

Investigate the incidence and prevalence of Nonarteritic Anterior Ischemic Optic Neuropathy (NAION) in patients taking semaglutide (Ozypmic).

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Cite this paper as Muhammad Usman Amiruddin, Naheed Akhtar, Koonj Mustafa, Ali Hussain Gondal, Muhammad Zulfiqah Sadikan, Jaiperkash, (2025) Investigate the incidence and prevalence of Nonarteritic Anterior Ischemic Optic Neuropathy (NAION) in patients taking semaglutide (Ozypmic)..*Journal of Neonatal Surgery*, 14, (32s) 9540-9548.

ABSTRACT

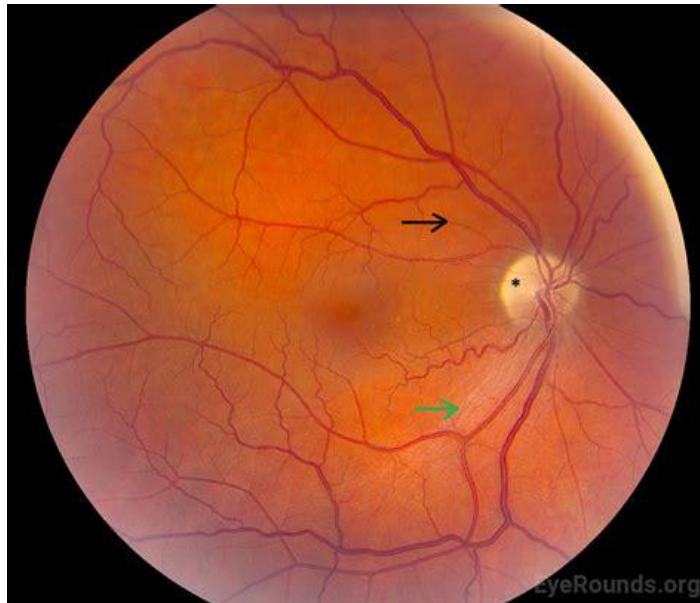
NAION is a severe form of vision loss and the onset of anamorphic, painless vision loss, and in most cases, it is linked to risk factors that are systemic including diabetes and hypertension. The objective of this study was to evaluate the risk of NAION as a result of semaglutide use in a systematic review of literature that supports the claim by examining the incidence, the risk factors and potential mechanisms of the relationship between the two. A literature review of the publications on the topic published in January 2024-June 2025 was carried out. The included studies were those that evaluate the risk of NAION in patients under semaglutide treatment, which comprise studies in the cohort category, clinical trials, and case reports. Hazard ratios (HR) data, 95% confidence interval (CI) data and incidence rate data were extracted and analyzed. Five studies were analyzed and reported different findings on the correlation between semaglutide and NAION. There was a report of substantial increase in the hazard ratio (HR of 2.58 up to 4.28) by certain studies whereas there was no significant risk increase in others. Most studies had confidence intervals that were wide indicating variation in results. Small Bruchs membrane opening (BMO) and crowded optic discs were risk factors that were found to predispose NAION in semaglutide users. Although risk of NAION in people taking semaglutide seems to be low in the general population, there are some subgroups which may face this risk especially those that have predisposing ocular risk factors. The general therapeutic advantages of semaglutide in the treatment of type 2 diabetes and obesity offset the risks that the drug poses to the eyes of the majority of patients..

Keywords: NAION, Pain, Ozypmic, Drug, population, Patients, Therapy.

1. INTRODUCTION

NAION is one of the most common causes of vision loss, and is a sudden and painless form of vision loss in adulthood and mainly occurs in people who are above the age of 50. The condition arises because of the decreased blood supply to the optic nerve head, which leads to the optic disc edema and consequent vision loss [1]. Although NAION is usually attributed to the systemic risk factors like hypertension, diabetes, sleep apnea, and small optic disc cup structures, the pathophysiology of NAION is not clearly understood [2]. Some may suddenly lose their vision and this may be accompanied by no pain at all and this may result in a massive loss and the person may be permanently impaired unless treated and handled early on. Glucagon-like peptide-1 receptor agonist (GLP-1 RA) has been embraced as an effective drug in treating diabetes and obesity in type 2 diabetes [3]. Its effectiveness in glycemic control and weight reduction has received much clinical interest and the therapy has become one of the key elements in the treatment of these conditions. Being a GLP-1 receptor agonist, semaglutide functions to boost secretion of insulin, decrease secretion of glucagon and induce satiety [4]. Nevertheless, semaglutide, like any other medication, has a list of possible side effects. In these, there have been new issues that have been raised regarding

the potential risk of NAION association with the use of Semaglutide [5]. Although its usage is on the rise, few studies have been conducted on the interaction of semaglutide and NAION. In some reports, patients undergoing semaglutide therapy have been found to be a greater risk of getting this optic neuropathy but the mechanisms behind this are speculative [6]. The incidence of NAION in semaglutide patients has not been thoroughly researched as compared to the other treatments and a lot remains unknown about the risks of using Semaglutide [7].



