**Supplementary Tables**

**Table S1. Influence of the genotypes of TNF-α (rs1799964) on the phenotypes of patients with vitiligo**

|  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- |
| **S. No.** | **Heading** | **TNF-α (rs1799964)** | **Phenotypes positive(n)** | **Phenotypes negatives(n)** | **p value** | **OR** | **95% CI** |
|  | Females | TT Vs. CT + CC | 82 | 74 | 0.30 | 0.74 | 0.45 - 1.22 |
| CC | 14 | 18 | 0.87 | 1.06 | 0.48 - 2.36 |
| CT | 68 | 56 | 0.19 | 0.68 | 0.40 - 1.14 |
| TT | 49 | 59 | - | - | - |
|  | Early onset type | TT Vs. CT + CC | 62 | 94 | 0.85 | 0.92  | 0.56 - 1.52 |
| CC | 14 | 18 | 0.99 | 1.08 | 0.49 - 2.41 |
| CT | 48 | 76 | 0.74 | 0.88 | 0.52 -1.49 |
| TT | 45 | 63 | - | - | - |
|  | Family History | TT Vs. CT + CC | 28 | 128 | 0.25 | 1.59 | 0.78 - 3.25 |
| CC | 5 | 27 | 0.56 | 1.35 | 0.44 - 4.13 |
| CT | 23 | 101 | 0.23 | 1.66 | 0.79 - 3.47 |
| TT | 13 | 95 | - | - | - |
|  | Acrofacial vitiligo type | TT Vs. CT + CC | 54 | 102 | 0.10 | 0.64 | 0.38 - 1.05 |
| CC | 13 | 19 | 0.85 | 0.85 | 0.38 - 1.90 |
| CT | 41 | 83 | 0.10 | 0.61 | 0.36 - 1.05 |
| TT | 48 | 60 | - | - | - |
|  | Vulgaris type | TT Vs. CT + CC | 78 | 78 | 0.31 | 1.29 | 0.79 - 2.12 |
| CC | 14 | 18 | 1.00 | 1.01 | 0.45 - 2.23 |
| CT | 64 | 60 | 0.27 | 1.38 | 0.82 - 2.32 |
| TT | 47 | 61 | - | - | - |
|  | Active vitiligo | TT Vs. CT + CC | 120 | 36 | 0.70 | 1.16 | 0.66 - 2.06 |
| CC | 20 | 12 | 0.26 | 0.53 | 0.25 - 1.34 |
| CT | 100 | 24 | 0.29 | 1.45 | 0.78 - 2.71 |
| TT | 80 | 28 | - | - | - |

Chi-square test with Yate’s correction was used to analyze association of genotype and phenotype.

\*p value < 0.05 was considered statistically significant. All significant results are in bold font.

**Table S2. Influence of the genotypes of TNF-α (rs1800630) on the phenotypes of patients with vitiligo**

|  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- |
| **S. No.** | **Heading** | **TNF-α (rs1800630)** | **Phenotypes positive(n)** | **Phenotypes negatives(n)** | **p value** | **OR** | **95% CI** |
|  | Females | CC Vs. AC + AA | 53 | 59 | 0.60 | 1.17 | 0.71 - 1.91 |
| AA | 9 | 7 | 0.91 | 0.81 | 0.29 - 2.31 |
| AC | 44 | 52 | 0.47 | 1.24 | 0.74 - 2.07 |
| CC | 78 | 74 | - | - | - |
|  | Early onset type | CC Vs. AC + AA | 43 | 69 | 0.63 | 0.85 | 0.52 - 1.41 |
| AA | 5 | 11 | 0.56 | 0.62 | 0.20 - 1.88 |
| AC | 38 | 58 | 0.79 | 0.90 | 0.53 - 1.51 |
| CC | 64 | 88 | - | - | - |
|  | Family History | CC Vs. AC + AA | 20 | 92 | 0.46 | 1.35  | 0.69 - 2.64 |
| AA | 5 | 11 | 0.14 | 2.83 | 0.89 - 8.98 |
| AC | 15 | 81 | 0.83 | 1.15 | 0.56 - 2.36 |
| CC | 21 | 131 | - | - | - |
|  | Acrofacial vitiligo type | CC Vs. AC + AA | 39 | 73 | 0.33 | 0.75 | 0.45 - 1.25 |
| AA | 6 | 10 | 0.96 | 0.84 | 0.29 - 2.45 |
| AC | 33 | 63 | 0.32 | 0.74 | 0.43 - 1.25 |
| CC | 63 | 89 | - | - | - |
|  | Vulgaris type | CC Vs. AC + AA | 60 | 52 | 0.10 | 1.54 | 0.94 - 2.52 |
| AA | 9 | 7 | 0.42 | 1.72 | 0.60 - 4.86 |
| AC | 51 | 45 | 0.14 | 1.51 | 0.90 - 2.53 |
| CC | 65 | 87 | - | - | - |
|  | Active vitiligo | CC Vs. AC + AA | 85 | 27 | 0.96 | 1.01 | 0.57 - 1.79 |
| AA | 12 | 4 | 1.00 | 0.96 | 0.29 - 3.17 |
| AC | 73 | 23 | 0.94 | 1.02  | 0.56 - 1.85 |
| CC | 115 | 37 | - | - | - |

