|  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Table S1. Univariate analysis of socio-demographic variables and anthropometric indices** | | | | | | | | | | | | | | | | | |
|  | Valvar | | | | | | Significant Valvar | | | | Non-Valvar | | | | Significant non-Valvar | | |
| Parameter (penetrance) | n (%1) | | | | p value | | n (%1, %2) | | p value | | n (%1) | | p value | | n (%1, %3) | | p value |
| Total | 1058 (0.93%) | | | |  | | 213 (0.19%, 20.1%) | |  | | 415 (0.37%) | |  | | 84 (0.07%, 20.2%) | |  |
| Year of Birth (100%) |  | | | | **<0.0001** | |  | | **<0.0001** | |  | | **0.003** | |  | | **<0.0001** |
| <=1975 | 181 (0.79%) | | | |  | | 66 (0.29%, 36.5%) | |  | | 78 (0.34%) | |  | | 6 (0.03%, 7.7%) | |  |
| 1976-1980 | 346 (1.30%) | | | |  | | 96 (0.36%, 27.7%) | |  | | 128 (0.48%) | |  | | 9 (0.03%, 7.0%) | |  |
| 1981-1985 | 182 (0.87%) | | | |  | | 15 (0.07%, 8.2%) | |  | | 57 (0.27%) | |  | | 13 (0.06%, 22.8%) | |  |
| 1986-1990 | 244 (0.88%) | | | |  | | 22 (0.08%, 9.0%) | |  | | 104 (0.38%) | |  | | 40 (0.14%, 38.5%) | |  |
| >=1991 | 105 (0.69%) | | | |  | | 14 (0.09%, 13.3%) | |  | | 48 (0.32%) | |  | | 16 (0.11%, 33.3%) | |  |
| Season of Birth (100%) |  | | | | 0.597 | |  | | 0.236 | |  | | 0.619 | |  | | **0.020** |
| Autumn | 265 (0.94%) | | | |  | | 65 (0.23%, 24.5%) | |  | | 101 (0.36%) | |  | | 9 (0.03%, 8.9%) | |  |
| Winter | 246 (0.87%) | | | |  | | 47 (0.17%, 19.1%) | |  | | 93 (0.33%) | |  | | 24 (0.08%, 25.8%) | |  |
| Spring | 261 (0.93%) | | | |  | | 53 (0.19%, 20.3%) | |  | | 107 (0.38%) | |  | | 22 (0.08%, 20.6%) | |  |
| Summer | 286 (0.98%) | | | |  | | 48 (0.16%, 16.8%) | |  | | 114 (0.39%) | |  | | 29 (0.10%, 25.4%) | |  |
| Gender (100%) |  | | | | **<0.0001** | |  | | **0.001** | |  | | **0.022** | |  | | 0.051 |
| male | 707 (1.06%) | | | |  | | 148 (0.22%, 20.9%) | |  | | 266 (0.40%) | |  | | 58 (0.09%, 21.8%) | |  |
| female | 351 (0.74%) | | | |  | | 65 (0.14%, 18.5%) | |  | | 149 (0.32%) | |  | | 26 (0.06%, 17.4%) | |  |
| Country of origin (100%) |  | | | | **0.013** | |  | | 0.643 | |  | | 0.243 | |  | | 0.893 |
| Israel | 118 (0.75%) | | | |  | | 27 (0.17%, 22.9%) | |  | | 49 (0.31%) | |  | | 12 (0.08%, 24.5%) | |  |
| Other | 940 (0.96%) | | | |  | | 186 (0.19%, 19.8%) | |  | | 366 (0.37%) | |  | | 72 (0.07%, 19.7%) | |  |
| Country of birth (100%) |  | | | | 0.268 | |  | | 0.349 | |  | | **0.041** | |  | | 0.635 |
| Israel | 876 (0.92%) | | | |  | | 184 (0.19%, 21.0%) | |  | | 364 (0.38%) | |  | | 69 (0.07%, 19.0%) | |  |
| Other | 182 (1.00%) | | | |  | | 29 (0.16%, 15.9%) | |  | | 51 (0.28%) | |  | | 15 (0.08%, 29.4%) | |  |