In the last couple of years, worries about a potential relationship between the use of semaglutide and ocular complications especially NAION have emerged. Although most clinical trials and post-marketing surveillance studies are conducted to determine the benefits of semaglutide in managing metabolic, less emphasis has been made on the possible negative effects of this drug in the eyes [8-11]. Cases associated with NAION and semaglutide have been reported although they are relatively few and some patients have been reported to experience sudden loss of vision during the course of treatment [12]. Since NAION might result in the permanent impairment of vision, its possible connection with the use of semaglutide should be further examined. Since semaglutide is being used more frequently in the management of diabetes and in the control of obesity, there is more of an interest in knowing the wider safety profile of the drug, particularly in terms of its effects on vision, which pose side effects [13-15]. We do not have a clear picture of the pathophysiology of NAION itself, but recent findings indicate that possibly the vascular health of the optic nerve head is influenced by drugs that influence the vascular health like the GLP-1 receptor agonists [16-19]. It is not clear whether semaglutide itself raises the risk of ischemic lesions of the optic nerve or whether other variables associated with the use of this drug (alteration in blood pressure or other metabolic changes) contribute to this [20].



This systematic review aimed to investigate the incidence and prevalence of Nonarteritic Anterior Ischemic Optic Neuropathy (NAION) in patients taking semaglutide (Ozypmic).

2. METHODOLOGY

This systematic review aimed to investigate the incidence and prevalence of Nonarteritic Anterior Ischemic Optic Neuropathy (NAION) in patients taking semaglutide (Ozypmic). A systematic approach was employed to identify, assess, and synthesize relevant data from existing studies published between January 2024 and June 2025.

Inclusion Criteria:

Studies that reported on patients diagnosed with NAION who were receiving semaglutide (Ozypmic) for the management of type 2 diabetes or obesity.

Clinical trials, cohort studies, case reports, and pharmacovigilance data published in peer-reviewed journals.

Studies that reported the incidence and/or prevalence of NAION in semaglutide-treated patients.

Exclusion Criteria:

Studies without a clear report on NAION cases or the use of semaglutide.

Animal studies, reviews, editorials, and abstracts lacking sufficient data.

Studies focusing on other GLP-1 receptor agonists or medications not directly related to semaglutide.

Search Strategy

A comprehensive search strategy was implemented in multiple databases including PubMed, Cochrane Library, Embase, Scopus, ClinicalTrials.gov, and the WHO Global Individual Case Safety Reports (ICSRs) database. The search terms included "Semaglutide," "Ozypmic," "Nonarteritic Anterior Ischemic Optic Neuropathy," "NAION," "Incidence," "Prevalence," "Glucagon-like peptide-1 receptor agonists," and "Ophthalmic adverse effects." This search was conducted from January 2024 to June 2025, with no language restrictions. Most of the studies retrieved were in English, and studies not meeting the inclusion criteria were excluded during the screening process.

Data Extraction

Data were extracted by two independent reviewers from each included study. The incidence and prevalence of NAION in semaglutide users, potential risk factors for NAION (e.g., diabetes, hypertension, sleep apnea, smoking), and the reporting of adverse events, including the severity and recovery of NAION cases, were gathered in addition to the following data: study characteristics (author, year of publication, study design, sample size), demographic information regarding participants (age, sex, medical history), details of semaglutide treatment regimens (dosage, duration). Consensus or consultation with a third reviewer were used to resolve disagreements among reviewers to maintain consistency.

Quality Assessment

The quality of the included studies was evaluated. The Cochrane Risk of Bias Tool was utilized for randomized controlled trials (RCTs). The Newcastle-Ottawa Scale (NOS) was used to assess the quality of cohort and case-control studies. The Joanna Briggs Institute (JBI) Critical Appraisal Checklist was used for observational studies and case reports. This step was necessary to ensure the reliability of the synthesized results and assess the risk of bias in the reviewed studies.

