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Research article

The causal effect of oxidative stress on the risk of glaucoma

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ABSTRACT

Glaucoma is a complex multifactorial disease. Oxidative stress has been implicated in its pathogenesis. However, establishing a causal relationship between oxidative stress and glaucoma is challenging due to confounding and reverse causality. In this study, we performed bidirectional two-sample Mendelian randomization (MR) analyses based on genetic instrumental variables as proxies for 11 biomarkers of oxidative stress injury to investigate the causal relationship between oxidative stress and glaucoma. Eight significant associations were identified. Increased circulating levels of catalase (OR = 0.915, 95 % CI: 0.848–0.987, $P = 0.022$), retinol (OR = 0.481, 95 % CI: 0.248–0.932, $P = 0.044$) and superoxide dismutase (OR = 0.779, 95 % CI: 0. 616-0.986, $P = 0.038$) are associated with a decreased risk of glaucoma, whereas an increased myeloperoxidase level (OR = 2.145, 95 % CI: 1.119–4.111, $P = 0.029$) is associated with an increased risk of glaucoma. Glaucoma was causally associated with lower levels of total bilirubin (OR = 0.961, 95 % CI: 0.927–0.997, $P = 0.039$), glutathione peroxidase (OR = 0. 934, 95 % CI: 0.890–0.981, $P = 0.006$), paraoxonase (OR = 0.883, 95 % CI: 0.810–0.963, $P = 0.005$) and albumin (OR = 0.988, 95 % CI: 0.978–0.998, $P = 0.014$). The bidirectional MR analysis revealed a causal relationship between oxidative stress and glaucoma. These findings provide a greater understanding of the underlying mechanisms of glaucomatous neurodegeneration and imply a potential therapeutic approach for glaucoma through targeting oxidative stress pathways.

1. Introduction

As one of the leading causes of irreversible blindness throughout the world, glaucoma is characterized by the degeneration of retinal ganglion cells and axons, resulting in a reduced visual field [1]. The global prevalence of glaucoma is estimated at 111.8 million cases by the year 2040 [2].

Glaucoma is a multifactorial disease influenced by genetic and environmental factors. Oxidative stress has emerged as a potential factor in the development and progression of glaucoma, although the exact mechanisms underlying its pathogenesis are not fully understood. Dysregulation of oxidative stress leads to the generation of significant amounts of free radicals, which trigger cellular

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autophagy and deposition of extracellular matrix components [3]. Due to the involvement of free radicals in many biological processes, oxidative stress has emerged as a recognized risk factor for several diseases [4,5]. Previous studies have suggested an association between oxidative stress and glaucoma, as abnormal levels of oxidative stress injury biomarkers (OSIBs) have been observed in glaucoma patients' serum and aqueous humor [6]. Observational studies have consistently shown elevated levels of total oxidation status (TOS) and oxidative stress index (OSI) in the aqueous humor of glaucoma patients compared to non-glaucoma subjects [7]. Furthermore, increased activities of superoxide dismutase (SOD) and glutathione peroxidase (GPX) have been observed in the aqueous humor of patients with primary open-angle glaucoma (POAG) and primary angle-closure glaucoma (PACG), accompanied by decreased levels of vitamin C and vitamin E [8]. In patients with normal-tension glaucoma (NTG), decreased serum levels of vitamin C and retinol, and increased levels of serum uric acid (UA) have been reported [9,10]. These findings suggest a strong link between biomarkers of oxidative stress injury and the pathogenesis of glaucoma. Further investigation of OSIB holds great promise for identifying novel therapeutic targets for glaucoma. However, published studies have yielded conflicting results. For example, while Wang and Singh et al. found that high-dose vitamin C supplementation was associated with reduced odds of glaucoma, Han and Fu et al. reported the opposite [11,12]. The discrepancies in these studies may be due to the susceptibility of observational studies to confounding, which may obscure the true association between variables.

Mendelian randomization (MR) is an instrumental variable-based approach that uses genetic variants as proxies for modifiable risk factors to infer causality in observational studies. It leverages the random assortment of genetic variants during meiosis, miming a randomized controlled trial and reducing confounding bias. MR studies have been widely used to investigate causal relationships between risk factors and disease, providing valuable insights into disease etiology.

This study aims to investigate the causal relationship between oxidative stress and glaucoma using a bidirectional two-sample Mendelian randomization approach. By using large genome-wide association study datasets for oxidative stress and glaucoma, we can overcome the limitations of observational studies and make more robust causal inferences. This bidirectional analysis will allow us to examine both the effect of oxidative stress on glaucoma development and potential reverse causality.

2. Materials and methods

2.1. Data sources

GWAS summary data of OSIB were obtained from the IEU OpenGWAS database (https://gwas.mrcieu.ac.uk/). Specifically, we retrieved data for 11 relevant biomarkers of oxidative stress injury, including glutathione S-transferase (GST), catalase (CAT), myeloperoxidase (MPO), paraoxonase (PON), SOD, GPX, retinol, vitamin C, vitamin E, albumin, total bilirubin (TBIL). Sample sizes for the different OSIBs ranged from 1322 to 342,829 participants, as summarized in Table 1. To minimize potential bias due to population heterogeneity, all study participants included in the analysis were European ancestry. Detailed information on these data can be found in previous studies [13–15].

