

The Heritability of Liability to Talipes Equinovàrus and Genetic Counseling

Metin Atasu, D.V.M.** / Talât Göğüş, M.D.*** /
Burhan Say, M.D.****

Some conditions not fitting into simple Mendelian inheritance are nevertheless thought to be hereditary in origin, since their incidence among the relatives of patients seems to be much greater than those observed in the general population. The heritability of liability in such conditions is not as easy to calculate as it is in the quantitative characters. Talipes equinovàrus is a good example in this respect since there are many hypothesis about its inheritance. Palmer has pointed out that there are two types of talipes; one of them is dominant and shows 40 per cent penetrance while in the other, affecting males only, the role of heredity has yet to be established. In this latter type of case the heredity is determined with additive influence of more than one allele genes. It is necessary to estimate the heritability in order to find out this proposed influence.¹

The study presented below has been made in order to estimate this liability.

Materials and Methods

At the Orthopedic Department of Hacettepe University 110 talipes cases were studied. As a general population 9,947 newborn cases have been taken from Ankara Maternity Hospital.² The heritability of liability to talipes was estimated according to Falconer's method.³

* From the Departments of Pediatrics, Orthopedic Surgery and Division of Clinical Genetics, Hacettepe University, Ankara, Turkey.

** Instructor in Clinical Genetics and Statistics

*** Associate Professor of Orthopedics

**** Professor of Pediatrics

Application and Results

Since talipes equinovàrus have not been observed on the parents of the cases, they are accepted as heterozygotes. According to this hypothesis, analyses have been made and the results suggested that there is no sex-linked or autosomal dominant inheritance in talipes. Therefore, the heritability of liability has been estimated by the following equations.

$$b = \frac{x_g - x_r}{a_g} \quad (1)$$

$$h^2 = 2.b \quad (2)$$

The standard error of h^2 is found as

$$V_b = \frac{I}{(a_g)^2} \times \frac{P}{(a_r)^2 \times A} \quad (3)$$

and

$$SE (h^2) = 2 \times \sqrt{V_b} \quad (4)$$

The following symbols have been used for the equations:

q : Frequency of affected individuals

p : 1-q

x_g and a_g : The values connected with q in the general population and found from Table I.

x_r and a_r : The values connected with q which is estimated from the sibs of patients and found from Table I.

b : Regression value of patients' relatives

V_b : Sampling variance of b

h^2 : The heritability of liability

N : Number of individuals in the sample

A : Observed number of affected individuals in the sample.

The incidence of talipes equinovàrus among brothers and sisters of the male patients as well as among the brothers and sisters of the female patients have been estimated. From equation (1) when we replace the observed values, the following b value in male sibs of male patients becomes,