Chi-square test with Yate’s correction was used to analyze association of genotype and phenotype.

\*p value < 0.05 was considered statistically significant. All significant results are in bold font.

**Table S3. Influence of the genotypes of TNF-α (rs1799724) on the phenotypes of patients with vitiligo**

|  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- |
| **S. No.** | **Heading** | **TNF-α (rs1799724)** | **Phenotypes positive(n)** | **Phenotypes negatives(n)** | **p value** | **OR** | **95% CI** |
|  | Females | CC Vs. CT + TT | 22 | 25 | 0.79 | 1.14  | 0.60 - 2.15 |
| TT | 2 | 2 | 0.99 | 1.00 | 0.13 - 7.29 |
| CT | 20 | 23 | 0.78 | 1.161 | 0.60 - 2.23 |
| CC | 109 | 108 | - | - | - |
|  | Early onset type | CC Vs. CT + TT | 16 | 31 | 0.40 | 0.71 | 0.36 - 1.38 |
| TT | 0 | 4 | 0.23 | 0.15 | 0.01 - 2.89 |
| CT | 16 | 27 | 0.68 | 0.82 | 0.41 - 1.61 |
| CC | 91 | 126 | - | - | - |
|  | Family History | CC Vs. CT + TT | 10 | 37 | 0.26 | 1.62 | 0.73 - 3.59 |
| TT | 1 | 3 | 0.46 | 2.00 | 0.20 - 19.8 |
| CT | 9 | 34 | 0.25 | 1.58 | 0.69 - 3.63 |
| CC | 31 | 186 | - | - | - |
|  | Acrofacial vitiligo type | CC Vs. CT + TT | 19 | 28 | 0.91 | 1.09 | 0.57 - 2.08 |
| TT | 2 | 2 | 0.96 | 1.61 | 0.22-11.69 |
| CT | 17 | 26 | 0.98 | 1.05 | 0.54 - 2.06 |
| CC | 83 | 134 | - | - | - |
|  | Vulgaris type | CC Vs. CT + TT | 21 | 26 | 0.74 | 0.87 | 0.46 - 1.65 |
| TT | 2 | 2 | 1.00 | 1.08 | 0.15 - 7.85 |
| CT | 19 | 24 | 0.73 | 0.86 | 0.44 - 1.66 |
| CC | 104 | 113 | - | - | - |
|  | Active vitiligo | CC Vs. CT + TT | 34 | 13 | 0.57 | 0.80 | 0.39 - 1.63 |
| TT | 3 | 1 | 1.00 | 0.92 | 0.09 - 9.0 |
| CT | 31 | 12 | 0.56 | 0.79 | 0.37 - 1.65 |
| CC | 166 | 51 | - | - | - |

Chi-square test with Yate’s correction was used to analyze association of genotype and phenotype.

\*p value < 0.05 was considered statistically significant. All significant results are in bold font.