In addition, GWAS summary data for glaucoma and its three subtypes (POAG, PACG and NTG) provided by the FinnGen consortium were obtained from the IEU OpenGWAS database (https://gwas.mrcieu.ac.uk/). The sample sizes for glaucoma ranged from 210,789 to 218,792 participants. All participants included in these studies were of European ancestry. More detailed information on the GWAS data, including sample sizes and ancestry, is provided in Table 1.

Table 1
Detailed information regarding studies and datasets used in the present study.

Exposure or Outcome	GWAS ID	Year	Sample size	Ancestry	Build	Reference
OSIB						
GST	prot-a-1283	2018	3301	European	HG19/GRCh37	[13]
CAT	prot-a-367	2018	3301	European	HG19/GRCh37	[13]
SOD	prot-a-2800	2018	3301	European	HG19/GRCh37	[13]
GPX	prot-a-1265	2018	3301	European	HG19/GRCh37	[13]
MPO	ebi-a-GCST90012031	2020	21,758	European	HG19/GRCh37	[14]
PON	ebi-a-GCST90010252	2020	1322	European	HG19/GRCh37	[15]
Retinol	ukb-b-17406	2018	62,991	European	HG19/GRCh37	/
VC	ukb-b-19390	2018	64,979	European	HG19/GRCh37	/
VE	ukb-b-6888	2018	64,979	European	HG19/GRCh37	/
Albumin	met-*d*-Albumin	2018	115,060	European	HG19/GRCh37	/
TBIL	ukb-*d*-30840_raw	2018	342,829	European	HG19/GRCh37	/
Glaucoma diseases						
Glaucoma	finn-b-H7_GLAUCOMA	2021	8591/210,201	European	HG19/GRCh37	/
POAG	finn-b-H7_GLAUCPRIMOPEN	2021	4433/210,201	European	HG19/GRCh37	/
PACG	finn-b-H7_GLAUCCLOSEPRIM	2021	588/210,201	European	HG19/GRCh37	/
NTG	finn-b-H7_GLAUCOMA_NTG	2021	892/210,201	European	HG19/GRCh37	/

Sample size shown as a total number for quantitative traits and Cases/Controls for binary traits.

2.2. Study design

Bidirectional two-sample MR analysis was used to investigate the causal relationship between 11 biomarkers related to oxidative stress damage and glaucoma (Fig. 1). Instrumental variables (IVs) for both OSIB and glaucoma were obtained from the IEU OpenGWAS database. To estimate the causal effect between exposure (OSIB) and outcome (glaucoma), we used several MR methods, including MR-Egger, weighted median, and inverse variance weighted (IVW) with random-effects and fixed-effects models. We also conducted sensitivity analyses using MR-Egger, MR-PRESSO, Cochran's Q, Rucker's Q and leave-one-out analysis to assess the robustness of the MR results. Our bidirectional two-sample MR analysis was based on the following assumptions: (1) the single nucleotide polymorphisms (SNPs) used as IVs were strongly associated with exposure (OSIB); (2) the IVs were independent of confounders that could influence both exposure and outcome; (3) the IVs influenced outcome only by exerting their effects through the exposure variable. These assumptions are the basis for causal inference in MR analysis [16].

2.3. Selection of IVs

We conducted a selection process with strict quality control measures to identify suitable SNPs for the IVs in our MR analysis. Our strict selection criteria aimed to avoid weak IVs, which could lead to an underestimation of the association strength and introduce a bias in the causal relationship. To ensure a robust correlation between the IVs and the exposure variable, we selected SNPs with an F statistic greater than 10 ($F = Beta^2/SE^2$) [17]. When identifying SNPs strongly associated with the exposure variable ($P < 1 \times 10^{-5}$), we also applied clumping ($R^2 < 0.001$, clumping distance = 10,000 kb) to remove any linkage disequilibrium bias [18]. In addition, we excluded any SNPs associated with confounders using the PhenoScanner database (http://www.phenoscanner.medschl.cam.ac.uk/phenoscanner) [19,20]. Finally, palindromic SNPs were excluded to ensure that the effect of SNPs on exposure corresponded to the same alleles as their effect on the outcome variable [21].

2.4. Statistical analysis

Several rigorous statistical methods were used to investigate the causal relationship between OSIB and glaucoma, including IVW (fixed effects) [22], IVW (random effects) [23], MR-Egger regression [24], weighted median [25], and MR-PRESSO [26]. The IVW results were considered unbiased without horizontal pleiotropy [27]. IVW (fixed effects) was used when no heterogeneity was found [22]. Conversely, IVW (random effects) results were considered more reliable when substantial heterogeneity was present [23]. The MR-Egger regression allowed for pleiotropy in all SNPs and satisfied the instrument strength independent of the direct effect (InSIDE) hypothesis. In cases where pleiotropy was present, MR-Egger results were considered more reliable [24]. The weighted median method provided consistent estimates even when up to half of the weight came from invalid IVs. It had smaller type I errors than IVW and complemented MR-Egger analysis [25]. The MR-PRESSO analysis corrected for horizontal pleiotropy by removing outliers and performed a significance difference test for causal estimates before and after outlier removal [26].

