

Study of Neutrophil-To-Lymphocyte Ratio and its Correlation with Glycemic Status in Diabetic Senile Cataract Patients

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ABSTRACT

Background Systemic inflammation is associated with cataractogenesis in diabetes remains controversial. Recently, Neutrophil-to-Lymphocyte Ratio (NLR) is used as a reliable biomarker for inflammation in various diseases. However, the NLR also act as risk factor in the pathogenesis of diabetic senile cataract is still unknown.

Objectives The objective of the current study is to investigate NLR and other hematological parameter levels and to find out any association with diabetic senile cataract compared to normal healthy individuals without cataract.

Subjects and methods This case-control study consists of 100 type 2 DM patient with senile cataract (cases) and 100 normal healthy individuals without cataract (control) in the age group from 40 to 75 years of both genders. Complete blood count indices were estimated by autoanalyzer and NLR was calculated by dividing the neutrophil count by lymphocyte count.

Results The present study shows significantly increased NLR and Absolute Neutrophil Count (ANC) levels and decreased level of Absolute Lymphocyte Count (ALC) in diabetic senile cataracts when compared to normal healthy individuals without cataract. A significant positive correlation of HbA1c with NLR and ANC were observed. Multiple linear regression analysis showed significantly positive influence of NLR with respect to HbA1c.

Conclusion NLR levels are increased in diabetic senile cataracts which indicate that systemic inflammation also plays an important role in the early development of cataract formation and act as risk factor of diabetic senile cataract.

Keywords

Neutrophil-to-Lymphocyte Ratio, Senile Cataract, Diabetic Senile cataract

Introduction

Cataract is a major cause of visual impairment and could be considered as an earliest complication of diabetes mellitus. Cataractogenesis is much faster and earlier in diabetic patients than non-diabetics. [1–4]. The systemic inflammation may play a role in the pathogenesis of age-related cataract. [5]. Literatures have reported an increase in the inflammatory markers levels such as C-reactive protein (CRP), interleukin (IL)-1, IL-6 and tumor necrosis factor (TNF)-alpha in diabetes mellitus patients. [3,4]

Recently, Neutrophil-to-lymphocyte ratio (NLR) has emerged as a new inflammatory biomarkers of T2DM. [6–8] This index is a rapid, easy and cost-effective method which is a calculated index derived from a routine complete blood count test in clinical practice.[9]

The NLR was yet to study in the pathogenesis of diabetes induced senile cataract. The present study was designed to evaluate NLR and other hematological parameters in Type 2 diabetes with senile cataract patients and compared to normal healthy individuals without cataract.

Materials and methods

This case-control study population consisted of 100 Type 2 DM patients with senile cataract (Group I) as cases and 100 age and gender matched normal healthy individuals without cataract (Group II) as controls. The study was conducted between March 2017 to April 2018 in the Department of Biochemistry in collaboration with Department of Ophthalmology in a tertiary care hospital. The study protocol was approved by the Institutional Human Ethics Committee. Informed consent form was obtained from all participants. The cataract was confirmed by using slit-lamp examination and purely nuclear type of cataract was included according to lens opacities classification system III by ophthalmologist.

Inclusion criteria Type 2 Diabetes mellitus patients having more than 5 years of duration who are under treatment of oral hypoglycemic drugs with senile cataract and the healthy controls without cataracts were recruited from the hospital who came for health check-up having without any eye disease, and the exclusion criteria were the same as for the cataract group were included in this study.

Exclusion criteria Subjects who had history of cardiovascular disease, renal dysfunction, hepatic disease, traumatic or toxic cataract, and other systemic diseases were excluded from the study.

Sample collection and processing

5 ml of venous fasting blood sample was drawn from the patient and collected in EDTA and sodium fluoride-Potassium oxalate anticoagulant vacutainers. Estimation of plasma glucose done by hexokinase method using Beckman Coulter Olympus AU400 auto-analyzer. Whole blood was used for the estimation of glycated hemoglobin (HbA1c) by HPCL method using Biorad D10 HbA1c analyser and the complete blood count such as Hb (hemoglobin), RBC count, Total WBC count, PCV (packed cell volume), MCV (Mean red cell corpuscular volume), MCHC (Mean corpuscular hemoglobin concentration) of patients were measured using a Horiba-Pentra DF Nexus automated hematology analyzer. NLR was calculated as ratio between the absolute neutrophil counts (ANC) by absolute lymphocyte counts (ALC).

