



Data Article

Retrospective case-control data of serum nitrotyrosine level and clinical biomedical indices in primary glaucoma patients

Yuan Lei^{a,b,1,*}, Yanting Gao^{c,1}, Maomao Song^{a,b,1}, Wenjun Cao^{d,*},
Xinghuai Sun^{a,b,e,*}

^a Department of Ophthalmology & Visual Science, Eye & ENT Hospital, Shanghai Medical College, Fudan University, Shanghai 200031, China

^b NHC Key Laboratory of Myopia (Fudan University), Key Laboratory of Myopia, Chinese Academy of Medical Science (Fudan University), and Shanghai Key Laboratory of Visual Impairment and Restoration (Fudan University), Shanghai 200031, China

^c Department of Laboratory Medicine, Shanghai General Hospital, Shanghai Jiao Tong University School of Medicine, Shanghai 200031, China

^d Department of Clinical Laboratory, Eye & ENT Hospital, Shanghai Medical College, Fudan University, Shanghai 200031, China

^e State Key Laboratory of Medical Neurobiology, Institutes of Brain Science and Collaborative Innovation Center for Brain Science, Fudan University, Shanghai 200031, China

ARTICLE INFO

Article history:

Received 13 April 2020

Revised 6 May 2020

Accepted 7 May 2020

Available online 16 May 2020

Keywords:

Nitrotyrosine

Glaucoma

Biochemical indices

ABSTRACT

From April to December 2017, the case-control data were collected in the Department of Ophthalmology & Visual Science, Eye & ENT Hospital, Fudan University. One hundred primary angle closure glaucoma (PACG), one hundred primary open angle glaucoma (POAG) patients and two hundred control participants were consecutively recruited. The serum nitrotyrosine (NT) levels was not significant different in PACG or POAG patients stratified by gender (1,868.17±427.13 nmol/L vs. 1,768.77±410.17 nmol/L, $p>0.05$; 1,734.04±460.74 vs. 1,696.46±405.73 nmol/L, $p>0.05$). Serum NT level was not significantly associated with glaucoma severity in either PACG group or POAG group based on mean deviation (MD) (mild, $n=30$; moderate, $n=24$; severe, $n=19$; blinding, $n=27$, $p>0.05$, in Table 3 for PACG; mild, $n=9$; moder-

* Corresponding authors.

E-mail addresses: lilian0167@hotmail.com (Y. Lei), wgkjk@aliyun.com (W. Cao), xhsun@shmu.edu.cn (X. Sun).

¹ These authors are contributed equally to this work.

ate, n=20; sever, n=21; blinding, n=40; $p > 0.05$, in Table 4 for POAG). Multivariable logistic regression analysis indicated that the risk of developing PACG were significantly associated with serum total triglyceride (TG) and uric acid (UA) levels (OR=1.638, 95%CI: 1.059-2.531, $p=0.026$ for TG, OR=0.003, 95%CI: 0-0.461, $p=0.024$ for UA). Serum TG, gamma-glutamyl transferase (GGT) and total bilirubin (TB) levels were significantly associated with POAG (OR=2.00, 95%CI: 1.363-2.934, $p < 0.001$ for TG; OR=0.972, 95%CI: 0.949-0.996, $p=0.022$ for GGT; OR=1.115, 95%CI: 1.042-1.194, $p=0.002$ for TB). Descriptions of the data are also available in our recent paper published in Nitric Oxide, "Peroxynitrite is a novel risk factor and treatment target of glaucoma" [1].

© 2020 Published by Elsevier Inc.

This is an open access article under the CC BY-NC-ND license. (<http://creativecommons.org/licenses/by-nc-nd/4.0/>)

Specifications Table

Subject	Ophthalmology
Specific subject area	Risk factor and treatment target in glaucoma
Type of data	Table, Figure
How data were acquired	Retrospective analysis of a case-control data
Data format	Raw and analyzed data
Parameters for data collection	According to the inclusion/ exclusion criteria
Description of data collection	The case-control data were conducted from April to December 2017 and 100 PACG, 100 POAG and 200 controls were consecutively recruited. Participants' ocular parameters were collected from the standardized ophthalmic examination; serum nitrotyrosine levels were measured by competitive ELISA kit and other serum biochemical indices were acquired by respective commercially available kits in Roche biochemical automatic analyzer.
Data source location	Eye & ENT Hospital, Fudan University, Shanghai, China
Data accessibility	With the article
Related research article	Yuan Lei, Yanting Gao, Maomao Song, Wenjun Cao, Xinghuai Sun, Peroxynitrite is a novel risk factor and treatment target of glaucoma, Nitric Oxide 99 (2020) 17-24. Doi: 10.1016/j.niox.2020.03.006.