Sensitivity analyses were carried out to assess the potential bias in the MR results. Horizontal pleiotropy was detected by the MR-

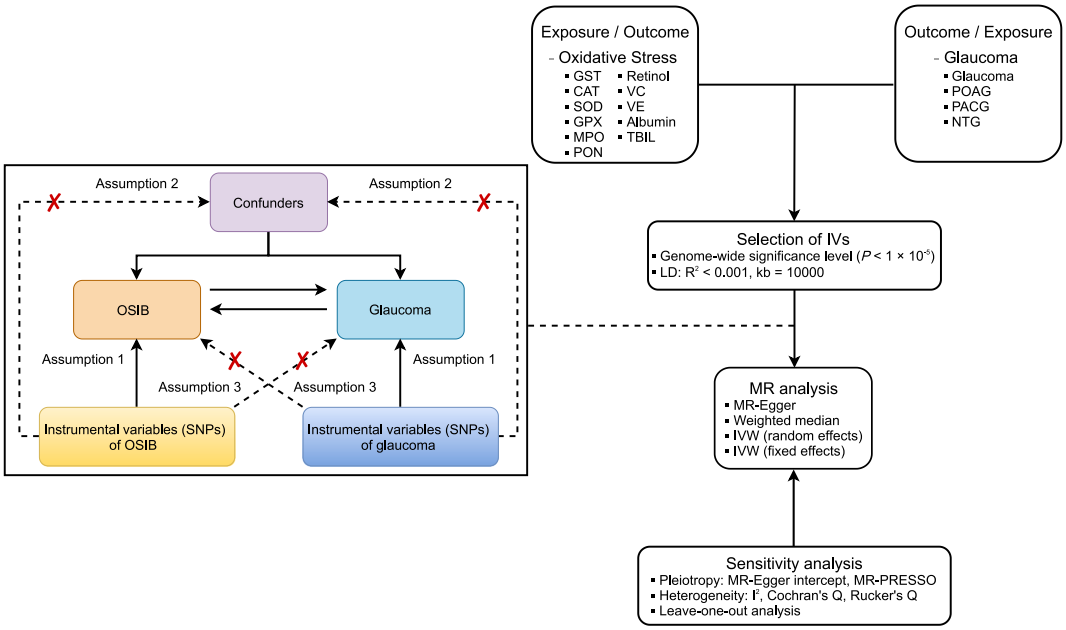

Fig. 1. Flow chart of the bidirectional MR study design.

Egger intercept test and the MR-PRESSO global test. Statistical significance level of $P < 0.05$ indicates the presence of horizontal pleiotropy [24,26]. The I^2 statistic, Cochran's Q statistic for the MR-IVW method, and Rucker's Q statistic for the MR-Egger method were used to determine the heterogeneity of the MR analysis, with $I^2 < 50$ % or $P > 0.05$ indicating no heterogeneity [28]. Finally, leave-one-out analysis was used to examine the influence of individual SNPs on the IVW estimates [29,30].

All statistical analyses were conducted using R (version 4.2.2) with the packages TwoSampleMR (version 0.5.6) [31] and MR-PRESSO (version 1.0) [26]. A causal relationship between biomarkers of oxidative stress injury and glaucoma was considered significant if $P < 0.05$.

3. Results

3.1. The causal effect of genetically predicted OSIB on glaucoma

The two-sample MR analysis provided insight into the causal effect of OSIB on glaucoma, as shown in Fig. 2. The results showed significant associations between genetically predicted levels of CAT and reduced risk of POAG (OR = 0.915, 95 % CI: 0.848–0.987, P = 0.022), retinol and reduced odds of glaucoma (OR = 0.481, 95 % CI: 0.248–0.932, P = 0.044), SOD and decreased incidence of PACG (OR = 0.779, 95 % CI: 0.616–0.986, P = 0.038), and MPO and increased incidence of PACG (OR = 2.145, 95 % CI: 1.119–4.111, P = 0.029) (Fig. 2). Importantly, the MR-PRESSO test did not identify any outlier SNPs among these OSIB.

The MR-Egger intercept did not significantly deviate from zero, with p-values of 0.204 for CAT on POAG, 0.089 for retinol on glaucoma, 0.834 for SOD on PACG, and 0.142 for MPO on PACG, respectively. Furthermore, statistical analyses, including MR-PRESSO, Cochran's Q test, and Rucker's Q test did not yield statistically significant results ($P > 0.05$), indicating no evidence of pleiotropy or heterogeneity in the MR analysis. Additionally, the leave-one-out test demonstrated that the MR results were not significantly affected by individual SNPs (Fig. 4), indicating the reliability and stability of the results. Further details on the results of the additional forward MR and the sensitivity analyses can be found in Supplementary Table S1 and Table S3.