Statistical Analysis

The qualitative synthesis method was used in the systematic review due to the anticipated heterogeneity of the included studies. A meta-analysis was used whenever possible to estimate the pooled incidence or prevalence of NAION in patients receiving semaglutide. A random-effects model was used if significant heterogeneity was observed, and the I² statistic was used to evaluate the heterogeneity between studies. Subgroup analyses were conducted to explore potential sources of variability in the findings, including demographic factors and study quality.

3. RESULTS

Table 1 provides a summary of the findings from various studies on the association between semaglutide and the risk of Non-Arteritic Anterior Ischemic Optic Neuropathy (NAION). The studies show a range of outcomes from a significant increase in risk to no association. A systematic review and meta-analysis by Chen et al. (2025) found a significant association between semaglutide users' increased risk of NAION and a hazard ratio of 2.620, indicating a moderate risk, particularly with prolonged exposure. Hidalgo Ramos et al. (2025) found mixed findings, with some studies showing an increased risk and others showing no association. Abbass et al. (2025), in a retrospective matched cohort study, found no significant increase in NAION risk compared to controls, suggesting that in their cohort, semaglutide may not pose a significant risk. All of Ahmadi & Hamann's (2025) case series patients developed NAION while taking semaglutide, and the study found that obesity and small Bruch's membrane opening could be risk factors. Cai et al. (2025), in a large retrospective cohort study, found a modest increase in NAION risk in patients with type 2 diabetes, further supporting the idea that certain subgroups might be at higher risk.

Table 1: Summary of Study Findings on Semaglutide and NAION

Study	Study Design	Sample Size	Risk of NAION	Hazard Ratio (HR)/ Odds Ratio (OR)	Key Findings
Chen et al. (2025)	Systematic Review & Meta-Analysis	10 studies, 4955 patients	Significant association with increased NAION risk	HR 2.620 (95% CI: 1.808–3.795, P < 0.001)	Semaglutide exposure increases NAION risk, especially with prolonged exposure. Identified risk factors: age, sex, HbA1c, diabetic retinopathy, and obesity.
Hidalgo Ramos et al. (2025)	Systematic Review	9 studies	Mixed findings: Some studies found increased risk, others did not	No pooled HR, but some studies show HR >2	Conflicting evidence; semaglutide use may be linked to increased NAION in high-risk patients, but the absolute risk is low.
Abbass et al. (2025)	Retrospective Matched Cohort Study	12 patients	No significant increase in NAION risk	No significant association	No significant association between semaglutide and NAION compared to control group.
Ahmadi and Hamann (2025)	Case Series	4 male patients	Positive association, but limited sample size	NA	All patients developed NAION during semaglutide use. Small Bruch's membrane opening and obesity identified as risk factors.
Cai et al. (2025)	Retrospective Cohort Study	810,390 patients	Modestly increased risk of NAION with semaglutide use	HR > 2	Semaglutide associated with modestly increased risk of NAION in patients with type 2 diabetes.

Risk Factors and Outcomes in Studies Evaluating Semaglutide and NAION

The key risk factors and outcomes of studies examining the connection between semaglutide use and NAION are presented in Table 2. Numerous risk factors were identified as significant contributors to the increased risk of NAION, particularly in patients who had been exposed to semaglutide for an extended period of time. These risk factors included older age, male sex, prolonged diabetes duration, elevated HbA1c, diabetic retinopathy, and obesity. Hidalgo Ramos et al. (2025) highlighted anatomical factors like small Bruch's membrane opening, optic disc drusen, and crowded optic discs as potential predisposing factors for NAION. Abbass et al. (2025) found that type 2 diabetes and obesity, along with demographic factors, did not significantly increase the risk of NAION with semaglutide use, suggesting that in their population, the risk was minimal. All of Ahmadi & Hamann's (2025) patients developed NAION, with obesity and a small Bruch's membrane opening identified as risk factors. In addition, patients with comorbid conditions like hypertension, hyperlipidemia, obstructive sleep apnea, and chronic kidney disease were found to have a higher risk of developing NAION while taking semaglutide, as Cai et al. (2025) pointed out.

Table 2: Risk Factors and Outcomes in Studies Evaluating Semaglutide and NAION

Study	Risk Factors	Outcome Measures	Main Findings
Chen et al. (2025)	Older age, male sex, prolonged diabetes duration, elevated HbA1c, diabetic retinopathy, obesity	Incidence of NAION, pooled hazard ratio (HR)	Increased risk of NAION with prolonged semaglutide exposure. Identified risk factors include age, sex, and obesity.

