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The association between vitiligo and diabetes mellitus: A systematic review and meta-analysis

To the Editor: Vitiligo is an acquired disorder of depigmentation resulting from a loss of cutaneous melanocytes.[1] Aside from cosmetic concerns, many genetic and epidemiology studies have demonstrated an association of vitiligo with several comorbid systemic diseases.[2] Diabetes mellitus (DM) is a chronic disease featuring an impaired ability to process blood sugar. The prevalence of DM is increasing throughout the world, and its complications are associated with substantial morbidity and mortality.[3] To our knowledge, no large quantitative study has evaluated the association between vitiligo and DM; we therefore conducted this meta-analysis.

We identified all studies published before February 28, 2019, and included case-control studies describing the prevalence of DM in vitiligo patients and controls or the prevalence of vitiligo in DM patients and controls. Review articles, case series, and conference abstracts were excluded. The quality of each study was evaluated by using the Newcastle-Ottawa scale. A random effects model was used for the meta-analysis. Odds ratios (ORs) with 95% confidence intervals (CIs) were used to compare the prevalence of DM in patients with vitiligo and controls. Subgroup analyses were performed according to the type of DM (type 1, type 2, or mixed). Heterogeneity across studies was assessed using the χ^2 statistic and I^2 statistic, and the risk of publication bias was assessed using the Egger test. All analyses were performed with Comprehensive Meta Analysis version 3 (Biostat, Englewood, NJ).

Nine studies with a total of 15,657 vitiligo patients met the inclusion criteria. A summary of the characteristics of included studies is shown in Table I. Seven studies reported the prevalence of DM (5 with mixed-type DM and 2 with type 1 DM) among vitiligo patients, and 2 studies reported the prevalence of vitiligo among type 2 DM patients. The pooled estimate of 9 studies showed that vitiligo was significantly associated with DM (OR 2.515, 95% CI 1.972-3.208; $P < .001$; Fig 1). The subgroup analysis showed that vitiligo was significantly associated with type 1 DM (OR 2.899, 95% CI 1.532-5.482; $P = .001$) and also type 2 DM (OR 2.371, 95% CI 1.712-3.283; $P < .001$; Fig 1). No significant publication bias was noted ($P = .66654$), and a leave-1-out sensitivity analysis also confirmed the robustness of our findings.

The significant correlation between vitiligo and type 1 DM might result from a similar pathogenesis of autoreactive cytotoxic T-cell–mediated destruction in both diseases.[1,4] Current results also showed that type 2 DM was comparably associated with vitiligo. Oxidative stress is thought to be involved in the pathogenic mechanism of both vitiligo and type 2 DM.[5] These findings suggest that both autoimmune and nonautoimmune components are involved in the pathogenesis of vitiligo. Limitations of the current study included insufficient data for subgroup analyses of different vitiligo variants or ethnicity.

Table I. Basic characteristics of included studies for meta-analysis

Study*	Country	Group	Type 1 DM, n	Type 2 DM, n	Total, n	Age, y, mean (SD) or range	Sex, M:F, n	NOS†
Birlea et al, 2006	Romania	Vitiligo	3	NA	31	53.0 (17.1)	10:21	6
		Nonvitiligo	1	NA	33	NA	NA	
Gopal et al, 2007	India	Vitiligo	30 (mixed)		150	23	81:69	8
		Nonvitiligo	5 (mixed)		100	matched	matched	
Nejad et al, 2013	Iran	Vitiligo	4 (mixed)		85	28.11 (12.5)	33:52	8
		Nonvitiligo	3 (mixed)		85	32.60 (13.8)	35:50	
Afkhami-Ardekani et al, 2014	Iran	Vitiligo	NA	54	74	16-95 [DM]	589:511 [DM]	7
		Nonvitiligo	NA	1046	2126	10-98 [non-DM]	609:491 [non-DM]	
Gopal et al, 2014	India	Vitiligo	24 (mixed)		150	24 (10.28)	83:67	8
		Nonvitiligo	5 (mixed)		100	26 (9.81)	54:46	
Chen et al, 2015	Taiwan	Vitiligo	15	NA	14,883	44	6391:8492	8
		Nonvitiligo	21	NA	59,532	44	25,564:33,968	
Al Houssien et al, 2017	Saudi Arabia	Vitiligo	31 (mixed)		61	45 (19)	17:44	8
		Nonvitiligo	20 (mixed)		61	40 (17)	17:44	
Mubki et al, 2017	Saudi Arabia	Vitiligo	9 (mixed)		115	29.53 (9.22)	51:64	8
		Nonvitiligo	4 (mixed)		89	30.73 (10.56)	37:52	
Raveendra et al, 2017	India	Vitiligo	NA	72	108	55.07 [DM]	72:36	8
		Nonvitiligo	NA	528	1092	48.47 [non-DM]	NA	