$$b = \frac{2.989 - 2.226}{3.273} = 0.233$$

TABLE I
NORMAL DEVIATE VALUES CORRESPONDING TO Q AND THE MEAN
DEVIATIONS OF AFFECTED INDIVIDUALS

q%	x	a	q%	x	a	q%	x	a	q%	x	a
			0.50	2.576	2.892	1.00	2.326	2.665	1.50	2.170	2.525
0.01	3.719	3.960	0.51	2.569	2.886	1.01	2.323	2.662	1.51	2.167	2.522
0.02	3.540	3.790	0.52	2.562	2.880	1.02	2.310	2.658	1.52	2.165	2.520
0.03	3.432	3.687	0.53	2.556	2.853	1.03	2.315	3.655	1.53	2.162	2.518
0.04	3.353	3.613	0.54	2.549	2.868	1.04	2.312	2.652	1.54	2.160	2.515
0.05	3.291	3.554	0.55	2.543	2.862	1.05	2.308	2.649	1.55	2.157	2.513
0.06	3.239	3.507	0.66	2.536	2.856	1.06	2.304	2.654	1.56	2.155	2.511
0.07	3.195	3.464	0.57	2.530	2.850	1.07	2.301	2.642	1.57	2.152	2.508
0.08	3.156	3.429	0.58	2.524	2.845	1.08	2.297	2.639	1.58	2.149	2.506
0.09	3.121	3.397	0.59	2.518	2.839	1.09	2.294	2.636	1.59	2.147	2.502
0.10	3.090	3.367	0.60	2.512	2.834	1.10	2.209	2.633	1.60	2.144	2.507
0.11	3.062	3.341	0.61	2.506	2.829	1.11	2.287	2.630	1.61	2.142	2.499
0.12	3.036	3.317	0.62	2.501	2.823	1.12	2.283	2.627	1.62	2.139	2.494
0.13	3.012	3.294	0.63	2.495	2.818	1.13	2.280	2.624	1.63	2.137	2.495
0.14	2.989	3.273	0.64	2.489	2.813	1.14	2.277	2.921	1.64	2.135	2.493
0.15	2.968	3.253	0.65	2.484	2.808	1.15	2.273	2.618	1.65	2.132	2.491
0.16	2.948	3.234	0.66	2.478	2.803	1.16	2.270	2.615	1.66	2.130	2.489
0.17	2.929	3.217	0.67	2.473	2.798	1.17	2.267	2.612	1.67	2.127	2.485
0.18	2.911	3.201	0.68	2.462	2.793	1.18	2.264	2.609	1.68	2.125	2.484
0.19	2.894	3.185	0.69	2.462	2.789	1.19	2.260	2.606	1.69	2.122	2.482
0.20	2.878	3.170	0.70	2.457	2.457	1.20	2.257	2.603	1.70	2.120	2.480
0.21	2.863	3.156	0.71	2.452	2.779	1.21	2.254	2.600	1.71	2.118	2.478
0.22	2.848	3.142	0.72	2.447	2.775	1.22	2.251	2.597	1.72	2.115	2.476
0.23	2.834	3.129	0.73	2.442	2.770	1.23	2.248	2.594	1.73	2.113	2.474
0.24	2.820	3.117	0.74	2.437	2.766	1.24	2.244	2.591	1.74	2.111	2.474
0.24	2.820	3.117	0.74	2.437	2.766	1.24	2.244	2.591	1.74	2.111	2.474
0.25	2.807	3.104	0.75	2.432	2.761	1.25	2.241	2.589	1.75	2.108	2.70
0.26	2.794	3.093	0.76	2.428	2.757	1.26	2.238	2.586	1.76	2.106	2.467
0.27	2.782	3.081	0.77	2.423	2.753	1.27	2.235	2.583	1.77	2.104	2.465
0.28	2.770	3.070	0.78	2.418	2.748	1.28	2.232	2.580	1.78	2.101	2.463
0.29	2.759	3.060	0.79	2.414	2.744	1.29	2.229	2.578	1.79	2.099	2.461
0.30	2.748	3.050	0.80	2.409	2.740	1.30	2.226	2.575	1.80	2.097	2.499
0.31	2.737	3.040	0.81	2.404	2.736	1.31	2.223	2.572	1.81	2.095	2.457
0.32	2.727	3.030	0.82	2.400	2.732	1.32	2.220	2.570	1.82	2.092	2.455
0.33	2.716	3.021	0.83	2.395	2.728	1.33	2.217	2.567	1.83	2.090	2.453
0.34	2.706	3.012	0.84	2.391	2.724	1.34	2.124	2.564	1.84	2.088	2.451
0.35	2.697	3.003	0.85	2.387	2.720	1.35	2.211	2.562	1.85	2.086	2.449
0.36	2.687	2.994	0.86	2.382	2.716	1.36	2.209	2.559	2.86	2.084	2.447
0.37	2.678	2.986	0.87	2.378	2.712	1.37	2.206	2.557	1.87	2.081	2.445
0.38	2.669	2.978	0.88	2.374	2.708	1.38	2.203	2.554	1.88	2.079	2.444
0.39	2.661	2.969	0.89	2.370	2.704	1.39	2.200	2.552	1.89	2.077	2.442
0.40	2.652	2.962	0.90	2.366	2.701	1.40	2.197	2.549	1.90	2.075	2.440
0.41	2.644	2.954	0.91	2.361	2.697	1.41	2.194	2.547	1.91	2.073	2.438
0.42	2.636	2.947	0.92	2.357	2.693	1.42	2.192	2.544	1.92	2.071	2.436
0.43	2.628	2.939	0.93	2.353	2.690	1.43	2.189	2.542	1.93	2.068	2.434
0.44	2.620	2.932	0.94	2.349	2.686	1.44	2.186	2.539	1.94	2.066	2.432
0.45	2.612	2.925	0.95	2.346	2.683	1.45	2.183	2.537	1.95	2.064	2.430
0.46	2.605	2.918	0.96	2.342	2.679	1.46	2.181	2.534	1.96	2.062	2.428
0.47	2.597	2.911	0.97	2.338	2.767	1.47	2.178	2.532	1.97	2.060	2.426
0.48	2.590	2.905	0.98	2.334	2.672	1.48	1.275	2.529	1.98	2.058	2.225
0.49	2.583	2.898	0.99	2.330	2.669	1.49	2.173	2.527	1.99	2.056	2.423
0.50	2.576	2.892	2.00	2.326	2.665	1.50	2.170	2.525	2.00	2.054	2.421