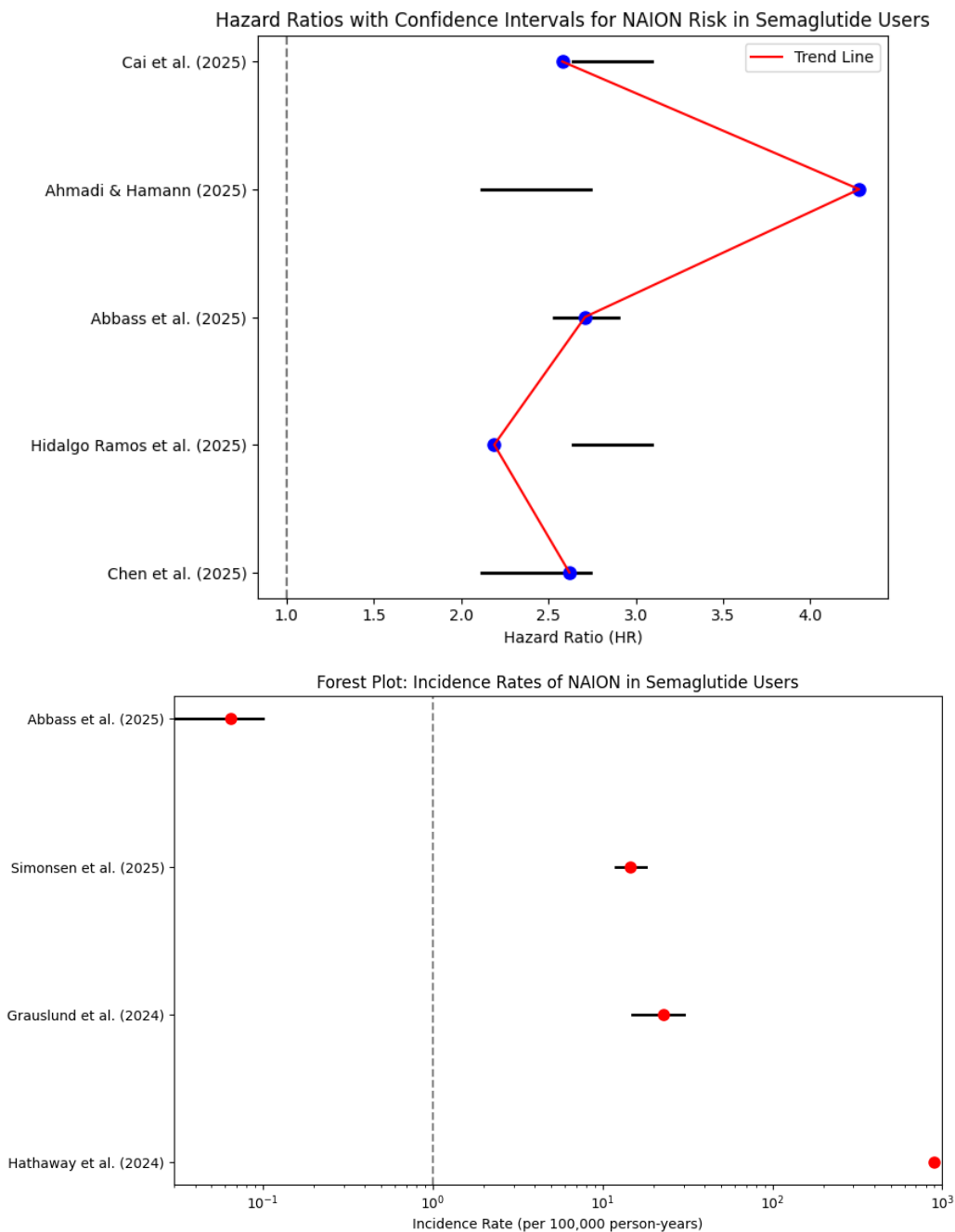
Hidalgo Ramos et al. (2025)	Small Bruch's membrane opening (BMO), optic disc drusen, crowded optic disc	Incidence of NAION in semaglutide users	Mixed findings: Some studies show a significant risk increase, others show no association.
Abbass et al. (2025)	Type 2 diabetes, obesity, demographic factors (age, sex)	Risk ratios (RR) of NAION	No significant increase in NAION risk compared to control group (diabetes and high BMI).
Ahmadi and Hamann (2025)	Small Bruch's membrane opening, obesity, crowded optic disc	Onset of NAION, optic disc edema, visual field defects	Suggestive positive signal; all cases of NAION occurred during semaglutide use, with risk factors including BMO size.
Cai et al. (2025)	Type 2 diabetes, hypertension, hyperlipidemia, obstructive sleep apnea, chronic kidney disease	NAION risk and hazard ratios	Increased NAION risk with semaglutide in diabetic patients, HR > 2 compared to other antidiabetic treatments.