Value of the Data

- The data are very important to the glaucoma and nitric oxide research community since a large set of clinical data from PACG and POAG patients are reported.
- The clinical data may be used by basic science researchers for further insights into the mechanism of action of peroxynitrite in glaucoma etiology.
- The clinical data can also be used to design further experimental models to understand how peroxynitrite contributes to ocular hypertension.

1. Data Description

From April to December 2017, the case-control data were collected in the Department of Ophthalmology & Visual Science, Eye & ENT Hospital, Fudan University. One hundred primary angle closure glaucoma (PACG), one hundred primary open angle glaucoma (POAG) patients and two hundred control participants were consecutively recruited.

Table 1

Baseline characteristics and nitrotyrosine level of primary angle-closure glaucoma patients stratified by gender

Demographic Parameters	Male (n=40)	Female (n=60)	p value
age, y	61.78±10.19	62.80±10.60	0.497
duration of disease, y	1.03±2.50	0.87±2.95	0.664
intraocular pressure, mmHg	23.57±11.15	20.44±12.32	0.040
mean deviation, dB	13.99±8.81	12.02±8.01	0.271
vertical cup-to-disc ratio	0.68±0.23	0.62±0.23	0.162
axial length, mm	22.57±0.95	22.19±0.82	0.005
central corneal thickness, µm	553.08±34.85	547.68±48.96	0.255
anterior chamber depth, mm	2.00±0.55	2.05±0.93	0.629
total triglyceride, mmol/L	1.53±0.98	1.58±1.00	0.825
total cholesterol, mmol/L	4.48±0.76	5.05±0.96	0.002
gamma-glutamyl transferase, U/L	27.60±19.34	19.17±10.30	0.010
uric acid, mmol/L	0.37±0.09	0.26±0.07	≤0.001
total bilirubin, µmol/L	14.80±8.18	10.77±4.96	0.060
nitrotyrosine, nmol/L	1,868.17±427.13	1,768.77±410.17	0.192

Data are showed as mean ± SD. Statistical methods used here are Independent Student's t-tests and Mann-Whitney U tests.

Table 2

Baseline characteristics and nitrotyrosine level of primary open angle glaucoma patients stratified by gender

Demographic Parameters	Male (n=59)	Female (n=41)	p value
age, y	51.42±16.91	52.20±14.94	0.798
duration of disease, y	2.85±3.39	2.59±4.43	0.289
intraocular pressure, mmHg	22.27±8.70	20.37±7.26	0.209
mean deviation, dB	17.96±8.83	12.60±9.07	0.004
vertical cup-to-disc ratio	0.85±0.12	0.77±0.15	0.008
axial length, mm	25.32±2.40	24.98±2.03	0.464
central corneal thickness, µm	542.17±40.27	530.48±30.67	0.255
anterior chamber depth, mm	2.98±0.64	2.85±0.50	0.206
total triglyceride, mmol/L	2.04±1.60	1.68±1.03	0.437
total cholesterol, mmol/L	4.54±0.80	4.99±1.03	0.022
gamma-glutamyl transferase, U/L	20.93±20.49	20.17±14.59	≤0.001
uric acid, mmol/L	0.37±0.09	0.28±0.74	≤0.001
total bilirubin, µmol/L	14.04±7.14	10.83±5.81	0.006
nitrotyrosine, nmol/L	1,734.04±460.74	1,696.46±405.73	0.716

Data are showed as mean ± SD. Statistical methods used here are Independent Student's t-tests and Mann-Whitney U tests.

Tables 1 and 2 listed baseline characteristics data and serum NT level in PACG or POAG patients stratified by gender. There was no difference in serum NT levels of PACG or POAG patients of different gender.