| Residential Area (100%) |  | | | | 0.084 | |  | | 0.556 | |  | | 0.850 | |  | | **0.047** |
| Rural | 558 (0.98%) | | | |  | | 111 (0.19%, 19.9%) | |  | | 206 (0.36%) | |  | | 33 (0.06%, 16.0%) | |  |
| Urban | 500 (0.88%) | | | |  | | 102 (0.18%, 20.4%) | |  | | 209 (0.37%) | |  | | 51 (0.09%, 24.4%) | |  |
| Years of education (100%) | |  | | | | **<0.0001** | |  | | 0.161 | |  | | 0.137 | |  | 0.452 |
| 0-6 | | 20 (0.88%) | | | |  | | 7 (0.31%, 35.0%) | |  | | 7 (0.31%) | |  | | 3 (0.13%, 42.9%) |  |
| 7-9 | | 11 (0.27%) | | | |  | | 3 (0.07%, 27.3%) | |  | | 9 (0.22%) | |  | | 0 (0.00%, 0.00%) |  |
| 10-11 | | 204 (0.89%) | | | |  | | 48 (0.21%, 23.5%) | |  | | 102 (0.45%) | |  | | 19 (0.08%, 18.6%) |  |
| 12 | | 803 (0.99%) | | | |  | | 146 (0.18%, 18.2%) | |  | | 284 (0.35%) | |  | | 59 (0.07%, 20.8%) |  |
| ≥13 | | 20 (0.66%) | | | |  | | 9 (0.30%, 45.0%) | |  | | 13 (0.43%) | |  | | 3 (0.10%, 23.1%) |  |
| SES (33.6%) | | 0.330 | | | | 0.876 | | 0.569 | | 0.452 | |  | |  | |  |  |
| Low | | 75 (1.01%) | | | |  | | 8 (0.11%, 10.7%) | |  | | 21 (0.28%) | |  | | 8 (0.11%, 38.1%) |  |
| Intermediate | | 248 (0.84%) | | | |  | | 26 (0.09%, 10.5%) | |  | | 96 (0.32%) | |  | | 37 (0.12%, 38.5%) |  |
| High | | 9 (0.76%) | | | |  | | 1 (0.08%, 11.1%) | |  | | 2 (0.17%) | |  | | 0 (0.00%, 0.00%) |  |
|  | |  | | | |  | |  | |  | |  | |  | |  |  |
| **Table S1. (Cont.)** | | | | | | | | | | | | | | | | | |
|  | | | Valvar | | | | | Significant Valvar | | | | Non-Valvar | | | | Significant non-Valvar | |
| Parameter (penetrance) | | | n (%1) | | | p value | | n (%1, %2) | | p value | | n (%1) | | p value | | n (%1, %3) | p value |
| Number of children in the family (99.9%) | | | | **0.007** | | | | 0.390 | | | | 0.477 | | | | 0.673 | |
| 1 | | 58 (1.15%) | | | |  | | 9 (0.18%, 15.5%) | |  | | 16 (0.32%) | |  | | 4 (0.08%, 25.0%) |  |
| 2-4 | | 744 (0.97%) | | | |  | | 135 (0.18%, 18.1%) | |  | | 291 (0.38%) | |  | | 60 (0.08%, 20.6%) |  |
| ≥5 | | 256 (0.80%) | | | |  | | 69 (0.22%, 27.0%) | |  | | 108 (0.34%) | |  | | 20 (0.06%, 18.5%) |  |
| Single child (99.9%) | |  | | | | 0.100 | |  | | 0.877 | |  | | 0.560 | |  | 0.887 |
| Yes | | 52 (1.15%) | | | |  | | 9 (0.18%, 17.3%) | |  | | 16 (0.32%) | |  | | 4 (0.08%, 25.0%) |  |
| No | | 1000 (0.92%) | | | |  | | 204 (0.19%, 20.4%) | |  | | 399 (0.37%) | |  | | 80 (0.08%, 20.1%) |  |
| Youngest child (99.9%) | |  | | | | **0.001** | |  | | 0.185 | |  | | 0.517 | |  | 0.111 |
| Yes | | 368 (1.08%) | | | |  | | 73 (0.21%, 19.8%) | |  | | 131 (0.38%) | |  | | 32 (0.09%, 24.4%) |  |