DM, Diabetes mellitus; *NA*, not available; *NOS*, Newcastle-Ottawa scale; *SD*, standard deviation.

*Birlea S, Birlea M, Cimponeriu D, et al. Autoimmune diseases and vitamin D receptor Apa-I polymorphism are associated with vitiligo in a small inbred Romanian community. Acta Derm Venereol. 2006;86(3):209-14.

Gopal KV, Rama Rao GR, Kumar YH, Appa Rao MV, Vasudev P; Srikant. Vitiligo: a part of a systemic autoimmune process. Indian J Dermatol Venereol Leprol. 2007;73(3):162-5.

Nejad SB, Qadim HH, Nazeman L, Fadaii R, Goldust M. Frequency of autoimmune diseases in those suffering from vitiligo in comparison with normal population. Pak J Biol Sci. 2013;16(12):570-4.

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Gopal KV, Rao GR, Kumar YH. Increased prevalence of thyroid dysfunction and diabetes mellitus in Indian vitiligo patients: a case-control study. Indian Dermatol Online J. 2014;5(4):456-60.

Chen YT, Chen YJ, Hwang CY, et al. Comorbidity profiles in association with vitiligo: a nationwide population-based study in Taiwan. J Eur Acad Dermatol Venereol. 2015;29(7):1362-9.

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Raveendra L, Hemavathi RN, Rajgopal S. A study of vitiligo in type 2 diabetic patients. Indian J Dermatol. 2017;62(2):168-70.

†Scale for case-control studies (score: 0-9).