Tables 3 and 4 showed ocular parameters and serum NT level in PACG or POAG subjects stratified according to glaucoma severity. Based on MD, there was no significant difference regarding serum NT level with the severity of PACG or POAG (mild, n=30; moderate, n=24; severe, n=19; blinding, n=27; p>0.05, in Table 3 for PACG; mild, n=9; moderate, n=20; severe, n=21; blinding, n=40; p>0.05, in Table 4 for POAG).

Table 5 listed the methods and intra- and inter-assay coefficient of variations (CV).

Figs. 1 and 2 showed the association between age, gender, biochemical indices and PACG or POAG. Multivariable logistic regression analysis indicated that the risk of developing PACG were significantly associated with serum TG and UA levels (OR=1.638, 95%CI: 1.059-2.531, p=0.026 for TG, OR=0.003, 95%CI: 0-0.461, p=0.024 for UA). There was no association between age, gender,

Table 3

Ocular parameters and serum nitrotyrosine level of primary angle-closure glaucoma subjects, stratified according to glaucoma severity

Demographic Parameters	Mild(n=30)	Moderate(n=24)	Severe(n=19)	Blinding(n=27)	p value
age, y	60.07±10.12	63.33±8.65	64.00±10.68	63.00±11.96	0.402
duration of disease, y	0.80±2.09	1.42±4.14	0.84±2.58	0.70±2.03	0.760
intraocular pressure, mmHg	33.27±12.42	35.65±13.28	28.29±14.11	38.10±13.62	0.114
mean deviation, dB	3.64±1.68	9.03±2.03	16.07±2.77	24.05±2.11	≤0.001 ^a
vertical cup-to-disc ratio	0.53±0.17	0.56±0.19	0.65±0.23	0.84±0.17	≤0.001 ^b
axial length, mm	22.22±0.73	22.24±1.28	22.38±0.80	22.51±0.67	0.587
central corneal thickness, μm	547.93±32.25	560.52±55.69	548.53±59.09	543.48±29.72	0.832
anterior chamber depth, mm	2.08±0.81	1.82±0.61	2.08±1.05	2.13±0.75	0.558
nitrotyrosine, nmol/L	1,757.14±381.29	1,834.94±410.71	1,898.16±526.70	1,779.08±388.14	0.675

Data are showed as mean ± SD. Statistical methods used here are χ^2 tests, one-way ANOVA and Kruskal-Wallis tests.

^a $p < 0.001$ for the difference among all subgroups of PACG, except the difference between moderate subgroups and sever subgroups (Kruskal-Wallis test with the Bonferroni post hoc test).

^b $p < 0.001$ for the difference between blindness subgroup and mild, moderate or severe subgroup (Kruskal-Wallis test following Bonferroni post hoc test).

Table 4

Ocular parameters and serum nitrotyrosine level in primary open angle glaucoma subjects, stratified according to glaucoma severity

Demographic Parameters	Mild(n=19)	Moderate(n=20)	Severe(n=21)	Blinding(n=40)	p value
age, y	48.21±15.48	52.90±13.45	56.14±17.47	50.53±16.74	0.336
duration of disease, y	1.74±3.43	3.40±5.13	3.05±3.15	2.73±3.62	0.297
intraocular pressure, mmHg	27.14±12.88	30.96±11.09	29.93±15.07	26.22±6.93	0.484
mean deviation, dB	2.87±1.59	9.00±1.84	15.54±2.34	25.39±3.62	≤0.001 ^a
vertical cup-to-disc ratio	0.73±0.17	0.75±0.15	0.85±0.08	0.89±0.09	≤0.001 ^b
axial length, mm	24.80±1.64	25.43±2.56	25.23±1.96	25.20±2.51	0.862
central corneal thickness, μm	551.11±30.89	525.85±36.49	527.14±26.88	542.50±41.97	0.076
anterior chamber depth, mm	2.84±0.57	3.11±0.67	3.01±0.49	2.83±0.59	0.157
nitrotyrosine, nmol/L	1,654.99±392.08	1,777.71±482.61	1,779.46±359.50	1,687.40±477.47	0.535

Data are showed as mean ± SD. χ^2 test, one-way ANOVA and Kruskal-Wallis test were used.

^a $p < 0.001$ for the difference between mild subgroup and sever subgroup, between blinding subgroup and mild, moderate or severe subgroup (Kruskal-Wallis test with the Bonferroni post hoc test).