3.2. The causal effect of genetically predicted glaucoma on OSIB

To investigate the potential causal effect of glaucoma on OSIB, reverse MR analysis was performed, as shown in Fig. 3. After excluding two SNPs with abnormalities, the results of the reverse MR analysis showed a significant causal association between genetically predicted glaucoma and reduced TBIL levels (OR = 0.961, 95 % CI: 0.927–0.997, P = 0.039). The IVW (fixed effects) estimate indicated a significant association between genetically predicted PACG and decreased levels of GPX (OR = 0.934, 95 % CI: 0.890–0.981, P = 0.006). Furthermore, the IVW (fixed effects) analysis demonstrated a significant causal relationship between PACG and decreased PON activity (OR = 0.883, 95 % CI: 0.810–0.963, P = 0.005), with consistent estimates obtained using the weighted median method (OR = 0.874, 95 % CI: 0.769–0.994, P = 0.041). The IVW (fixed effects) analysis also showed significant causality between POAG and decreased albumin levels (OR = 0.988, 95 % CI: 0.978–0.998, P = 0.014). Sensitivity analyses revealed no

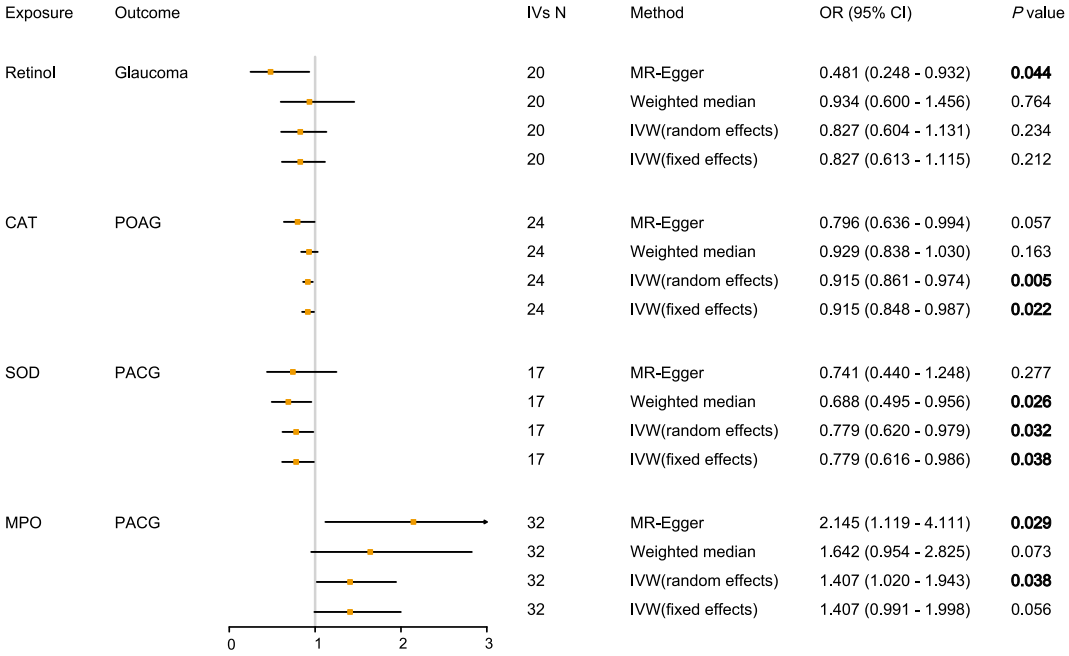

Fig. 2. Associations between genetically predicted OSIB and glaucoma.

