

Supplementary archives

Supplementary table 1. Scientific articles on GC polymorphisms and vitamin D levels in the Brazilian population

| study | database | authors | acess link | population | region/ city/ town | gene | SNP | effect or minor allele | effect or minor allele frequency | prevalence of vitamin D deficiency (95% CI) | prevalence of vitamin D insufficiency (%) | p-value | 25OHD (ng/ml) mean ± sd | p-value | beta 25OHD (ng/ml) | CI 95% se | p-value | OR | p-value | DBP (ug/ml) | p-value | N | age (years) mean ± sd (range) | % female | ethnicity (% whites) | Hardy-Weinberg equilibrium (p-value) | correction for population stratification | type of study | comments |
|---|----------|-----------------------|---|--|---------------------------|------|---------------------------|------------------------|----------------------------------|---|---|----------------------------|-------------------------|-----------|--------------------|-----------|---------|----|---------|-------------|---------|---|---|--------------|----------------------|--------------------------------------|--|--|--|
| Genetic, sociodemographic and lifestyle factors associated with serum 25-hydroxyvitamin D concentrations in Brazilian adults: the Pró-Saúde Study | PUBMED | Bezerra et al. (2022) | https://pubmed.ncbi.nlm.nih.gov/35043885/ | university civil servants | Rio de Janeiro, RJ | GC | rs2282679 | C | 0.222 | 55.0 | <0.001 | 48.0 ± 19.1 nmol/l | <0.001 | | | | | | | | | 491 | 45-54 (43.8%) | 51.1 | in equilibrium | no | cross-sectional | | |
| Genetic polymorphisms related to the vitamin D pathway in patients with cirrhosis with or without hepatocellular carcinoma (HCC) | PUBMED | Brait et al. (2022) | https://pubmed.ncbi.nlm.nih.gov/35919232/ | patients with cirrhosis & controls | São José do Rio Preto, SP | GC | rs4588; rs7041 | A; G | rs4588 A: 0.30 cases: 0.28 | 30.0 cases/35.0 controls | | 48.2 | 50.3 (28.3) | reference | | | | | | | | | 383 | 16-81; 20-84 | 21.5; 43.6 | in equilibrium | no | case-control | reduced levels of vitamin D in cases showed association with genotypes with at least one mutant allele (A) for GC rs4588 (77.8%) compared to controls (14.3%; p = 0.0406). |
| "Effect of vitamin D serum levels and GC gene polymorphisms in liver fibrosis due to chronic hepatitis C | PUBMED | Azevedo et al. (2017) | https://pubmed.ncbi.nlm.nih.gov/28809744/ | adult patients with chronic hepatitis C genotype 1 | Porto Alegre, RS | GC | rs4588; rs7041 | T; C | 0.213; 0.461 | 50.0 | 27.3 | 0.02 | 19.9 (14.0-29.4) | | | | | | | | | 132 | 53 (± 9) | 46.2 | in equilibrium | no | cross-sectional | 25OHD levels differences between haplotypes too. | |
| Prevalence of vitamin D deficiency in women from southern Brazil and association with vitamin D-binding protein levels and GC-DBP gene polymorphisms | PUBMED | Santos et al. (2019) | https://pubmed.ncbi.nlm.nih.gov/31830090/ | women with no evidence of clinical disease | Porto Alegre, RS | GC | rs4588; rs7041; rs2282679 | A; G; C | 0.293; 0.484; 0.283 | 39.7 | | 22.80 (± 8.32) | | | | | | | | | | 443 | 53.4 (± 9.4) | 100 | 0.23, 0.09, 0.68 | no | cross-sectional | | |
| Genetic variant in vitamin D-binding protein is associated with metabolic syndrome and lower 25-hydroxyvitamin D levels in polycystic ovary syndrome: A cross-sectional study | PUBMED | Santos et al. (2017) | https://pubmed.ncbi.nlm.nih.gov/28278285/ | women of reproductive age | Porto Alegre, RS | GC | rs4588; rs7041; rs2282679 | A; G; C | 0.230; 0.535; 0.225 | 42.2 | 45.1 | 21.48 ± 7.25; 21.50 ± 6.90 | | | | | | | | | | 291 (191 PCOS + 100 controls)/102 (54 PCOS + 48 controls) with 25OHD levels | 22.89 ± 6.66 PCOS/25.18 ± 7.72 controls | 100 | 80 | in equilibrium | no | cross-sectional | LD rs4588 & rs7041 r ² = 0.44 |
| Variations in the vitamin D-binding protein (DBP) gene are related to lower 25-hydroxyvitamin d levels in healthy girls: a cross-sectional study | PUBMED | Santos et al. (2013) | https://pubmed.ncbi.nlm.nih.gov/23548751/ | healthy female students | Curitiba, PR | GC | rs4588; rs7041 | A; G | 0.267; 0.485 | | | 22.1 ± 5.9 | | | | | | | | | | 198 | 13.17 ± 1.74 | 100 | 93.9* | in equilibrium | no | cross-sectional | LD rs4588 & rs7041 r ² = 0.38 |

