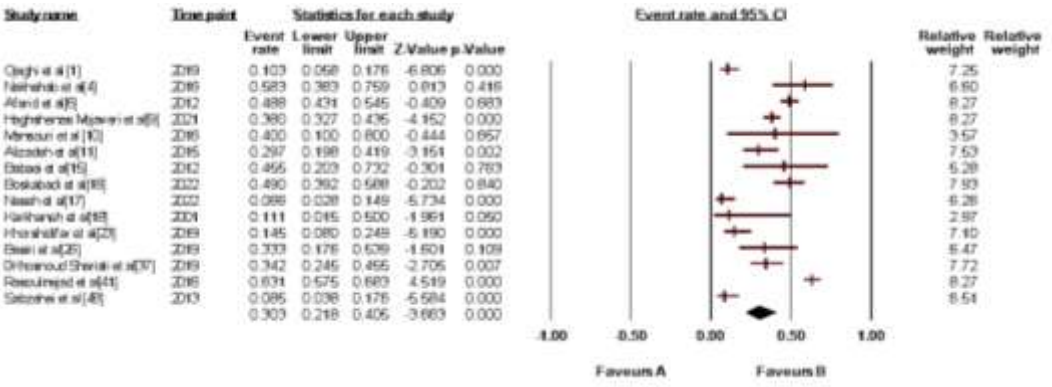

Fig. 7: The prevalence of Sage II of prematurity with ROP in Iran

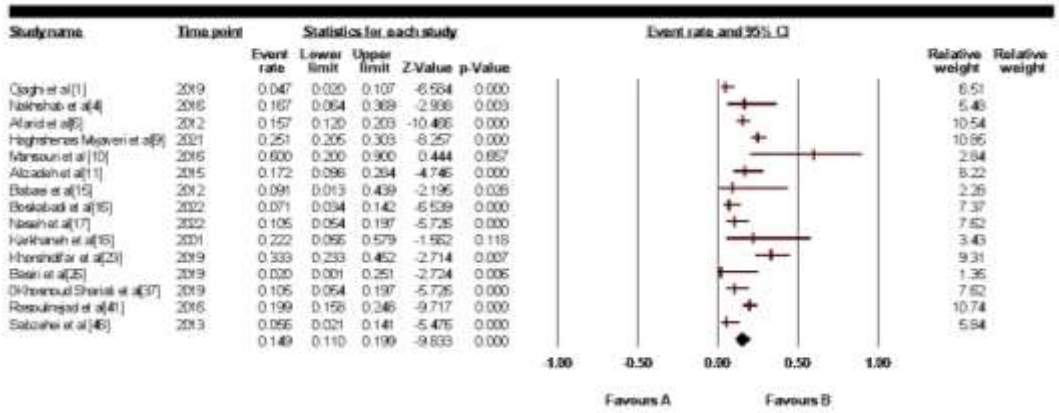

Fig. 8: The prevalence of Sage I of prematurity with ROP in Iran

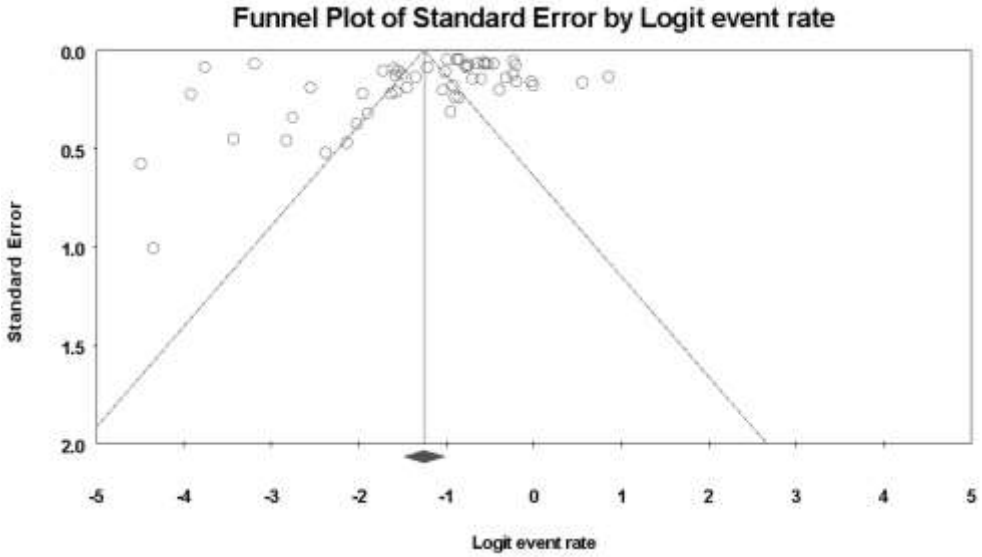

Fig. 9: Publication bias in the studies

4- DISCUSSION

Infants, as one of the vulnerable age groups, experience different types of crises from birth to childhood and adolescence (67-69). Premature birth is one of the causes of infant mortality and its prevalence is high in developing countries such as Iran. In a meta-analysis by Sharifi et al. (2017) in 19 articles and with a sample size of 41,773, its prevalence was reported to be 10% (70), and in the meta-analysis by Vakilian et al. with 14 articles and a sample size of 156,461, its prevalence was reported as 9.2% (71). While the global prevalence of preterm delivery has decreased by 5.26%, the mortality rate in infants has decreased by 41.47% from 1990 to 2019 (72). For this reason, paying attention to complications related to premature birth is a priority. So, this meta-analysis aimed to determine the prevalence and outcome of ROP disease in Iranian infants.

Based on the results, the prevalence of ROP was 22.2% (95% CI: 18.5-26.5). In the meta-analysis by Azami et al. in Iran, where 42 articles were reviewed, the prevalence of ROP was reported as 23.5% (13).

Table-1: Specifications of articles published in the field of retinopathy of prematurity included in the study

No.	Author	Years	City	Samples	Male	Female	gestational age	Weight to grams	Prevalence	Zone I	Zone II	Zone III	stage I	stage II	stage III
1	Ojaghi et al (14)	2019	Ardabil	400	229(57.2)	297(74.2)	-	1909.8 gr±404.2	107(26.8)	4(3.7)	29(27.1)	74(69.2)	91(85)	11(10.3)	5(4.7)
2	Naderian et al(15)	2011	Isfahan Tehran	200	100(50)	100(50)	-	-	(35.5)	-	-	-	-	-	-
3	Abrishami et al(16)	2013	Mashhad	122	57	65	30.54	-	32(26.2)	-	-	-	-	-	-
4	Nakhshab et al(17)	2016	Sari	146	-	-	30.33(21.2)	1325.6±430.65	24(16.44)	-	-	-	6	14	4
5	Fayyazi et al(18)	2009	Tabriz	399	-	-	-	-	29(7.26)	-	-	-	-	-	-