Data Analysis The present study results were expressed as mean \pm standard deviation (SD) for normal distribution and abnormal distribution were expressed as Median and interquartile ranges. Data was analysed using JASP 8.4. The Shapiro-Wilk test was used to check the normal distribution for the variables and the statistical significant differences between groups were

analysed using the Student's t-test and the Mann-Whitney U-test. Spearman's correlation coefficient (ρ) was used to assess the association between the variables. Multiple regression analysis was performed to assess independent relationship between glycemic status and inflammation. A p value of ≤ 0.05 was considered as statistically significant.

Results

Table 1 shows glycemic status between diabetic senile cataracts and Normal healthy individuals without cataract. There was no significant difference was observed in age group between group I (59 ± 08) and group II (60 ± 08), $p=0.625$. Mean fasting plasma glucose and HbA1c levels were significantly elevated in group I [$132(99,190)$, $7.8(6.4, 10.2)$], $p<.001$ when compared to group II [90 ± 15 , 5.5 ± 0.5]

In type 2 diabetes with senile cataract patients, mean NLR [$2.09(1.72,3.23)$, $p=0.019$], and ANC [$4.83(4.04,5.89)$, $p<.001$] levels were significantly increased whereas mean Hb [(10.26 ± 1.78) , $p<.001$], RBC[(4.08 ± 0.55) $p<.001$], MCHC[$(30.65)p<.001$], MCV[$(87(82,90)$ $p<.001$], Hematocrit [$(30.77 \pm 5.35)p<.001$]and ALC[$(2.24 \pm 0.92)p<.001$] levels were significantly decreased when compared to Normal healthy individuals without cataract. However, there were no significant differences observed for Total WBC count, Platelet, MCH, and PCV between two groups as shown in table 2.

Spearman's correlation analysis showed a significant negative correlation of HbA1C with Hb ($r=-0.144$), RBC($r=-0.329$), MCHC($r=-0.367$), MCV ($r=-0.288$), Hematocrit($r=-0.144$), ALC($r=-0.236$) and positive correlation of HbA1C with NLR($r=0.329$), PLR($r=0.209$), ANC($r=0.172$). In addition, there was a significant positive correlation of FBS with NLR($r=0.274$), ANC($r=0.162$), and negative correlation of FBS with RBC($r=-0.296$), MCHC($r=-0.242$), ALC($r=-0.165$) respectively as shown in table 3 and 4. Table 5 represent the results of Multiple linear regression analysis which showed significantly positive influence of NLR ($p=0.016$) and total WBC count ($p=0.039$) with respect to HbA1c.

Table 1: Glycemic status of group I and group II

Parameters	Group I - Type 2 DM patients with cataract (n=100)	Group II- Normal healthy individuals without cataract (n=100)	p Value
	Mean (Min, Max)	Mean \pm SD	
Fasting plasma glucose (mg/dL)	132(99,190)	90 \pm 15	<.001*
HbA1c (%)	7.8(6.4,10.2)	5.5 \pm 0.5	<.001*

* $p<0.05$ significant

Table 2: Comparison of Hematology indices between Group I and Group II

Parameters	Group I - Type 2 DM patients with cataract (n=100)	Group II - Normal healthy individuals without cataract (n=100)	p Value
Hb (g/dl)	10.26 ± 1.78	11.09 ± 1.67	<.001*
RBC count (million/cumm)	4.08 ± 0.55	4.65 ± 0.53	<.001*
Total WBC count (10 ⁹ /L)	8.20(7,9.9)	8.12 ± 1.73	0.177
Platelet (10 ⁹ /L)	275.10 ± 76.20	280(235.5,319.8)	0.740
MCH(pg)	27.55(27.23,28.77)	27.68 ± 2.85	0.243
MCHC(%)	30.65(30.52,31)	31.65(32.29,34)	< .001*
MCV(fl/cell)	87(82,90)	90(85,93)	< .001*
Hematocrit(%)	30.77 ± 5.35	33.26 ± 5.01	< .001*
PCV(%)	36.28 ± 4.97	36.27 ± 5.06	0.991
ANC (10 ⁹ /L)	4.83(4.04,5.89)	4.37(3.44,5.2)	< .001*
ALC (10 ⁹ /L)	2.24 ± 0.92	2.88 ± 0.85	< .001*
NLR	2.09(1.72,3.23)	1.5(1.23,1.9)	0.019*