Supplementary table 2. Scientific articles on *VDR* gene polymorphisms and vitamin D levels in the Brazilian population

| Study | Database | Authors | Access link | Population | Region/ city/town | Gene | SNP | Effect or minor allele | Effect or minor allele frequency | Prevalence of vitamin D deficiency (95% CI) | p-value | Prevalence of vitamin D insufficiency (%) | p-value | 25OHD (ng/ml) mean ± sd | p-value | N | Age (years) mean ± SD (range) | % female | Ethnicity (% white) | Beta 25OHD (ng/ mL) | 95% CI/ SE | p-value | OR | CI 95% | p-value ^a | Hardy- Weinberg equilibrium (p-value) | Correction for population stratification | Type of study | Comments |
|---|----------|------------------------------|---|---|----------------------------|------|--|------------------------------|-------------------------------------|--|----------------------------|--|------------------------------------|----------------------------------|---------|-------|-------------------------------------|-------------|---------------------------|------------------------------|---------------|---------|------|--------------|----------------------|--|--|---|---|
| Vitamin D deficiency is a risk factor for delayed tooth eruption associated with persistent primary tooth (PPT) | PUBMED | Xavier et al. (2021) | https://pubmed.ncbi.nlm.nih.gov/33944665/ | children with primary teeth with exfoliation time expired for more than a year (persistent primary tooth) and children with regular primary teeth exfoliation time (controls) | Ribeirão Preto, SP | VDR | rs2228570; rs739837 | A; G | 26.7 PPT/0.0 controls | 14.2-37.4 PPT; 21.9-48.2 controls | 30 (15 PPT + 15 controls) | 9.4 ± 1.8 | 43.3 | | | | | | | | | | | not reported | no | case-control | data showed no association between genetic polymorphisms in VDR and serum 25OHD levels (p>0.05). | | |
| Genetic polymorphisms in vitamin D pathway influence 25(OH)D levels and are associated with atopy and asthma | PUBMED | Galvão et al. (2020) | https://pubmed.ncbi.nlm.nih.gov/32834827/ | SCAALA cohort (children from deprived areas) | Salvador, BA | VDR | rs10875694; rs11168287; rs219480; rs2853561; rs2853564; rs4237855; rs4328262; rs59128934; rs739837; rs7963776; rs79656274; rs7967152; rs9729 | G; C; G; G; G; T; A; C | 20.8 | 40.7 | 27.33 ± 9.60 | 792 | (11-19) | 47.6 | | | | | | | | | | | in equilibrium | individual genetic ancestry using 269 AlMs | cross-sectional nested in cohort | write to them to ask the DBP (GC) SNPs vs 25OHD levels. | |
| *Variants rs1544410 and rs2228570 of the vitamin D receptor gene are associated with serum levels in adolescents from Northeast Brazil | PUBMED | Neves et al. (2019) | https://pubmed.ncbi.nlm.nih.gov/31710844/ | adolescents who did not present any chronic disease | João Pessoa, PB | VDR | rs1544410; rs2228570 | B = A; f = T | 0.395; 0.332 | 50.0 | 28.0 (28.4-30.7) | 208 | 17.7 (± 1.14) | 62.5 | | | | | | | | | 1.78 | 1.12, 2.83 | 0.014 | rs1544410 out of HWE (calculated by us) | no | cross-sectional | rs9729 C allele increases VDR expression (p = 0.0007) in GTEx. Rs9729 is in strong LD with rs731236 (TaqI). |
| Polymorphism in the vitamin D receptor gene is associated with maternal vitamin D concentration and neonatal outcomes: A Brazilian cohort study | PUBMED | Pereira Santos et al. (2019) | https://pubmed.ncbi.nlm.nih.gov/31070844/ | pregnant women who lived in the urban area of the municipality and received prenatal services | Santo Antônio de Jesus, BA | VDR | rs731236; rs7975232 | G; C | 0.300; 0.400 | 23.0 | 43.0 | 72.62 ± 31.51 nmol/l | 270 | 26.73 ± 5.85 | 100 | 18.15 | nmol/L | | | | | | | 0.24; 0.94 | no | prospective cohort | | | |
| Association of vitamin D3, VDR gene polymorphisms, and LL-37 with a clinical form of Chagas Disease | SciELO | Junior et al. (2019) | https://www.scielo.br/scielo.php?script=sci_arttext&pid=27QwDmFg7Ndz6RxRtbJG8SK?lng=en | adult male patients with indeterminate and cardiac form of chronic Chagas Disease (CD) | Botucatu, SP | VDR | rs1544410; rs2228570; rs731236; rs7975232 | 0.40; 0.44; 0.26; 0.31 | 10.9 | 53.1 | 0.207; 0.767; 0.617; 0.837 | 29.3 ± 5.8; 25.4 ± 7.3 | 64 (46 indeterminate + 18 cardiac) | 60.3 ± 8.1; 62.2 ± 11.0 | 0 | 76.6 | | | | | | | | not reported | no | cross-sectional | | | |