6	Afarid et al(19)	2012	Shiraz	787	389(49.4)	398 (50.6)	30.87 ± 2.37	1397 ± 303.776	293(37.2)	-	-	-	33.4	48.8	15.7
7	Bayat-Mokhtari et al(20)	2010	Shiraz	199	106 (53)	93 (47)	30.8 (2.1)	1393.1 (327.2)	84(42)	-	-	-	-	-	-
8	Kasiri et al(21)	2021	Ahvaz	812	382(47.0)	430(52.9)	-	-	316(39)	-	-	-	-	-	-
9	Haghshenas Mojaveri et al(22)	2021	Babol	828	405	418	-	-	303(36.6)	62	156	77	106	115	76
10	Mansouri et al (23)	2016	Sanandaj	47	22	25	31.6 ± 2.54	1580 ± 320	5(10.6)	-	-	-	3	2	3
11	Alizadeh et al(24)	2015	Rasht	310	170 (54.8)	140 (45.2)	30.18 ± 2.28	1727.41 ± 471.05	64(20.6)	-	-	-	31(48)	19(29)	11(17)
12	Daraie et al(25)	2016	Semnan	270	-	149(55.2)	33	1961(565)	3(1.1)	-	-	-	-	-	-
13	Sadeghzadeh et al(26)	2016	Zanjan	78	-	-	-	1586.21 ±540.53	1(1.2)	-	-	-	-	-	-
14	Abbasi et al (27)	2022	Mashhad	253	149(58.9)	104(41.1)	32.1(2.9) weeks	1697.2 ± 566.5 g	112 (44.3)	-	-	-	-	-	-
15	Babaei et al(28)	2012	Kermansha h	84	40(47.62)	44(51.38)	-	1302.73±185.8	11(13.1)	-	-	-	5 (45.5)	5 (45.5)	1(9.1)
16	Boskabadi et al(29)	2022	Mashhad	154	-	-	-	-	98(63.6)	3.8%	46.3%	45%	43(43.9)	48 (49)	7(7.1)
17	Naseh et al(30)	2022	Tehran	415	207	208	33.36 ±1.2	1886±446	76 (18)	-	-	-	7 (30.4)	5 (21.7)	8(34.8)
18	Karkhaneh et al(31)	2001	Tehran	150	74(49.3)	76(50.7)	33.46 ±2.63	1814.46±491	9(6)	-	-	-	6(66.7)	1(11.1)	2(22.2)
19	Ghaseminejad et al(32)	2011	Kerman	83	-	-	30.17±1.8	1247.92±237.1	24(29)	-	-	-	-	-	-
20	AhmadpourKacho et al(33)	2014	Babol	155	-	-	-	-	70(45.2)	-	-	-	-	-	-
21	Khalesi et al(34)	2015	Tehran	120	-	-	-	-	60(50)						
22	Mousavi et al(35)	2010	Tehran	690	320(52.9)	364(60.2)	31.4 ±2.3	1562(443)	105(31.4)	-	-	-	-	-	-
23	Khorshidifar et al(36)	2019	Tehran	207	107(51.7)	100(48.3)	32±3; 32	1701±610; 1650	69(33.3)	3(4.3)	40(58)	26(37.7)	36(52.2)	10(14.5)	23(33.3)
24	Feghhi et al (37)	2012	Ahvaz	576	212	181	-	-	183(32)	-	-	-	-	-	-
25	Farajzadeh et al(38)	2020	Kurdistan	159	55	104	33.34 ±4.15	2277 ± 71	5(3.1)	-	-	-	-	-	-
26	Basiri et al(39)	2019	Hamadan	80	-	-	-	1210.12, ±297.23	24(30)	-	-	-	16	8	0
27	Alizadeh et al(40)	2022	Guilan	716	-	-	31.4 ± 2.8	1629 ± 502	164(22.9)	-	-	-	-	-	-