**Table S4. Influence of the genotypes of TNF-α (rs1800629) on the phenotypes of patients with vitiligo**

|  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- |
| **S. No.** | **Heading** | **TNF-α (rs1800629)** | **Phenotypes positive(n)** | **Phenotypes negatives(n)** | **p value\*** | **OR** | **95% CI** |
|  | Females | GG Vs. AG + AA | 82 | 78 | 0.59 | 0.85 | 0.52 - 1.39 |
| AA | 1 | 1 | 0.93 | 0.89 | 0.05 - 14.63 |
| AG | 81 | 77 | 0.59 | 0.85 | 0.52 - 1.39 |
| GG | 49 | 55 | - | - | - |
|  | Early onset type | GG Vs. AG + AA | 54 | 106 | **0.008** | **0.49** | **0.29 – 0.81** |
| AA | 1 | 1 | 0.49 | 0.96 | 0.05 – 15.81 |
| AG | 53 | 105 | **0.007** | **0.48** | **0.29 - 0.80** |
| GG | 53 | 51 | - | - | - |
|  | Family History | GG Vs. AG + AA | 26 | 134 | 0.82 | 1.15 | 0.57 - 2.29 |
| AA | 0 | 2 | 1.00 | 1.15 | 0.052 - 25.24 |
| AG | 26 | 132 | 0.78 | 1.16 | 0.58 - 2.33 |
| GG | 15 | 89 | - | - | - |
|  | Acrofacial vitiligo type | GG Vs. AG + AA | 62 | 98 | 0.93 | 1.01 | 0.60 - 1.68 |
| AA | 1 | 1 | 0.68 | 1.60 | 0.09- 26.32 |
| AG | 61 | 97 | 0.91 | 1.00  | 0.60 - 1.67 |
| GG | 40 | 64 | - | - | - |
|  | Vulgaris type | GG Vs. AG + AA | 79 | 81 | 0.48 | 1.23 | 0.74 - 2.01 |
| AA | 1 | 1 | 1.00 | 1.26 | 0.076 - 20.72 |
| AG | 78 | 80 | 0.49 | 1.22 | 0.74 - 2.02 |
| GG | 46 | 58 | - | - | - |
|  | Active vitiligo | GG Vs. AG + AA | 121 | 39 | 0.95 | 0.98 | 0.55 - 1.74 |
| AA | 2 | 0 | 1.00 | 1.60 | 0.07 - 34.53 |
| AG | 119 | 39 | 0.90 | 0.96 | 0.54 - 1.72 |
| GG | 79 | 25 | - | - | - |

Chi-square test with Yate’s correction was used to analyze association of genotype and phenotype.

\*p value < 0.05 was considered statistically significant. All significant results are in bold font.

**Table S5. Influence of the genotypes of TNF-α (rs361525)) on the phenotypes of patients vitiligo**

|  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- |
| **S. No.** | **Heading** | **TNF-α (rs361525)** | **Phenotypes positive(n)** | **Phenotypes negatives(n)** | **p value\*** | **OR** | **95% CI** |
|  | Females | GG Vs. AG + AA | 32 | 19 | **0.04** | **0.51** | **0.27 - 0.96** |
| AA | 23 | 12 | **0.04** | **0.45** | **0.21 - 0.95** |
| AG | 9 | 7 | 0.62 | 0.67 | 0.24 -1.88 |
| GG | 99 | 114  | - | - | - |
|  | Early onset type | GG Vs. AG + AA | 22 | 34 | 0.94 | 0.97 | 0.53 – 1.78 |
| AA | 15 | 25 | 0.91 | 0.90 | 0.45- 1.81 |
| AG | 7 | 9 | 0.96 | 1.17 | 0.42 – 3.26 |
| GG | 85 | 128 | - | - | - |
|  | Family History | GG Vs. AG + AA | 10 | 41 | 0.49 | 1.43 | 0.65 - 3.15 |
| AA | 8 | 27 | 0.31 | 1.74 | 0.72 - 4.17 |
| AG | 2 | 14 | 0.82 | 0.84 | 0.18 - 3.87 |
| GG | 31 | 182 | - | - | - |
|  | Acrofacial vitiligo type | GG Vs. AG + AA | 17 | 34 | 0.48 | 0.75 | 0.39 - 1.43 |
| AA | 14 | 21 | 0.86 | 1.00 | 0.48 – 2.08 |
| AG | 3 | 13 | 0.15 | 0.34 | 0.09- 1.25 |
| GG | 85 | 128 | - | - | - |
|  | Vulgaris type | GG Vs. AG + AA | 24 | 27 | 0.96 | 0.98 | 0.53 - 1.81 |
| AA | 16 | 19 | 1.00 | 0.93 | 0.45 - 1.91 |
| AG | 8 | 8 | 1.00 | 1.10 | 0.40 - 3.06 |
| GG | 101 | 112 | - | - | - |
|  | Active vitiligo | GG Vs. AG + AA | 38 | 13 | 0.85 | 0.92 | 0.45 - 1.86 |
| AA | 27 | 8 | 1.00 | 1.06 | 0.45 - 2.48 |
| AG | 11 | 5 | 0.54 | 0.69 | 0.23 - 2.08 |
| GG | 162 | 51 | - | - | - |

Chi-square test with Yate’s correction was used to analyze association of genotype and phenotype.

\*p value < 0.05 was considered statistically significant. All significant results are in bold font.