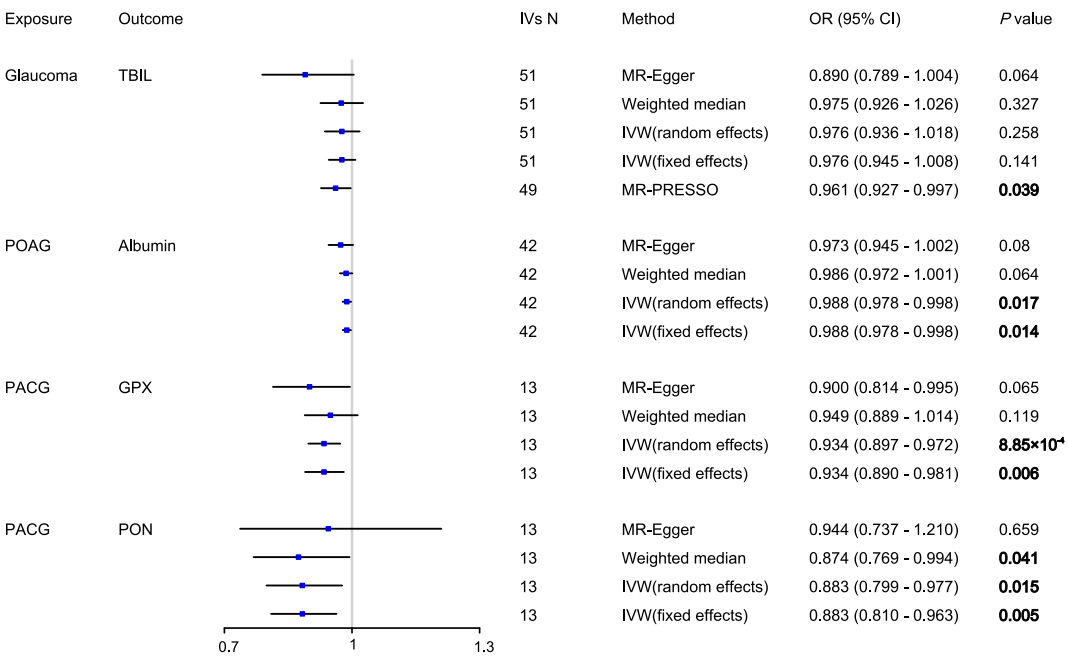

Fig. 3. Associations between genetically predicted glaucoma and OSIB.

evidence of pleiotropy or heterogeneity in the reverse MR analysis ($P > 0.05$). The leave-one-out test is presented in Fig. 5, and the MR results are not significantly affected by individual SNPs, indicating the robustness of the results. Additional results of reverse MR and sensitivity analysis are provided in Supplementary Table S2 and Table S4.

4. Discussion

This study investigated the causal relationship between oxidative stress and glaucoma risk in individuals of European ancestry using a bidirectional two-sample MR approach combined with robust genetic tools and large data sets. We observed a significant association between genetically predicted CAT and a lower risk of POAG, suggesting that higher levels of CAT may protect against the development of this form of glaucoma. Furthermore, our results indicate a significant causal relationship between retinol and glaucoma, implying that higher retinol levels may be associated with reduced risk. For PACG, we observed that genetically predicted SOD was associated with lower disease incidence, suggesting a potential protective effect of SOD against PACG development. Conversely, MPO was significantly associated with a higher incidence of PACG, suggesting that higher levels of MPO may increase the risk of developing this form of glaucoma. These findings highlight a potential role for oxidative stress biomarkers in the pathogenesis of PACG. In addition to investigating the effect of oxidative stress on glaucoma, we also investigated reverse causality by examining the effect of glaucoma on OSIB. Our results showed significant associations between genetically predicted glaucoma and lower TBIL levels, suggesting that glaucoma may have a causal effect in reducing TBIL levels. Similarly, we found that PACG was associated with decreased levels of GPX and reduced activity of PON, suggesting a potential influence of PACG on these biomarkers of oxidative stress. Moreover, POAG was significantly associated with reduced albumin levels, suggesting a possible causal effect of POAG on albumin levels.

Observational studies have previously reported associations between OSIB and glaucoma. MPO, an enzyme in heme metabolism, produces reactive oxygen species (ROS) under normal physiological conditions using hydrogen peroxide and chloride ions to fight invading microorganisms [32]. However, excessive production of oxidative substances catalyzed by MPO can overwhelm the body's antioxidant capacity, leading to pathological processes and tissue damage. Several studies have demonstrated that MPO interacts with retinal nerve compounds and proteins associated with cell death, potentially inducing inflammatory responses and nerve cell damage, thereby contributing to the onset and progression of glaucoma [33,34]. Zhang et al. observed elevated levels of cathepsin D in aqueous humor samples from patients with primary POAG compared to those with cataracts, whereas MPO levels were not significantly different between groups [35]. Our results are consistent with these studies, as we also found no association between MPO levels and the risk of POAG.

Antioxidant enzymes, such as GST, CAT, SOD, GPX, and PON, play a critical role in removing toxic by-products generated during oxidative stress reactions and protecting cells from free radical damage. Sobot et al. investigated the relationship between polymorphisms of several genes encoding antioxidant enzymes involved in mitochondria and susceptibility to POAG. They found that individuals carrying GSTO2*GG and GSTO1*AA variants were at risk of developing POAG [36]. A meta-analysis study suggested that zero genotypes of GSTM1 may be significantly associated with glaucoma risk [37]. The results of this study did not demonstrate a causal relationship between GSTA1 and glaucoma, but further investigation is needed to determine whether other GST subtypes are