No.	Author	Years	City	Samples	Male	Female	gestational age	Weight to grams	Prevalence	Zone I	Zone II	Zone III	stage I	stage II	stage III
28	Naderian et al(41)	2009	Isfahan	796	51%	49%	29 ± 2.5	1300 ± 290	134(16.8)						
29	Naderian et al(42)	2010	Isfahan	604	324(53.6)	280(46.4)	31 ± 2.6	1375.35, ±299.80	106(17.5)	-	-	-	-	-	-
30	Khatami et al (43)	2008	Mashhad	50	-	-	-	-	14(28)	-	-	-	-	-	-
31	Fouladinejad et al (44)	2009	Gorgan	89	45	44	-	-	5(5.6)	5(100)	0(0)	0(0)	-	-	-
32	Kazemi Rad et al(45)	2019	Mashhad	1247	-	-	-	-	553(44)	-	-	-	-	-	-
33	Zarei et al(46)	2019	Tehran	1990	-	-	32.29 ± 2.75	-	543(27.28)	-	-	-	-	-	-
34	Roohipoor et al (47)	2016	Tehran	1932	-	-	32±2.7	1713 ±516	570(30)	-	-	-	-	-	-
35	Nakshab et al (48)	2003	Sari	68	-	-	32.3±2.7	1695.9 ±476.8	8(11.7)	-	-	-	-	-	-
36	Mousavi et al (49)	2010	Tehran	1053	-	-	-	-	380(36.1)	-	-	-	-	-	-
37	0Khosnoud Shariati et al(50)	2019	Tehran	154		59 (38.3)	28.53±1.82	1049.66±236.94 g	76(49.4)	-	-	-	55.26%	34.2%	10.53%
38	Palizban et al (51)	2022	Tehran	10830	-	-	-	-	2.28	-	-	-	-	-	-
39	Karkhaneh et al (52)	2005	Tehran	185	110(59.5)	75(49.5)	31.64 ± 2.67	1620.68 ± 467.6	23(12.4)	-	-	-	-	-	-
40	Mousavi et al (53)	2008	Tehran	693	-	-	-	1404±414	219(31.6)	-	-	-	-	-	-
41	Rasoulinejad et al(54)	2016	Babol	680	425(62.5)	255(37.5)	31.45 ± 2.21	1713.9 ± 416.7	306(45)	-	-	-	52(16.99)	193(63.07)	61(19.93)
42	Rasoulinejad et al(55)	2022	Babol	828	-	-	-	-	303(36.59)	-	-	-	-	-	-
43	Hosseini et al (56)	2009	Shiraz	1024	-	-	28±2.6	1189±295	20(1.95)	-	-	-	-	-	-
44	Karkhaneh et al (57)	2008	Tehran	953	-	-	31.1(2.6)	1542(473)	329(34.5)	-	-	-	-	-	-
45	Riazi-Esfahani et al (58)	2007	Tehran	99	52(52.5)	47(47.5)	-	-	40(24.24)	-	-	-	-	-	-
46	Ebrahim et al (59)	2010	Babol	173	-	-	32.24±2.36	1680.64±462.5	33(19.1)	-	-	-	-	-	-
47	Saeidi et al (60)	2009	Mashhad	47	23	24	-	-	4(8.5)	-	-	-	-	-	-
48	Sabzehei et al (61)	2013	Tehran	414	208(50.2)	206(49.8)	30.45 ± 2.29	1268.57 ± 192.19	71(17.14)	-	-	-	3.4%	8.7%	5.1%
49	Ebrahimiadib et al (62)	2016	Tehran	1896	-	-	-	-	570(30.06)	-	-	-	-	-	-
50	Mousavi et al (63)	2009	Tehran	797	120 (55.6)	96 (44.4)	29.9±2.7	1410±432	257(32.24)						
51	Mansouri et al (64)	2007	Tehran	147	74	73	33.2±3.3	1386±356	42(29)	-	-	-	-	-	-
52	Sadeghi et al (65)	2006	Tabriz	150	84(56)	66(44)	-	-	26(17.3)	-	-	-	-	-	-
53	Ahmadpour-kacho et al (66)	2014	Babol	256	127(49.6)	129(50.4)	-	-	180(70.3)	-	-	-	-	-	-