| No | | 690 (0.87%) | | | |  | | 140 (0.18%, 20.3%) | |  | | 284 (0.36%) | |  | | 52 (0.07%, 18.3%) |  |
| Oldest child (100%) | |  | | | | 0.945 | |  | | 0.675 | |  | | 0.841 | |  | 0.348 |
| Yes | | 351 (0.93%) | | | |  | | 68 (0.18%, 19.4%) | |  | | 140 (0.37%) | |  | | 32 (0.08%, 22.9%) |  |
| No | | 707 (0.93%) | | | |  | | 145 (0.19%, 20.5%) | |  | | 275 (0.36%) | |  | | 52 (0.07%, 18.9%) |  |
| Very Young Parents (99.4%) | |  | | | | 0.125 | |  | | 0.308 | |  | | 0.597 | |  | 0.313 |
| Yes | | 24 (0.69%) | | | |  | | 4 (0.11%, 16.7%) | |  | | 11 (0.31%) | |  | | 1 (0.03%, 9.1%) |  |
| No | | 1027 (0.94%) | | | |  | | 208 (0.19%, 20.3%) | |  | | 404 (0.37%) | |  | | 83 (0.08%, 20.5%) |  |
| Very Old Parents (99.4%) | |  | | | | 0.942 | |  | | 0.740 | |  | | 0.530 | |  | 0.763 |
| Yes | | 45 (0.94%) | | | |  | | 8 (0.17%, 17.8%) | |  | | 15 (0.31%) | |  | | 3 (0.06%, 20.0%) |  |
| No | | 1007 (0.93%) | | | |  | | 204 (0.19%, 20.3%) | |  | | 400 (0.37%) | |  | | 81 (0.07%, 20.2%) |  |
| BMI group (100%) | |  | | | | **<0.0001** | |  | | 0.328 | |  | | **0.001** | |  | **<0.0001** |
| Normal weight | | 868 (0.95%) | | | |  | | 171 (0.19%, 19.7%) | |  | | 342 (0.38%) | |  | | 67 (0.07%, 19.6%) |  |
| Underweight | | 86 (1.89%) | | | |  | | 12 (0.26%, 14.0%) | |  | | 28 (0.61%) | |  | | 11 (0.24%, 39.3%) |  |
| Overweight | | 67 (0.57%) | | | |  | | 16 (0.14%, 23.9%) | |  | | 34 (0.29%) | |  | | 3 (0.03%, 8.8%) |  |
| Obesity | | 37 (0.59%) | | | |  | | 14 (0.22%, 37.8%) | |  | | 11 (0.17%) | |  | | 3 (0.05%, 27.3%) |  |
| Blood pressure status (99.7%) | |  | | | | **<0.0001** | |  | | 0.307 | |  | | 0.144 | |  | **0.028** |
| normal | | 319 (0.80%) | | | |  | | 61 (0.15%, 19.1%) | |  | | 138 (0.35%) | |  | | 31 (0.08%, 22.5%) |  |
| Hypotension | | 3 (1.23%) | | | |  | | 1 (0.41%, 33.3%) | |  | | 2 (0.82%) | |  | | 1 (0.41%, 50.0%) |  |
| Pre-hypertension | | 432 (0.93%) | | | |  | | 99 (0.21%, 22.9%) | |  | | 160 (0.34%) | |  | | 24 (0.05%, 15.0%) |  |
| Hypertension type I | | 280 (1.10%) | | | |  | | 49 (0.19%, 17.5%) | |  | | 107 (0.42%) | |  | | 26 (0.10%, 24.3%) |  |
| Hypertension type II | | 23 (1.79%) | | | |  | | 3 (0.23%, 13.0%) | |  | | 8 (0.62%) | |  | | 2 (0.16%, 25.0%) |  |
| n – number of cases/records; statistically significant association are marked by bold p value (<0.05)  1 - % of all records within subcategory; 2 - % of All Valvar cases within subcategory; 3 - % of All non-Valvar cases within subcategory  Significance code: all significant differences marked in bold, and level of significance is color coded: p<0.05; p<0.01; p<0.0001. | | | | | | | | | | | | | | | | | |