Supplementary table 3. Scientific articles on polymorphisms in genes other than *GC* and *VDR* and vitamin D levels in the Brazilian population

| study | database | authors | access link | population | region/ city/town | gene | SNP | effect or minor allele frequency | effect or minor allele | prevalence of vitamin D deficiency (95% CI) | prevalence of vitamin D insufficiency (%) | p-value | 25OHD (ng/ ml) mean ± sd | p-value | beta 25OHD (ng/ml) | CI 95%/se | p-value | OR | CI 95% | p-value | N | age (years) mean ± sd (range) | % female | ethnicity (% whites) | Hardy- Weinberg equilibrium (p-value) | correction for population stratification | type of study | comments |
|---|----------|-----------------------|---|--|---------------------------|--------------------------|---|--|-----------------------------------|--|--|--------------|--------------------------------|---------|--------------------------|-----------|---------|----|--------|------------------------------|-----------------------------|-------------------------------------|----------------|---|--|--|---|----------|
| Genetic, sociodemographic and lifestyle factors associated with serum 25-hydroxyvitamin D concentrations in Brazilian adults: the Pró-Saúde Study | PUBMED | Bezerra et al. (2022) | https://pubmed.ncbi.nlm.nih.gov/35043885/ | university civil servants | Rio de Janeiro, RJ | CYP2R1; NADSYN1; CYP24A1 | rs10741657; rs12785878; rs013897 | G; T; T | | 55.0 | 48.0 ± 19.1 nmol/l | | | | | | | | | | 491 | 45.54 (43.8%) | 51.1 | rs12785878 & rs013897 in HWD and not analysed | no | cross-sectional | | |
| Genetic polymorphisms in vitamin D pathway influence 25(OH)D levels and are associated with atopy and asthma | PUBMED | Galvão et al. (2020) | https://pubmed.ncbi.nlm.nih.gov/32834827/ | SCAALA cohort (children from deprived areas) | Salvador, BA | CYP2R1; CYP24A1 | rs10500804; rs294714; rs2245153; rs34043203; rs3886163; rs4809960; rs56229249 | G, A; C, A, T, C, G | rs10741657 G GG GA AA | 0.705 59.2 49.5 56.8 | 0.119 median (IQR) 46.0 (25.6) 50.0 (28.3) 49.5 (22.8) | 27.33 ± 9.60 | | | | | | | | | 792 | (11-19) | 47.6 | in equilibrium | individual genetic ancestry using 269 AIMs | cross-sectional nested in cohort | write to them to ask the DBP (GC) SNPs vs 25OHD levels. | |
| Genetic polymorphisms related to the vitamin D pathway in patients with cirrhosis with or without hepatocellular carcinoma (HCC) | PUBMED | Brait et al. (2022) | https://pubmed.ncbi.nlm.nih.gov/35919232/ | patients with cirrhosis & controls | São José do Rio Preto, SP | CYP24A1 | rs8013897 | T | 0.72; 0.70 | 30.0; 35.0 | | | | | | | | | | 383 | 16-81; 20-84 | 21.5; 43.6 | in equilibrium | no | case-control | no association with vitamin D levels | | |
| Genetic polymorphisms of vitamin D metabolism genes and serum level of vitamin D in colorectal cancer | PUBMED | Vidigal et al. (2017) | https://pubmed.ncbi.nlm.nih.gov/28665452/ | colorectal cancer cases & controls | São Paulo, SP | CYP24A1; CYP27B1 | rs158552; rs7217119; rs013897; rs10877012 | T; A; T; G | 51.0; 43.3 | 18.4; 26.6 | 26.4 ± 17.6; 28.4 ± 19.2 | | | | | | | | | 473 (152 CRC + 321 controls) | 62.8 ± 13.0; 62.7 ± 10.4 | 46.7; 49.2 | not reported | no | case-control | | | |