* p<0.05 significant

Table 3: Association of Hematology indices and NLR with HbA1c

Parameter	HbA1C (rho Value)	p Value
Hb	-0.144	0.04*
RBC	-0.329	<0.001*
MCHC	-0.367	<0.001*
MCV	-0.288	<0.001*
Hematocrit	-0.144	0.04*
ANL	0.172	0.02*
ALC	-0.236	<0.001*
NLR	0.329	<0.001*

* p<0.05 significant

Table 4: Association of Hematology indices and NLR with fasting plasma glucose

Parameter	FBS (rho Value)	p Value
RBC count	-0.296	<0.001*
MCHC	-0.242	<0.001*
ALC	-0.165	0.019*
NLR	0.274	<0.001*
ANC	0.162	0.022*
ANL	0.172	0.02*
ALC	-0.236	<0.001*
NLR	0.329	<0.001*

* p<0.05 significant,

Table 5: Multiple linear regression analysis for Normal healthy individuals without cataract and diabetic senile cataract patients (Dependent variable: HbA1c)

Model	Coefficients			t	p Value
	Unstandardized coefficients B	Standard error	Standardized coefficients β		
NLR	0.063	0.026	0.170	2.438	0.016*
Total WBC count	0.173	0.083	0.145	2.080	0.039*

* P≤0.05 significant,

Discussions

Cataract is the leading cause of visual impairment in diabetes mellitus patients.[10] Inflammation is closely associated with insulin-resistance, because excess fat tissue producing pro-inflammatory adipokines results in low-grade chronic inflammation, impairing tissue response to insulin and leads to type 2 diabetes mellitus (T2DM).[11,12]

Although several inflammatory markers are available, NLR has been recently used as simple, inexpensive and novel inflammatory biomarker in chronic diseases, as well as prognostic predictors in cancer and cardiovascular disease.[13–17]

NLR is associated with diabetes and its complications.[18–22] The NLR level was significantly elevated in type 2 DM with cataract subjects when compared to normal healthy individuals without cataracts. Few studies have reported that NLR level was significantly elevated in type 2 DM patients with retinopathy compared to diabetes without retinopathy and healthy control subjects. [23–25] Another study have also shown that NLR was significantly higher in type 2 diabetic patients with nephropathy than those of diabetic patients without any microvascular complications and healthy control subjects.[22,26] NLR was increased in patients with diabetes and linked to poor glycemic control, insulin resistance and cardiovascular events.[7,23,24,27–29]

In our study, there was significantly positive correlation of HbA1C with NLR and in addition, multiple linear regression analysis showed that a significantly positive influence of NLR with respect to HbA1c in diabetes patients with cataract which indicates that NLR was an independent risk factor for diabetes induced cataract. Our results were consistent with the results studies done by Sefil et al., which showed that NLR was positively correlated with HbA1c levels in diabetes patient.[7] Although no literatures are available with reference to NLR levels in cataract subjects, our findings were supported with these reports.

In this present study, the Absolute neutrophil count (ANC) was significantly higher in diabetes with cataract patients than those of Normal healthy individuals without cataract which indicate that systemic inflammation is associated with cataractogenesis and neutrophil-mediated inflammation may play a significant role in the pathogenesis of diabetes induced cataract. Our results were in accordance with the study done by Woo et al, which revealed that elevated neutrophil count is associated with the severity of diabetic retinopathy.[33]

Waggiallah H et al, reported that significantly decrease in hemoglobin, RBCs, MCHC and MCH level in diabetes compared with controls.[27] Irace et al, showed mean hemoglobin, hematocrit and whole blood viscosity were significantly decreased in diabetic retinopathy compared with subjects without micro vascular complication, retinopathy.[28]

Similar results were observed in our study that, in diabetic cataract patients, mean hemoglobin, RBCs, MCHC, Hematocrit and MCV were significantly lower than in normal healthy individuals without cataract. This indicates that type 2 diabetes with cataract patients were more prone for anemia.