^b $p < 0.001$ for the difference between blindness subgroup and mild or moderate subgroup (Kruskal-Wallis test following Bonferroni post hoc test).

Table 5

Methods, intra- and inter-assay CV.

Biochemical indices	Method	Intra-assay CV (%)	Inter-assay CV (%)
total triglyceride, mmol/L	colorimetry	≤0.9	≤1.9
total cholestero, mmol/L	enzymatic colorimetry	≤0.6	≤1.6
gamma-glutamyl transferase, U/L	enzymatic colorimetry	≤3.3	≤3.7
uric acid, mmol/L	colorimetry	≤0.6	≤1.3
total bilirubi, μmol/L	diazotization	≤2.5	≤3.3

CV: coefficient of variations.

serum total cholesterol (TC), GGT, TB, total protein (TP) levels and PACG (Fig. 1). Serum TG, GGT, TB levels were significantly associated with POAG (OR=2.00, 95%CI: 1.363-2.934, $p < 0.001$ for TG; OR=0.972, 95%CI: 0.949-0.996, $p = 0.022$ for GGT; OR=1.115, 95%CI: 1.042-1.194, $p = 0.002$ for TB). There was no association between age, gender, serum TC, UA, TP levels and POAG (Fig. 2).

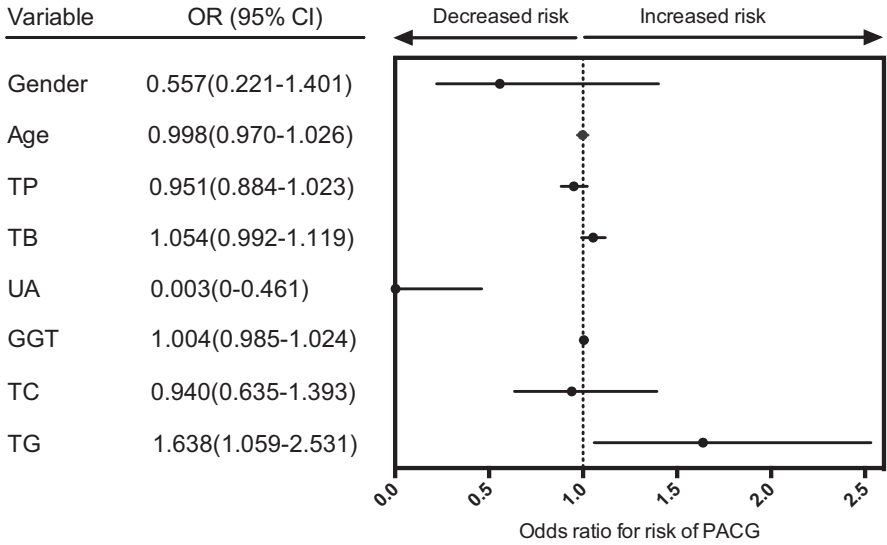


Fig. 1. Forest plot of the association between age, gender, biochemical indices and PACG. The overall OR displayed with black diamonds. 95% CI displayed with horizontal lines. No effect displayed in dashed vertical line (OR=1.0). PACG: primary angle closure glaucoma, CI: confidence interval, TG: total triglyceride, TC: total cholesterol, GGT: gamma-glutamyl transferase, UA: uric acid, TB: total bilirubin, TP: total protein.