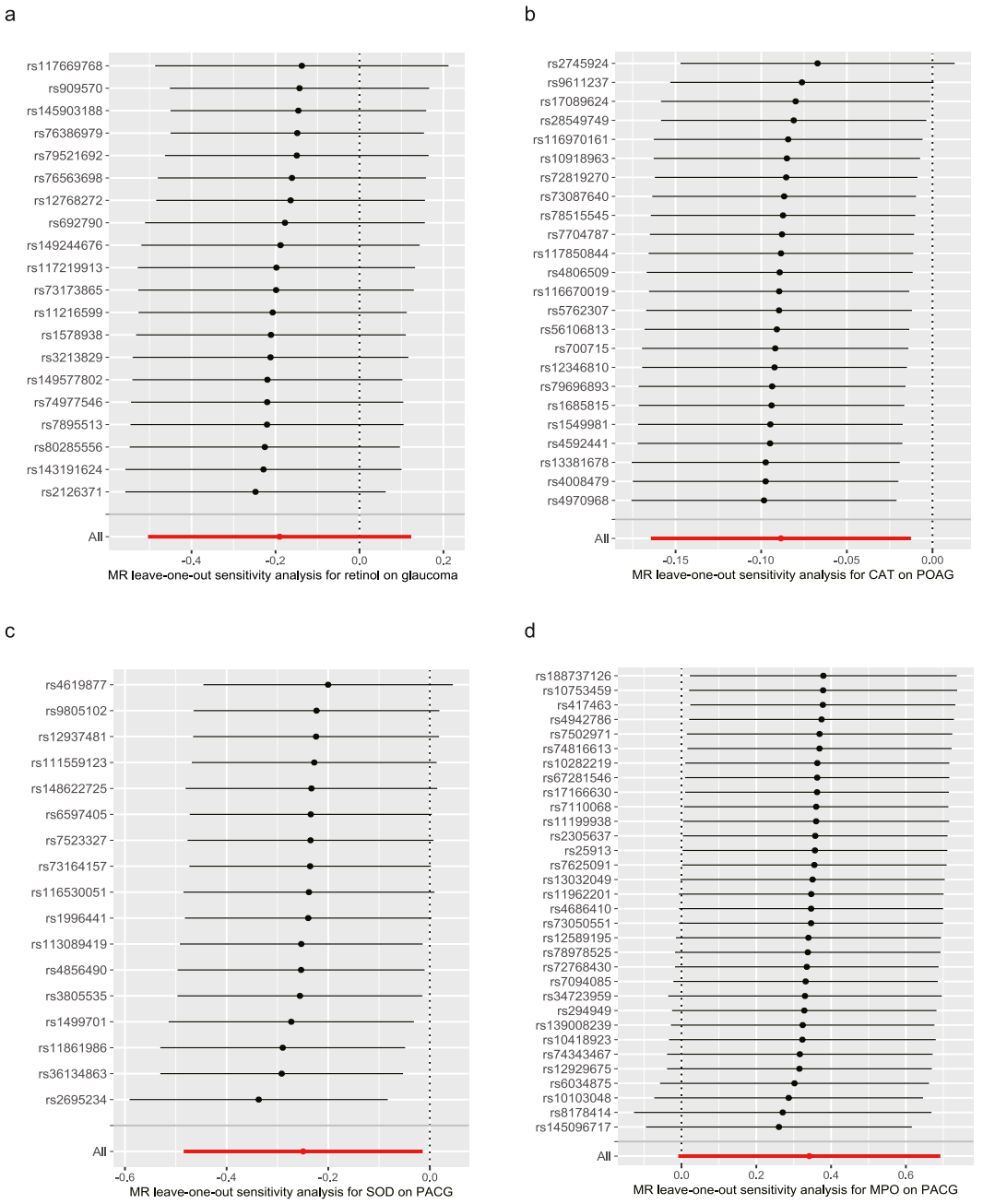

Fig. 4. Leave-one-out plots of the causal effects of OSIB on glaucoma. (a) MR leave-one-out sensitivity analysis for retinol on glaucoma. (b) MR leave-one-out sensitivity analysis for CAT on POAG. (c) MR leave-one-out sensitivity analysis for SOD on PACG. (d) MR leave-one-out sensitivity analysis for MPO on PACG.

involved in the pathogenesis of glaucoma. CAT, localized in cellular peroxisomes, facilitates the degradation of hydrogen peroxide to non-toxic water and molecular oxygen, thereby maintaining REDOX homeostasis [36,38]. Some studies found that the functional SNP rs769217 of the CAT gene was closely associated with POAG, suggesting that the CAT polymorphism plays an important role in the pathogenesis of POAG in the Chinese population [39]. SOD catalyzes the decomposition of highly reactive oxygen radicals to molecular oxygen and water. Experimental studies showed that the number of RGCs was reduced and dysfunction occurred in SOD1-deficient mice [40]. Celojevic et al. showed that gene variation in SOD1, SOD2, and SOD3 was not the main factor in the pathogenesis of POAG [41]. Our study showed a significant association between CAT and lower risk of POAG and a significant association between SOD and lower risk of PACG, which is consistent with previous research [39,42]. GPX, which uses glutathione as a reducing agent, eliminates hydrogen peroxide and other peroxides in the body. A case-control study conducted by the Medical