In the present study, absolute lymphocyte count was significantly decreased in diabetes with cataract patients compared to normal healthy individuals without cataract. Our results were in accordance with Okorie hope et al., which showed that Lymphocyte count was significantly reduced in gestational diabetic women when compared to controls. [29] The decrease in lymphocyte count might be due to glucose toxicity which affects the proliferation of the T and B lymphocyte cells.[34].

Conclusion

The current study indicates that hyperglycemia causes increased NLR level, a biomarker of systemic inflammation which also act as risk factor, play a significant role in the pathogenesis of diabetic senile cataracts.

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References

- [1] Klein, B.E.K., Klein, R. and Moss, S.E. (1995) Incidence of Cataract Surgery in the Wisconsin Epidemiologic Study of Diabetic Retinopathy. *American Journal of Ophthalmology*, **119**, 295–300. [https://doi.org/10.1016/S0002-9394\(14\)71170-5](https://doi.org/10.1016/S0002-9394(14)71170-5)
- [2] Kato, S., Oshika, T., Numaga, J., Kawashima, H., Kitano, S. and Kaiya, T. (2000) Influence of rapid glycemic control on lens opacity in patients with diabetes mellitus. *American Journal of Ophthalmology*, **130**, 354–5. [https://doi.org/10.1016/s0002-9394\(00\)00546-8](https://doi.org/10.1016/s0002-9394(00)00546-8)
- [3] de Rooij, S.R., Nijpels, G., Nilsson, P.M., Nolan, J.J., Gabriel, R., Bobbioni-Harsch, E. et al. (2009) Low-grade chronic inflammation in the relationship between insulin sensitivity and cardiovascular disease (RISC) population: associations with insulin resistance and cardiometabolic risk profile. *Diabetes Care*, **32**, 1295–301. <https://doi.org/10.2337/dc08-1795>
- [4] Garcia, C., Feve, B., Ferré, P., Halimi, S., Baizri, H., Bordier, L. et al. (2010) Diabetes and inflammation: fundamental aspects and clinical implications. *Diabetes & Metabolism*, **36**, 327–38. <https://doi.org/10.1016/j.diabet.2010.07.001>
- [5] Schaumberg, D.A., Ridker, P.M., Glynn, R.J., Christen, W.G., Dana, M.R. and Hennekens, C.H. (1999) High levels of plasma C-reactive protein and future risk of age-related cataract. *Annals of Epidemiology*, **9**, 166–71. [https://doi.org/10.1016/s1047-2797\(98\)00049-0](https://doi.org/10.1016/s1047-2797(98)00049-0)
- [6] Imtiaz, F., Shafique, K., Mirza, S.S., Ayoob, Z., Vart, P. and Rao, S. (2012) Neutrophil lymphocyte ratio as a measure of systemic inflammation in prevalent chronic diseases in Asian population. *International Archives of Medicine*, **5**, 2. <https://doi.org/10.1186/1755-7682-5-2>
- [7] Sefil, F., Ulutas, K.T., Dokuyucu, R., Sumbul, A.T., Yengil, E., Yagiz, A.E. et al. (2014) Investigation of neutrophil lymphocyte ratio and blood glucose regulation in patients with type 2 diabetes mellitus. *The Journal of International Medical Research*, **42**, 581–8. <https://doi.org/10.1177/0300060513516944>
- [8] İlgün, E., Akyürek, Ö., Kalkan, A.O., Demir, F., Demirayak, M. and Bilgi, M. (2016) Neutrophil/Lymphocyte Ratio and Platelet/Lymphocyte Ratio in Fibromyalgia. *Electronic Journal of General Medicine*, **13**, 100–4. <https://doi.org/10.15197/ejgm.1525>
- [9] Taylan, M., Demir, M., Kaya, H., Selimoglu Sen, H., Abakay, O., Carkanat, A.İ. et al. (2017) Alterations of the neutrophil-lymphocyte ratio during the period of stable and acute exacerbation of chronic obstructive pulmonary disease patients. *The Clinical Respiratory Journal*, **11**, 311–7. <https://doi.org/10.1111/crj.12336>
- [10] Harding, J.J., Egerton, M., van Heyningen, R. and Harding, R.S. (1993) Diabetes, glaucoma, sex, and cataract: analysis of combined data from two case control studies. *The British Journal of Ophthalmology*, **77**, 2–6.
- [11] Shoelson, S.E., Lee, J. and Goldfine, A.B. (2006) Inflammation and insulin resistance. *The Journal of Clinical Investigation*, **116**, 1793–801. <https://doi.org/10.1172/JCI29069>
- [12] Goldberg, R.B. (2009) Cytokine and cytokine-like inflammation markers, endothelial dysfunction, and imbalanced coagulation in development of diabetes and its complications. *The Journal of Clinical Endocrinology and Metabolism*, **94**, 3171–82.