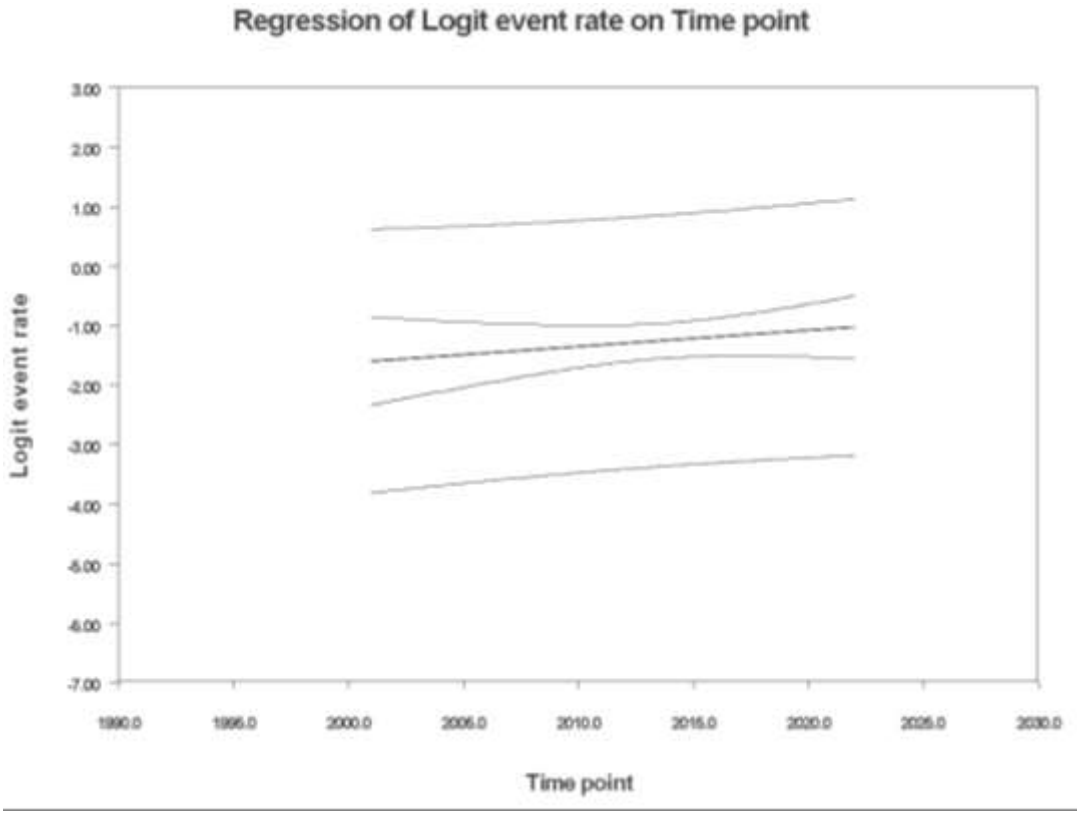

Fig. 10: Meta-regression of ROP prevalence based on years of studies' publications

Also, in the meta-analysis by Maroufizadeh et al. (2017) with 26 reviewed articles in Iran, the prevalence of ROP was reported as 26.1%, which indicates the high prevalence of ROP among Iranian infants (73). The difference between that study and the present one is the number of articles analyzed, which are more in our investigations. Also, in this study, the latest articles published in 2022 have been examined, while in the aforementioned studies, the last article reviewed was conducted in 2016. It seems that due to the expansion of health facilities and services, the prevalence of this disease has decreased.

Various original studies published in different countries on the prevalence of ROP have shown a significant prevalence of ROP in premature infants. For instance, Onyango et al. in Kenya reported the prevalence of ROP to be 41.7% and the majority of them were in stage 1 and 2 of the disease with involvement in Zone II (74). In another study by Dwivedi et al. in India, the prevalence of ROP in premature infants was 30%, and the zone of eye involvement was 31.49% in zone I, and 51.85% was in zone II (75). Van et al., in a cohort study, demonstrated that the prevalence of ROP in premature infants connected to ventilators was 21.8%. Moreover, they found that factors including low weight and severe apnea are related to the incidence of ROP (76).

5- CONCLUSION

Considering the high prevalence of ROP in premature infants in Iran, it is suggested to take necessary preventive measures in this field.

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