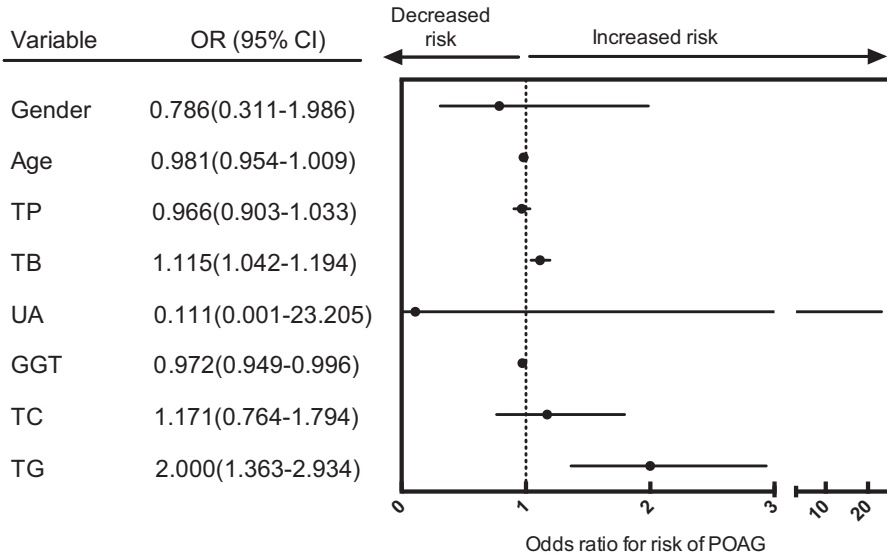


Fig. 2. Forest plot of the association between age, gender, biochemical indices and POAG. The overall OR displayed with black diamonds. 95% CI displayed with horizontal lines. No effect displayed in dashed vertical line (OR=1.0). POAG: primary open angle glaucoma, CI: confidence interval, TG: total triglyceride, TC: total cholesterol, GGT: gamma-glutamyl transferase, UA: uric acid, TB: total bilirubin, TP: total protein.

2. Experimental Design, Materials, and Methods

2.1. Participants

PACG patients (n=100) and POAG patients (n=100) were consecutively recruited from the Department of Ophthalmology & Visual Science, Eye & ENT Hospital, Fudan University between April 2017 and December 2017. Subjects participated in annual health screenings during this period were consecutively recruited as normal controls (n=200).

Each PACG or POAG patient accepted a standardized ophthalmic examination performed by glaucoma specialists. Those included assessments of slit-lamp biomicroscopy, refractive status, fundus examination, gonioscopy, intraocular pressure (IOP), axial length (AL), central corneal thickness (CCT), anterior chamber depth (ACD) and visual field (VF) examination. An automated perimeter (Octopus; Haag-Streit AG, Koeniz, Switzerland) was used to measure mean deviation (MD). A Goldmann applanation tonometry was used to measure IOP. A retinal camera (TRC-NW200, Topcon Corp., Tokyo, Japan) was used to acquire Fundus photography. AL, ACD, and CCT were acquired by A-scan ultrasound (A-Scan Pachymeter; Ultrasonic, Exton, PA, USA). Each normal control also accepted a basic ophthalmic examination by an expert ophthalmologist. Those included assessments of slit-lamp biomicroscopy, refractive status, and fundus examination. We chose data from the right eye even if both eyes of the patents diagnosed with glaucoma.

2.2. Inclusion/exclusion criteria of PACG and POAG

PACG subjects: 1) Age \geq 18 years old; 2) IOP $>$ 21 mmHg; 3) at least 180 degrees of iridotrabecular contact; 4) glaucomatous optic neuropathy with vertical cup-to-disc ratio (VCDR) \geq 0.7; 5) peripheral visual loss; 6) exclude secondary causes of glaucoma; 7) exclude other eye disorders (besides senile cataracts); 8) exclude infectious or systemic diseases such as hyperuricemia, diabetes, cardiac, acute or chronic inflammation, autoimmune disease, and cancer.

PACG can be classified according to the timing or suddenness of onset into acute PACG (APACG) or chronic PACG (CPACG) [2]. APACG, a severe type, was defined as 1) IOP $>$ 28 mmHg; 2) at least two of those symptoms: nausea, vomiting, ocular or periocular pain, or antecedent history of intermittent blurring of vision; and 3) at least three of those signs: corneal epithelial edema, conjunctival injection, shallow anterior chamber or mid-dilated nonreactive pupil. CPACG, also a severe type, diagnosed according to the PACG criteria listed above with no acute signs or symptoms. Subjects who received glaucoma medications were included too. We chose data from the right eye even if both eyes of the patents diagnosed with glaucoma. Patients can be divided into four subgroups based on perimetry, i.e., mild (MD \leq 6 dB), moderate (12 dB \geq MD $>$ 6 dB), severe (20 dB \geq MD $>$ 12 dB) and blinding (MD $>$ 20 dB) [3].

POAG subjects: 1) Age \geq 18 years old; 2) IOP $>$ 21 mmHg; 3) glaucomatous optic neuropathy with at least two of the following characteristics: VCDR \geq 0.7 in either eye, VCDR asymmetry \geq 0.2, diffuse or focal neural rim thinning, an optic disc hemorrhage, a notch and nerve fiber layer defect; 4) corresponding VF defect; 5) a normal anterior chamber and open angle; 6) exclude other eye disorders (besides senile cataracts); 7) exclude infectious or systemic diseases such as hyperuricemia, diabetes, cardiac, acute or chronic inflammation, autoimmune disease, and cancer.