From equation (2), the heritability of liability is found 46.6 per cent. Equation (3) gives the sampling variance:

$$V_b = \frac{1}{3.273^2} \times \frac{0.98701}{2.275^2 \times 1} = 0,0139$$

Then it is written as

$$V_b \times 10^4 = 1.39$$

From equation (4) the standard error of the heritability of liability is estimated as

$$SE (h^2) = 2 \times \sqrt{1.24} = \pm 2.358$$

Since there are no patients in the last three groups, the incidence is zero. As the incidence in females in talipes cases is small, the expected incidence will also be small. There is no difference between the estimated regression value and the incidence of zero.⁴ In fact, 0.95 confidence limits for the observed number is 3.66. This means that the incidence among the female sibs of the male cases is not different from 3.66/101. That is 3.20 per cent. Further calculations show that b is equal to 0.39 and h^2 is equal to 0.78. This is of course different from the first estimate.

h² and Genetic Counseling

If a mother who has a child affected with talipes equinovàrus wants to learn the risk of having another child affected similarly and if her child is male, the heritability of liability to talipes can be found by dividing the heritability figure by eight and replacing the obtained values in equation (1), as

$$0.466/8 = 0.0582 = \frac{2.989 - x_r}{3.273}$$

From this equation x_r is expected to be 0.063. From Table II at the line of 0.063 value we found 42 per cent. Accordingly the probability for the second child being affected similarly is 42/10 000.

Discussion

There are various observations on the subjects of the heredity of talipes equinovàrus. Isiggkeit reported that hereditary transmission of talipes is sex-linked recessive,⁵ while Staglietti pointed out that it is autosomal dominant,⁶ Palmer also thought it is autosomal dominant in some cases and sex-linked in others. He also suggested that in certain

patients no simple Mendelian inheritance could be demonstrated.⁶ Böö̈k showed that it is multifactorial.⁷ Falconer suggested a similar inheritance pattern with additive character.¹ Although Gö̈ğüş and Say could not rule out the possibility of sex-linked inheritance, they claimed that if the number of cases were increased, polygenic and additive inheritance may be also expected.⁸ Our results seem to confirm Falconer and Böö̈k's hypothesis. Furthermore, the heritability of liability as found by Falconer is approximately the same. According to this if there is no dominance in the talipes equinovàrus, there will be polygenic and additive inheritance.

TABLE II
STATISTICS CONNECTED WITH THE HERITABILITY OF LIABILITY
TO TALIPES EQUINOVARUS

	A	N	q	x	a	b	Vbx10 ⁴	h ² -SE
General Population								
Male	-	-	0.141	2.989	3.273	-	-	-
Female	-	-	0.080	3.156	3.429	-	-	-
Sibs of patients								
Male Male	1	77	1.300	2.226	2.575	0.233	1.39	0.466±2.358
Male Female	-	-	-	-	-	-	-	-
Female Male	-	-	-	-	-	-	-	-
Female Female	-	-	-	-	-	-	-	-

Summary

1. Pedigrees of talipes cases were analysed and it was suggested that this character had been determined by more than one and additive genes.

2. The heritability of liability to talipes equinovàrus in male sibs of male cases is 46.6±2.358 per cent.

3. The risk of having another male child affected with talipes is 42/10 000.

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