- <https://doi.org/10.1210/jc.2008-2534>
- [13] Kim, B.-J., Cho, S.-H., Cho, K.-I., Kim, H.-S., Heo, J.-H. and Cha, T.-J. (2016) The Combined Impact of Neutrophil-to-Lymphocyte Ratio and Type 2 Diabetic Mellitus on Significant Coronary Artery Disease and Carotid Artery Atherosclerosis. *Journal of Cardiovascular Ultrasound*, **24**, 115–22. <https://doi.org/10.4250/jcu.2016.24.2.115>
- [14] Urrejola, G.I., Bambs, C.E., Espinoza, M.A., Gellona, J., Zúñiga, Á.M., Molina, M.E. et al. (2013) Un índice neutrófilo/linfocito elevado se asocia a peor pronóstico en cáncer de colon etapa II resecado. *Revista Médica de Chile*, **141**, 602–8. <https://doi.org/10.4067/S0034-98872013000500008>
- [15] Rudiger, A., Burckhardt, O.A., Harpes, P., Müller, S.A. and Follath, F. (2006) The relative lymphocyte count on hospital admission is a risk factor for long-term mortality in patients with acute heart failure. *The American Journal of Emergency Medicine*, **24**, 451–4. <https://doi.org/10.1016/j.ajem.2005.10.010>
- [16] Tamhane, U.U., Aneja, S., Montgomery, D., Rogers, E.-K., Eagle, K.A. and Gurm, H.S. (2008) Association between admission neutrophil to lymphocyte ratio and outcomes in patients with acute coronary syndrome. *The American Journal of Cardiology*, **102**, 653–7. <https://doi.org/10.1016/j.amjcard.2008.05.006>
- [17] Yamanaka, T., Matsumoto, S., Teramukai, S., Ishiwata, R., Nagai, Y. and Fukushima, M. (2007) The baseline ratio of neutrophils to lymphocytes is associated with patient prognosis in advanced gastric cancer. *Oncology*, **73**, 215–20. <https://doi.org/10.1159/000127412>
- [18] Akbas, E.M., Demirtas, L., Ozcicek, A., Timuroglu, A., Bakirci, E.M., Hamur, H. et al. (2014) Association of epicardial adipose tissue, neutrophil-to-lymphocyte ratio and platelet-to-lymphocyte ratio with diabetic nephropathy. *International Journal of Clinical and Experimental Medicine*, **7**, 1794–801.
- [19] Shiny, A., Bibin, Y.S., Shanthirani, C.S., Regin, B.S., Anjana, R.M., Balasubramanyam, M. et al. (2014) Association of neutrophil-lymphocyte ratio with glucose intolerance: an indicator of systemic inflammation in patients with type 2 diabetes. *Diabetes Technology & Therapeutics*, **16**, 524–30. <https://doi.org/10.1089/dia.2013.0264>
- [20] Lou, M., Luo, P., Tang, R., Peng, Y., Yu, S., Huang, W. et al. (2015) Relationship between neutrophil-lymphocyte ratio and insulin resistance in newly diagnosed type 2 diabetes mellitus patients. *BMC Endocrine Disorders*, **15**, 9. <https://doi.org/10.1186/s12902-015-0002-9>
- [21] Yue, S., Zhang, J., Wu, J., Teng, W., Liu, L. and Chen, L. (2015) Use of the Monocyte-to-Lymphocyte Ratio to Predict Diabetic Retinopathy. *International Journal of Environmental Research and Public Health*, **12**, 10009–19. <https://doi.org/10.3390/ijerph120810009>
- [22] Huang, W., Huang, J., Liu, Q., Lin, F., He, Z., Zeng, Z. et al. (2015) Neutrophil-lymphocyte ratio is a reliable predictive marker for early-stage diabetic nephropathy. *Clinical Endocrinology*, **82**, 229–33. <https://doi.org/10.1111/cen.12576>
- [23] Ulu, S.M., Dogan, M., Ahsen, A., Altug, A., Demir, K., Acartürk, G. et al. (2013) Neutrophil-to-lymphocyte ratio as a quick and reliable predictive marker to diagnose the severity of diabetic retinopathy. *Diabetes Technology & Therapeutics*, **15**, 942–7. <https://doi.org/10.1089/dia.2013.0097>
- [24] Wang, R., Zhang, J., Li, Y., Liu, T. and Yu, K. (2015) Neutrophil–Lymphocyte ratio is associated with arterial stiffness in diabetic retinopathy in type 2 diabetes. *Journal of Diabetes and Its Complications*, **29**, 245–9. <https://doi.org/10.1016/j.jdiacomp.2014.11.006>
- [25] Verdoia, M., Schaffer, A., Barbieri, L., Aimaretti, G., Marino, P., Sinigaglia, F. et al. (2015)