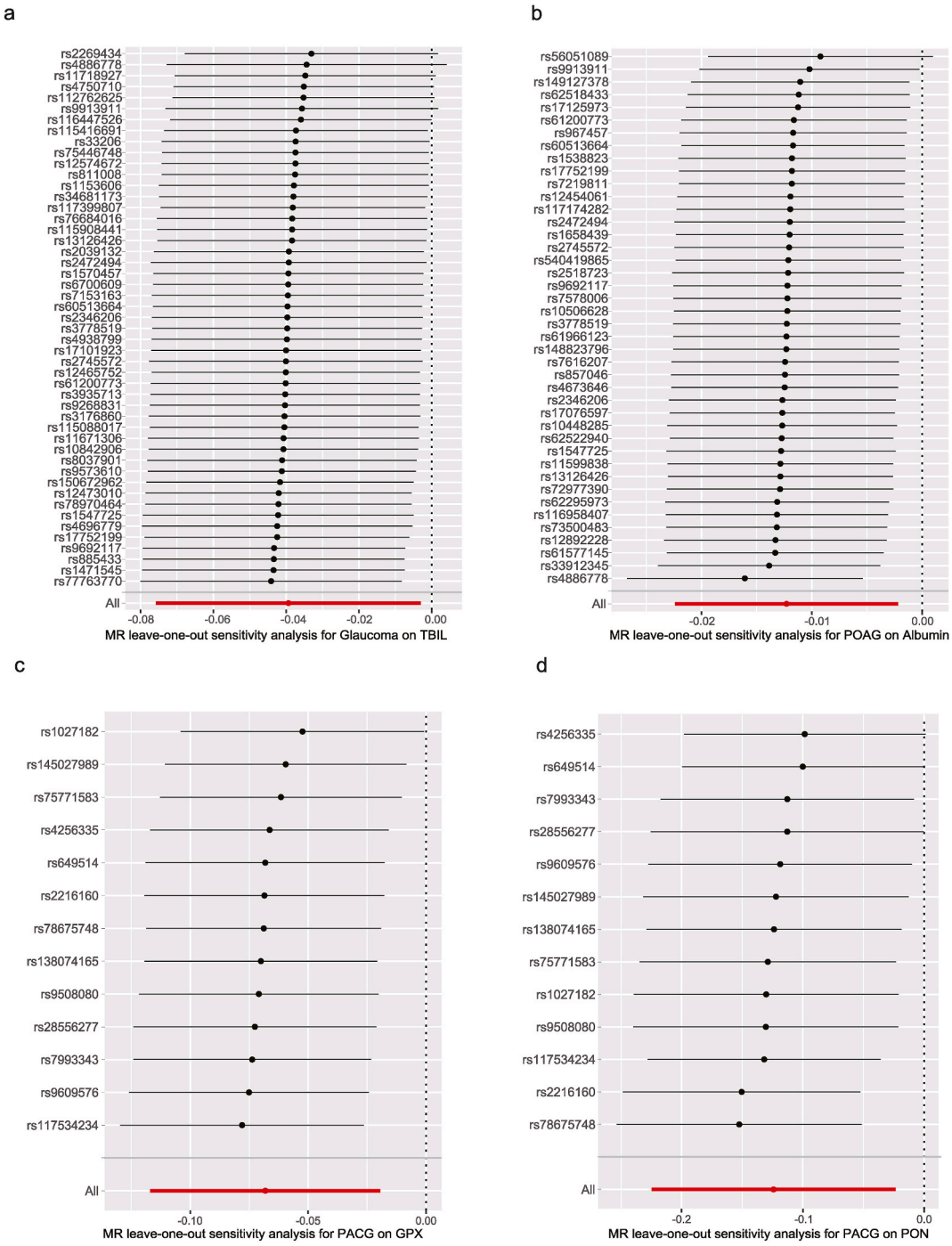

Fig. 5. Leave-one-out plots of the causal effects of glaucoma on OSIB. (a) MR leave-one-out sensitivity analysis for glaucoma on TBIL. (b) MR leave-one-out sensitivity analysis for POAG on albumin. (c) MR leave-one-out sensitivity analysis for PACG on GPX. (d) MR leave-one-out sensitivity analysis for PACG on PON.

University of Lodz found that GPX1 Pro198Leu gene polymorphisms conferred a protective effect against the development of POAG in the Polish population [43]. PON inhibits low-density lipoprotein (LDL) oxidation and prevents the production of lipid peroxides in ocular tissues, which could trigger an inflammatory response and cause cell damage [44]. Mumcu et al. reported that glaucoma patients had lower PON1 activity compared to controls and that the level of malondialdehyde (MDA), a marker of lipid peroxidation, showed a significant negative correlation with PON1 activity [45]. Other studies have shown that specific polymorphisms in the PON gene are associated with glaucoma risk [46]. Our study supports these findings by demonstrating a significant causal relationship

between PACG and lower levels of GPX and reduced levels of PON activity.