Subjects who received glaucoma medications were included too. We chose data from the right eye even if both eyes of the patents diagnosed with glaucoma. Four subgroups of POAG patients generated with the same methods used in PACG.

2.3. Inclusion/ exclusion criteria of the control group

1) Age \geq 18 years old. 2) The controls had normal physical and ocular examination data, no positive family history of glaucoma, and no infection or systemic diseases such as acute or

chronic inflammation, cardiovascular diseases, hyperuricemia, diabetes mellitus, autoimmune disease, and cancer. 3) All normal controls were randomly divided into two groups (n=100 per group), which were age-matched and gender-matched to PACG group and POAG group, respectively.

2.4. Biochemical measurement

Blood samples were obtained from subjects having fasted for 8 hours in the morning, which collected from the anterior elbow veins of the participants via anticoagulant tube. For complete clot formation, tubes were put in an vertical position for 30 min at room temperature, and then tubes were centrifuged at 2593g for 10 minutes. Then serum samples were collected and stored at -80°C within an hour. Serum levels of TG, TC, GGT, UA, TB and TP were obtained using respective commercially available kits (Roche Diagnostics GmbH, Mannheim, Germany). Table 5 listed the detection method and inter- and intra-assay CVs of those biochemical indices guided by the manufacturer. Further, we analyzed internal controls daily over the 3 years. The results showed that there was no significant changes of the values with typical monthly CVs of 2% to 4%.

2.5. Measurement of NT

Using competitive ELISA kits (Hycult Biotechnology b.v., Uden, The Netherlands), serum NT levels were measured following the manufacturer's instructions. The intensities of the color of the samples were detected at 450nm using an automatic microplate reader. The intra- and inter-assay CVs here were <10% respectively.

3. Statistical analysis

Data were analyzed using SPSS for Windows version 24.0 software (SPSS, Chicago, IL, USA). Independent Student's t-test and Mann-Whitney U test were used to compare the baseline characteristics and NT level in PACG or POAG patients stratified by gender (Table 1,2). The χ^2 test, one-way ANOVA and Kruskal-Wallis test followed by Bonferroni multiple comparison test were used to compare ocular parameters and serum NT levels in PACG or POAG subjects stratified by glaucoma severity (Table 3,4). The association between age, gender, biochemical indices and PACG or POAG was analyzed by multivariable logistic regression analysis (Fig. 1,2). In all cases, a P-value <0.05 was considered to be statistically significant.

Acknowledgments

Supported by Shanghai Clinical Medical Center of Ocular Disease (2017ZZ01020, XHS, China), State Key Program of National Natural Science Foundation of China (81430007, XHS, China), the Funds for International Cooperation of Ministry of Science and Technology (2015DFA31340, XHS, China), National Natural Science Foundation China (81100662, 81371015, YL, China), BrightFocus Foundation (G2018112, YL, USA), the 211 Project of Fudan University (EHF158351, YL, China), Young Scientists Program of EENT Hospital of Fudan University (YL, China).

Conflict of interest

The authors declare that they have no known competing financial interests or personal relationships which have, or could be perceived to have, influenced the work reported in this article.

Supplementary material

Supplementary material associated with this article can be found, in the online version, at doi:[10.1016/j.dib.2020.105706](https://doi.org/10.1016/j.dib.2020.105706).

References

- [1] Y. Lei, Y. Gao, M. Song, W. Cao, X. Sun, Peroxynitrite is a novel risk factor and treatment target of glaucoma, *Nitric Oxide* 99 (2020) 17–24.
- [2] X. Sun, Y. Dai, Y. Chen, D.Y. Yu, S.J. Cringle, J. Chen, X. Kong, X. Wang, C. Jiang, Primary angle closure glaucoma: What we know and what we don't know, *Prog Retin Eye Res* 57 (2017) 26–45.
- [3] P. Brusini, S. Filacorda, Enhanced Glaucoma Staging System (GSS 2) for classifying functional damage in glaucoma, *J Glaucoma* 15 (2006) 40–46.