- Impact of diabetes on neutrophil-to-lymphocyte ratio and its relationship to coronary artery disease. *Diabetes & Metabolism*, **41**, 304–11. <https://doi.org/10.1016/j.diabet.2015.01.001>
- [26] Moursy, E.Y., Megallaa, M.H., Mouftah, R.F.H. and Ahmed, S. (2015) Relationship Between Neutrophil-Lymphocyte Ratio and Microvascular Complications in Egyptian Patients with Type 2 Diabetes. <https://doi.org/10.11648/j.ajim.20150306.16>
- [27] Waggiallah, H. and Alzohairy, M. (2011) The effect of oxidative stress on human red cells glutathione peroxidase, glutathione reductase level, and prevalence of anemia among diabetics. *North American Journal of Medical Sciences*, **3**, 344–7. <https://doi.org/10.4297/najms.2011.3344>
- [28] Irace, C., Scarinci, F., Scoria, V., Bruzzichessi, D., Fiorentino, R., Randazzo, G. et al. (2011) Association among low whole blood viscosity, haematocrit, haemoglobin and diabetic retinopathy in subjects with type 2 diabetes. *The British Journal of Ophthalmology*, **95**, 94–8. <https://doi.org/10.1136/bjo.2009.172601>
- [29] Hope, O., Ifeanyi, O.E. and N, A.Q.B. (2019) Investigation of Some Haematological Parameters in Pregnant Women with Gestational Diabetes at Federal Medical Center, Owerri, Imo State, Nigeria. *Annals of Clinical and Laboratory Research*, **7**.
- [30] Guo, X., Zhang, S., Zhang, Q., Liu, L., Wu, H., Du, H. et al. (2015) Neutrophil:lymphocyte ratio is positively related to type 2 diabetes in a large-scale adult population: a Tianjin Chronic Low-Grade Systemic Inflammation and Health cohort study. *European Journal of Endocrinology*, **173**, 217–25. <https://doi.org/10.1530/EJE-15-0176>
- [31] Oh, Y., Kwon, G.C., Koo, S.H. and Kim, J. (2016) Association between Glycemic Control and Hematologic Indices in Type 2 Diabetic Patients. *Laboratory Medicine Online*, **6**, 134. <https://doi.org/10.3343/lmo.2016.6.3.134>
- [32] Demirtas, L., Degirmenci, H., Akbas, E.M., Ozcicek, A., Timuroglu, A., Gurel, A. et al. (2015) Association of hematological indices with diabetes, impaired glucose regulation and microvascular complications of diabetes. *International Journal of Clinical and Experimental Medicine*, **8**, 11420–7.
- [33] Woo, S.J., Ahn, S.J., Ahn, J., Park, K.H. and Lee, K. (2011) Elevated systemic neutrophil count in diabetic retinopathy and diabetes: a hospital-based cross-sectional study of 30,793 Korean subjects. *Investigative Ophthalmology & Visual Science*, **52**, 7697–703. <https://doi.org/10.1167/iovs.11-7784>
- [34] Twig, G., Afek, A., Shamiss, A., Derazne, E., Tzur, D., Gordon, B. et al. (2013) White blood cells count and incidence of type 2 diabetes in young men. *Diabetes Care*, **36**, 276–82. <https://doi.org/10.2337/dc11-2298>