Non-enzymatic antioxidants, such as retinol, vitamin C, vitamin E, albumin, and TBIL, were essential in maintaining a balance of oxidative stress. Retinol is critical for visual light absorption and eye structure development and is the primary circulating form of vitamin A in the blood [47]. Retinol could be converted by retinal dehydrogenase (RDH) and alcohol dehydrogenase (ADH) to the aldehyde isomer 11-cis-retinal, which binds to opsin in specific retinal cells to form rhodopsin, thereby influencing visual light transduction [48]. Furthermore, retinol could be converted to retinoic acid by several aldehyde dehydrogenases (ALDH). Studies have shown that dysregulation of the retinoic acid pathway activates the TGF-β pathway, increasing matrix production and fibrotic changes in the eye, thereby increasing the risk of glaucoma [49,50]. A Rotterdam study found that individuals with a high intake of retinol equivalents had a twofold lower risk of open-angle glaucoma (OAG) than those with a low intake [51]. This finding was further supported by a subsequent cross-sectional study of the Korean population [52]. A meta-analysis examining dietary vitamin C intake also reported a weak association with a reduced risk of glaucoma [53]. Vitamin E regulates retinal blood vessels through protein kinase C [54] and, in conjunction with activation of the Rho/ROCK system, has been suggested to be an important factor in inducing trabecular cell relaxation [55]. Experimental studies in rats have shown that vitamin E deficiency increases retinal ganglion cell (RGC) death compared to a normal diet [56]. Additionally, Moreno et al. found an inverse correlation between the multilocus genetic risk score (GRS) for POAG and plasma vitamin E concentration [57]. However, results from the SUN Project study suggested that the intake of vitamins A, C, and E alone may not confer a protective effect against glaucoma, but when taken together, they were associated with lower disease risk [58]. In our study, we observed a significant association between retinol and glaucoma. Both albumin and total bilirubin have been reported to have strong antioxidant properties, although their relationship with glaucoma remains largely unexplored. Transition metals, such as copper and iron, and polyunsaturated fatty acids serve as potent ROS generators upon reaction with oxygen, and albumin could bind to these substances while scavenging free radicals, thereby attenuating the onset of oxidative stress [59]. Experimental studies have shown that total bilirubin can effectively scavenge ROS and inhibit the activity of nicotinamide adenine dinucleotide phosphate (NADPH) oxidase, ultimately reducing oxidative stress [60]. Shao et al. demonstrated that high TBIL levels are a risk factor for POAG in men, but not in women [61]. A retrospective case-control study indicated that glaucoma patients had lower serum albumin and bilirubin levels than healthy controls [62]. Finally, the results of our study confirmed the association between albumin, TBIL, and glaucoma, suggesting that these antioxidants may be effective adjunctive treatments for glaucoma.

The present study has several strengths: First, it is the largest and most comprehensive MR study investigating the association between oxidative stress and glaucoma. Second, using MR analysis allowed the determination of a causal relationship between oxidative stress and glaucoma, minimizing confounding factors and reducing the problem of reverse causality. Finally, the inclusion of IVs derived exclusively from the European population reduced the potential impact of population stratification and increased the validity of the two-sample MR hypothesis. However, this study has several limitations. First, to ensure statistical efficiency in the MR analysis, a relatively lenient threshold of 1×10^{-5} was used for the p-value of the SNPs analyzed, which resulted in only a small proportion of the variance being explained by the association between IVs and specific exposures. Second, the MR analysis only examined causality, and further in-depth research is needed to elucidate the specific mechanisms by which oxidative stress increases the risk of glaucoma. In addition, the generalisability of the results to other ancestry groups may be limited because the MR analysis in this study was based on individuals of European ancestry. Future MR studies investigating the causal relationship between oxidative stress and glaucoma should consider diverse ethnic populations to increase the overall applicability of the findings.

5. Conclusions

In conclusion, the forward MR analysis performed in this study provides compelling evidence of a significant association between CAT and a reduced risk of POAG. In addition, the results establish a substantial causal relationship between glaucoma and retinol, while SOD and MPO show robust associations with the risk of PACG. In addition, the reverse MR analyses reveal remarkable associations, indicating that genetically predicted glaucoma is associated with reduced levels of TBIL, and PACG is associated with reduced levels of GPX and reduced activity of PON. Notably, this study also provides compelling evidence for a potential causal effect of POAG on albumin. Taken together, our study provides evidence for the role of oxidative stress in the development of glaucoma and sheds light on potential therapeutic targets for preventing or treating this sight-threatening disease. Further investigation of the causal pathways and clinical implications of these associations may ultimately lead to the development of novel glaucoma prevention and treatment interventions.

Data availability statement

Datasets analyzed in this study were publicly available from IEU OpenGWAS database (https://gwas.mrcieu.ac.uk/) and Supplementary material.

Ethics statement

This study only used published or publicly available data. Ethical approval for each study included in the investigation can be found in the original publications (including informed consent from each participant).

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CRediT authorship contribution statement

Ronghua Shi: Writing – original draft, Visualization, Methodology, Formal analysis, Data curation. **Yaxuan Wu:** Formal analysis. **He Chen:** Formal analysis. **Zicheng Zhang:** Investigation. **Siqi Bao:** Investigation. **Jia Qu:** Funding acquisition, Conceptualization. **Meng Zhou:** Writing – review & editing, Project administration, Conceptualization.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Abbreviations

OSIB	Oxidative stress injury biomarkers
GST	Glutathione S-transferase
CAT	Catalase
SOD	Superoxide dismutase
GPX	Glutathione peroxidase
MPO	Myeloperoxidase
PON	Paraoxonase
VC	Vitamin C
VE	Vitamin E
TBIL	Total bilirubin
POAG	Primary open-angle glaucoma
PACG	Primary angle-closure glaucoma
NTG	Normal tension glaucoma

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.heliyon.2024.e24852.

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