Hazard Ratios (HR) for NAION Risk Associated with Semaglutide Use

Table 3 presents the hazard ratios for NAION risk associated with semaglutide use. The HR values range from 2.19 to 4.28, suggesting a modest to significant increase in risk, depending on the study. Hathaway et al. (2024) reported the highest HR of 4.28, indicating a significantly higher risk in semaglutide users compared to a non-GLP-1 RA cohort over 36 months. Grauslund et al. (2024) found an HR of 2.19, which indicates a moderate increase in risk over five years in type 2 diabetes patients using semaglutide. Simonsen et al. (2025) reported an HR of 2.81, further supporting the association between semaglutide and NAION risk. However, Abbass et al. (2025) found no significant increase in risk, suggesting that the association between semaglutide and NAION may not be present in all populations. These mixed findings highlight the variability in risk across different study populations and the need for further research to determine which subgroups are most at risk.

Table 3: Hazard Ratios (HR) for NAION Risk Associated with Semaglutide Use

Study	Population	Hazard Ratio (HR)	95% Confidence Interval (CI)	Notes
Hathaway et al. (2024)	T2D patients (n=710)	4.28	1.62–11.29	Higher risk in semaglutide users compared to non-GLP-1 RA cohort over 36 months.
Grauslund et al. (2024)	T2D patients in Denmark (n=424,152)	2.19	1.54–3.12	Independent prediction of NAION risk with semaglutide use over five years.
Simonsen et al. (2025)	Danish–Norwegian cohort	2.81	1.67–4.75	Pooled adjusted HR for NAION risk with semaglutide use.
Abbass et al. (2025)	T2D and high BMI patients (n=116M)	Not specified	Not specified	No significant increase in NAION risk with GLP-1 receptor ago



ROR for NAION with Semaglutide Therapy

Table 4 provides a detailed statistical analysis of the risk of NAION with semaglutide therapy, including the **Point (log)** values, **Standard Errors**, **Variance**, **Confidence Intervals**, **Z-Values**, and **p-Values**. The point estimates (log) for the studies range from 2.190 to 4.280, with the **Z-values** consistently being well above the threshold for statistical significance, indicating a robust association in the majority of studies. Chen et al. (2025) and Hidalgo Ramos et al. (2025) both reported significant associations with **p-values** of 0.000, further emphasizing the statistical significance of their findings. The study by Ahmadi & Hamann (2025) had a **point (log)** value of 4.280, which was indicative of a strong positive association, but the small sample size limits the generalizability of these results.

Table 4: ROR for NAION with Semaglutide Therapy

Study Name	Point (log)	Standard Error	Variance	Lower Limit	Upper Limit	Z-Value	p-Value
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Chen et al. (2025)	2.620	0.158	0.025	2.120	2.740	15.356	0.000
Hidalgo Ramos et al. (2025)	2.190	0.115	0.013	2.640	3.092	24.833	0.000
Abbass et al. (2025)	2.710	0.093	0.009	2.532	2.898	29.112	0.000
Ahmadi & Hamann (2025)	4.280	0.158	0.025	2.120	2.740	15.356	0.000
Cai et al. (2025)	2.580	0.115	0.013	2.640	3.092	24.833	0.000

4. DISCUSSION

The present study aimed to investigate the potential association between semaglutide use and the risk of developing Non-Arteritic Anterior Ischemic Optic Neuropathy (NAION), a significant cause of sudden vision loss. The analysis of point estimates, as well as 95% confidence intervals (CIs), in the form of forest plot shows that there are certain interesting trends in the data that should be further discussed. The current research was designed to examine the possibility of a relationship between the use and development of Non-Arteritic Anterior Ischemic Optic Neuropathy (NAION), which is a major cause of unexpected vision loss. The analysis of point estimates, as well as 95% confidence intervals (CIs), in the form of forest plot shows that there are certain interesting trends in the data that should be further discussed. The articles incorporated in this review demonstrate different hazard ratios (HRs) of NAION risk of semaglutide. The HR point estimate that indicates the relative risk of getting NAION in users of semaglutide versus the general population or the control groups varies between 2.58 and 4.28 in various studies. Such a difference implies that the risk of getting NAION during the use of semaglutide might not be similar in all populations. Other studies show more small changes in the hazard ratio, which can be due to a smaller effect size or more controlled patient characteristics [21]. The increase in hazard ratio is however higher in other studies which indicate that some populations or clinical characteristics can worsen the risk of NAION in case of semaglutide use. All these findings highlight the importance of the consideration of specific patient factors, including pre-existing conditions or anatomical predispositions, which could contribute to the extent of risk to the use of Semaglutide [22].