Supplementary table 4. Single nucleotide polymorphisms in the *VDR* gene associated with complex traits according to the GWAS catalog

| Beta | CI | Mapped gene | Reported trait | Trait(s) | Study accession | Location |
|----------------------------|-----------------|---------------|---|---|-----------------|-------------|
| 0.063426755 unit decrease | [0.042-0.085] | VDR | basal cell carcinoma | basal cell carcinoma | GCST90013410 | 12:47844438 |
| 0.0481096 unit increase | [0.033-0.064] | VDR | total testosterone levels | testosterone measurement | GCST90012112 | 12:47860570 |
| 0.13136138 unit increase | [0.088-0.175] | VDR | medication use (diuretics) | Diuretic use measurement | GCST007928 | 12:47860570 |
| 0.3943 unit increase | [0.28-0.51] | VDR | diastolic blood pressure | diastolic blood pressure | GCST90132904 | 12:47860570 |
| 0.1314 unit increase | [0.088-0.175] | VDR | medication use (diuretics) | diuretic use measurement | GCST90018985 | 12:47860570 |
| | | VDR | cardiovascular disease | cardiovascular disease | GCST007072 | 12:47860570 |
| | | VDR | gout | gout | GCST001356 | 12:47862166 |
| 0.32741 unit increase | [0.18-0.47] | VDR | COVID-19 (hospitalized vs not hospitalized) | COVID-19 | GCST90104752 | 12:47873551 |
| 0.75 percent increase | | VDR | gut microbiota (beta diversity) | gut microbiome measurement | GCST003876 | 12:47876015 |
| | | VDR | eosinophil counts | eosinophil count | GCST007065 | 12:47879112 |
| 0.0138518615 unit increase | [0.0094-0.0183] | VDR | eosinophil percentage of white cells | eosinophil percentage of leukocytes | GCST90002382 | 12:47879112 |
| 47.572 unit increase | | VDR | serum immune biomarker levels | inflammatory biomarker measurement, YKL40 measurement | GCST010146 | 12:47914289 |
| 0.9905315 unit decrease | | VDR | sphingomyelin (d32:2) levels | sphingomyelin measurement | GCST90094889 | 12:47919236 |
| 0.57862 unit increase | [0.33-0.83] | VDR | S-6-hydroxywarfarin levels | S-6-hydroxywarfarin measurement | GCST90129565 | 12:47920142 |
| 0.86594 unit increase | [0.52-1.21] | VDR | R-6-hydroxywarfarin to R-warfarin ratio | R-6-hydroxywarfarin to R-warfarin ratio measurement | GCST90129572 | 12:47927031 |
| | | VDR | adolescent idiopathic scoliosis | adolescent idiopathic scoliosis | GCST006287 | 12:47927916 |
| | | VDR, TMEM106C | heel bone mineral density | heel bone mineral density | GCST007066 | 12:47943286 |
| 0.0304 unit increase | [0.024-0.037] | VDR, TMEM106C | glycated hemoglobin levels | HbA1c measurement | GCST90019509 | 12:47943286 |
| 0.0541 unit decrease | [0.038-0.07] | TMEM106C, VDR | glycated hemoglobin levels | HbA1c measurement | GCST90019509 | 12:47943734 |
| 0.049543403 unit increase | [0.032-0.067] | VDR, TMEM106C | medication use (calcium channel blockers) | calcium channel blocker use measurement | GCST007929 | 12:47944639 |
| | | TMEM106C, VDR | red blood cell count | erythrocyte count | GCST007069 | 12:47952685 |
| 0.015703138 unit increase | [0.011-0.02] | VDR, TMEM106C | lymphocyte percentage of white cells | lymphocyte percentage of leukocytes | GCST90002389 | 12:47963231 |