**Table S6: Results of previous studies: Association of TNF-α gene variants with vitiligo risk in other ethnics**

|  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- |
| **References** | **Ethnicity** | **Sample size** | **SNP/rsID** | **Allele/****Genotype** | **P value** | **Odds ratio,** **OR (95% CI)** | **Reference** |
| **Laddha et al.** | North Indian population | 729 generalized vitiligo and 990 controls | rs361525 | AA | <0.0001 | 6.35 (5.320–7.590) | (1) |
|  |  | 728 generalized vitiligo and 981controls | rs1800629 | AA | <0.0001 | 4.326 (3.623–5.165) |  |
|  |  | 728 generalized vitiligo and 984 controls | rs1799724 | TT | <0.0001 | 2.181 (1.885–2.524) |  |
|  |  | 728 generalized vitiligo and 984 controls | rs1800630 | AA | <0.0001 | 2.231 (1.894–2.629) |  |
|  |  | 733 generalized vitiligo and 989 controls | rs1799964 | CC | <0.0001 | 1.960 (1.675–2.294) |  |
| **Namian et al.** | Iranian population | 176 vitiligo and 575 controls | s1800629 | AA | 0.0004 | NA | (2) |
| **Yazici et al.,** | Turkish population | 61 patients with vitiligo and 123 controls | rs1800629 | AA | NS | NA | (3) |
| **Aydingoz et al.** | Turkish population | 105 patients with vitiligo and 211 controls | rs1800629 | AA | 0.22 | 0.27 (0.01–1.43) | (4) |
| **Salinas-Santander et al.** | Northeastern Mexican population | 198 vitiligo patients and 395 controls | rs1800629 | AA | 0.78  | 1.08 (0.60-1.96) | (5) |
| **Al Harthi et al.** | Saudi population | 123 vitiligo patients and 200 controls | rs1800629 | AA | 0.0001 | NA | (6) |
| **Nie et al.** | European Asian, North American | Meta-analysis 1391 vitiligo patients and 2455 healthy controls | rs1800629 | A allele | 0.188 | 0.65 (0.35-1.23) |  |
| **Wu et al** | European Asian, North American | Meta-analysis  | rs1800629 | A allele | 0.101 | 1.79 (0.89–3.58) | (7) |
| **Lee and Bae.** | Overall | Meta-analysis 1527 vitiligo patients and 2244 controls | rs1800629 | AA | 0.068 | 2.269 (0.941-5.471) | (8) |
|  | Middle Eastern populations | 360 vitiligo patients and 868 controls | rs1800629 | AA | 0.234 | 2.093 (0.021-7.059)  |  |

**References:**

1. Laddha NC, Dwivedi M, Begum R. Increased Tumor Necrosis Factor (TNF)-? and Its Promoter Polymorphisms Correlate with Disease Progression and Higher Susceptibility towards Vitiligo. Ahmed N, editor. PLoS ONE. 2012 Dec 20;7(12):e52298.

2. Namian A-M, Shahbaz S, Salmanpoor R, Namazi M-R, Dehghani F, Kamali-Sarvestani E. Association of interferon-gamma and tumor necrosis factor alpha polymorphisms with susceptibility to vitiligo in Iranian patients. Arch Dermatol Res. 2009 Jan;301(1):21–5.

3. Yazici AC, Erdal ME, Kaya TI, Ikizoglu G, Savasoglu K, Camdeviren H, et al. Lack of association with TNF-alpha-308 promoter polymorphism in patients with vitiligo. Arch Dermatol Res. 2006 Jun;298(1):46–9.

4. Aydıngöz IE, Kanmaz-Özer M, Gedikbaşi A, Vural P, Doğru-Abbasoğlu S, Uysal M. The combination of tumour necrosis factor-α -308A and interleukin-10 -1082G gene polymorphisms and increased serum levels of related cytokines: susceptibility to vitiligo. Clin Exp Dermatol. 2015 Jan;40(1):71–7.

5. Salinas-Santander M, Díaz-García D, Rojas-Martínez A, Cantú-Salinas C, Sánchez-Domínguez C, Reyes-López M, et al. Tumor necrosis factor-α -308G/A polymorphism is associated with active vitiligo vulgaris in a northeastern Mexican population. Exp Ther Med. 2012 May;3(5):893–7.

6. Al-Harthi F, Zouman A, Arfin M, Tariq M, Al-Asmari A. Tumor necrosis factor-α and -β genetic polymorphisms as a risk factor in Saudi patients with vitiligo. Genet Mol Res GMR. 2013 Jul 8;12(3):2196–204.

7. Wu D, Shi D, Zhu X. The association between tumor necrosis factor-α-308 G/A polymorphism and risk for vitiligo: a meta-analysis. Int J Dermatol. 2015 Sep;54(9):1045–53.

8. Lee YH, Bae SC. Associations between TNF-α polymorphisms and susceptibility to rheumatoid arthritis and vitiligo: a meta-analysis. Genet Mol Res GMR. 2015 May 25;14(2):5548–59.