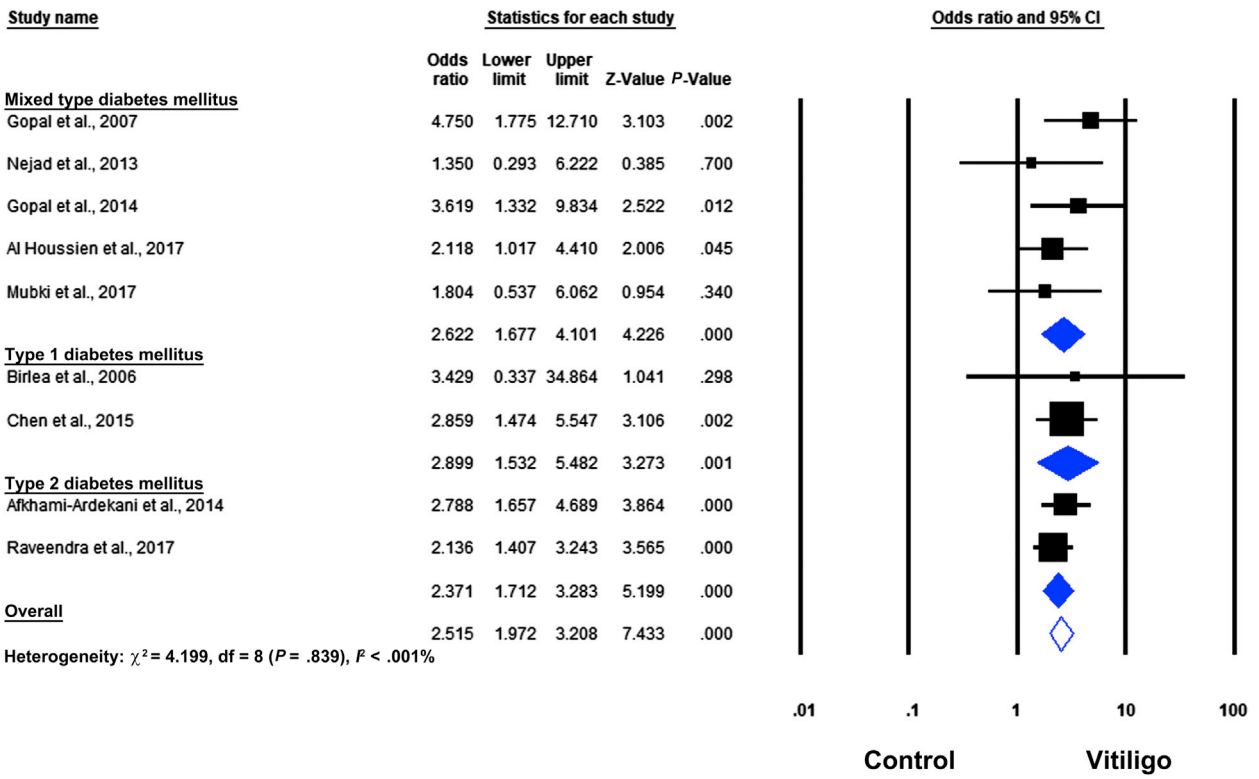

Fig 1. Forest plot of the association between vitiligo and diabetes mellitus and subgroup analysis of different types of diabetes mellitus. The following studies were included: Birlea S, Birlea M, Cimponeriu D, et al. Autoimmune diseases and vitamin D receptor Apa-I polymorphism are associated with vitiligo in a small inbred Romanian community. Acta Derm Venereol. 2006;86(3):209-14. Gopal KV, Rama Rao GR, Kumar YH, Appa Rao MV, Vasudev P; Srikant. Vitiligo: a part of a systemic autoimmune process. Indian J Dermatol Venereol Leprol. 2007;73(3):162-5. Nejad SB, Qadim HH, Nazeman L, Fadaii R, Goldust M. Frequency of autoimmune diseases in those suffering from vitiligo in comparison with normal population. Pak J Biol Sci. 2013;16(12):570-4. Afkhami-Ardekani M, Ghadiri-Anari A, Ebrahimzadeh-Ardakani M, Zaji N. Prevalence of vitiligo among type 2 diabetic patients in an Iranian population. Int J Dermatol. 2014;53(8):956-8. Gopal KV, Rao GR, Kumar YH. Increased prevalence of thyroid dysfunction and diabetes mellitus in Indian vitiligo patients: a case-control study. Indian Dermatol Online J. 2014;5(4):456-60. Chen YT, Chen YJ, Hwang CY, et al. Comorbidity profiles in association with vitiligo: a nationwide population-based study in Taiwan. J Eur Acad Dermatol Venereol. 2015;29(7):1362-9. Al Houssien AO, Al Houssien RO, Al Ajroush W, Al Kahtani HS. Chronic diseases among vitiligo patients. A case control study. Saudi Med J. 2017;38(4):400-404. Mubki T, Alissa A, Mulekar S, et al. Association of vitiligo with anemia vitamin B12 deficiency, diabetes mellitus, and thyroid dysfunction in Saudi Arab patients: a case control study. J Dermatol Dermatol Surg 2017;21(2):72-6. Raveendra L, Hemavathi RN, Rajgopal S. A study of vitiligo in type 2 diabetic patients. Indian J Dermatol. 2017;62(2):168-170. *CI*, Confidence interval; *df*, degrees of freedom.

In conclusion, our meta-analysis confirms a significant association of vitiligo with both type 1 and 2 DM. Clinicians should be aware of the risk of DM in patients with vitiligo.

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