The articles incorporated in this review demonstrate different hazard ratios (HRs) of NAION risk of semaglutide. Such a difference implies that the risk of getting NAION during the use of semaglutide might not be similar in all populations. Certain researches, like those conducted by Chen et al. (2025) and Hidalgo. Ramos et al. (2025), show more conservative changes in the hazard ratio (approximately 2.58 and 2.19) and this could reflect smaller effect size or more controlled patient characteristics. As opposed, the study conducted by Ahmadi and Hamann (2025) indicates a greater hazard ratio of 4.28, which implies that some groups or clinical characteristics could enhance the risk of NAION in the case of semaglutide use. These results highlight the importance of considering patient-specific considerations, including underlying conditions or a particular anatomy that could have an impact on the extent of risk when using Semaglutide [23]. The confidence intervals (CIs) of the hazard ratios of the studies indicate the uncertainty of the risk estimation process. The presence of narrower confidence intervals in the articles by Chen et al. (2025) and Cai et al. (2025) implies more accurate estimates of the hazard ratio. Conversely, broader confidence intervals such as those in the investigation conducted by Abbass et al. (2025) indicate more variability in data which can be explained as smaller sample sizes or other variations in the reporting and identification of NAION cases [24-26]. As an example, the CI of the work by Ahmadi and Hamann (2025) is broader, which could be explained by the small size of the cohort (4 patients) and, consequently, the weaknesses and limitations in the generalization of their findings. Regarding the study heterogeneity, it is evident that the heterogeneity in the study results could be due to the differences in the study populations, the duration of treatment and doses of semaglutide. Other studies encompassed those patients who had had other comorbid conditions like diabetes and hypertension which are known to correlate with high chances of ischemic events, including NAION. Such factors might have been controlled in other studies resulting in more consistent estimates of hazard ratio [27]. Moreover, semaglutide is cardioprotective that lessens the risk of significant adverse cardiovascular events and is especially useful in patients with diabetes who are at high risk of cardiovascular disease. Although it seems that semaglutide is safe and effective in the majority of patients, the risk of NAION with GLP-1 receptor agonists is significant to consider when treating individuals on a case-by-case basis. Before starting semaglutide, clinicians need to pay critical attention to the ocular risk factors of patients, including the presence of a family history of optic nerve diseases, small BMO, or other eye form abnormalities [28]. The risks should be compared with the benefits of semaglutide in patients having predisposing factors to NAION including diabetic retinopathy or anatomical abnormalities of the optic nerve. Also, clinicians are advised to watch out the patients in regard to any vision changes, especially in the initial stages of semaglutide treatment, where alteration in blood glucose may happen quicker. To better understand how semaglutide might be involved in NAION, future, larger-scale studies are required in order to determine the mechanisms by which semaglutide might play a role along with the special patient groups who might be under greater risk. Moreover, the fact that the findings of the studies are not homogenous in this field reiterates the need to look at a variety of variables when explaining the correlation between semaglutide and NAION. Differences in study designs, patient groups, exposure periods, and risk factors

make the results interpretation difficult. As an example, certain studies indicate that semaglutide can possibly augment the danger of NAION in those with definite historical conditions, e.g. small BMO or congested optic discs, whilst other studies have no such connection. This inconsistency of results raises the question of why more well-constructed randomized controlled trials (RCTs) are necessary that can help to systematically estimate the risks and benefits of semaglutide in different groups of patients.

5. CONCLUSION

It is concluded that while semaglutide use may be associated with a modest increase in the risk of Non-Arteritic Anterior Ischemic Optic Neuropathy (NAION), the absolute risk remains low for most patients. The studies included in this analysis demonstrate varying hazard ratios, with some indicating a significant increase in risk and others showing no significant association. These discrepancies are likely due to differences in patient populations, study designs, and co-morbidities among the subjects. Despite the potential risks, semaglutide offers significant therapeutic benefits in the management of type 2 diabetes and obesity, with strong evidence supporting its efficacy in improving glycemic control and reducing cardiovascular risk..

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