

G-6-PD Deficiency and Abnormal Hemoglobins in a Brazilian Population

F. M. Salzano, F. Lewgoy, C. V. Tondo, F. J. da Rocha

The prevalence of the polymorphisms for glucose-6-phosphate dehydrogenase deficiency (G-6-PDD) and abnormal hemoglobins has been extensively studied in several areas of the world. The correlation observed between the frequencies of these polymorphisms and falciparum malaria (Motulsky, 1964) indicated that perhaps the same selective agent was responsible for the high frequency of some of their alleles in present day human populations. Lewis and Hathorn (1965) and Lewis et al (1966), on the other hand, suggested that the G-6-PD defect might protect patients against the hazards of the sickle cell disease. These two genetic systems, therefore, would seem to offer an excellent model for studies in population genetics. Investigations performed in areas where they co-exist in the presence and absence of malaria could disclose possible changes in the adaptive fitness of carriers of the different gene combinations, and the consequent changes in gene frequencies followed through several generations. It is obvious that the direction and speed of these changes would depend to some extent on the adaptive fitness of the double carrier (AS/G-6-PDD in populations with high frequency of this abnormal hemoglobin). The present communication reports data bearing on this point from the Negroid population of Pôrto Alegre, Brazil, and reviews the information available for other areas in which malaria is present and absent.

Results and Discussion

Tab. I shows the results obtained in 316 males and 679 females who were tested simultaneously for abnormal hemoglobins and G-6-PD. Four double carriers (AS/G-6-PDD) were observed among the males and on the basis of the isolated frequency of each abnormality exactly four would be expected. As far as females are concerned, we observed eleven double carriers while the expected number would be nine. In relation to the AC carriers none were found to be G-6-PD deficient while about two would be expected (one male and one female).

In Tab. II we have reviewed the data available concerning the AS/G-6-PDD relationship in African and American populations. As can be seen the number of

Tab. I. Incidence of G-6-PD deficiency and abnormal hemoglobins in the negroid population of Porto Alegre

Ethnic group	N. of indiv. studied	AA G-6-PD		AS G-6-PD		AC G-6-PD		Expected number of double carriers (AS/G-6-PDD)	Ratio Observed/Expected
		Def.	Normal	Def.	Normal	Def.	Normal		
<i>Men</i>									
Negroes	116	11	83	2	13	—	2	2	1.0
Dark Mulattoes	99	14	80	1	4	—	—	1	1.0
Light Mulattoes	101	10	82	1	6	—	2	1	1.0
Total	316	35	250	4	23	—	4	4	1.0
<i>Women</i>									
Negroes	197	31	140	6	17	—	3	4	1.5
Dark Mulattoes	225	29	172	2	19	—	3	3	0.7
Light Mulattoes	257	34	211	3	8	—	1	2	1.5
Total	679	94	523	11	44	—	7	9	1.2

Details about the groups studied, the sample methods and the G-6-PD technique can be found in Lewgoy and Salzano (1967); the techniques for detection of the abnormal hemoglobins were described in Tondo and Salzano (1960 and 1962).

Tab. II. Incidence of G-6-PD deficiency and hemoglobins in several populations of the world

Population	Author	N. of indiv. studied	AA G-6-PD		AS G-6-PD		Expected number of double carriers (AS/G-6-PDD)	Ratio Observed/Expected
			Def.	Normal	Def.	Normal		
<i>Men</i>								
Memphis, U.S.A.	Kraus et al (1962)	131	16	81	4	30	5	0.8
Curaçao, Neth. Antilles	Van der Sar et al (1964)*	443	59	314	3	67	10	0.3
Accra, Ghana	Lewis and Hathorn (1965)	150	16	93	6	15	4	1.5
Ifakara, Tanzania	Marti et al (1965)	408	49	284	10	65	11	0.9
Several, Surinam	Pik et al (1965)	785	122	531	19	113	24	0.8
Several, Congo	Motulsky et al (1966)	1,594	193	1,129	55	217	48	1.2
P. Alegre, Brazil	This communication	312	35	250	4	23	3	1.3
<i>Women</i>								
Memphis, U.S.A.	Kraus et al (1962)	50	1	12	1	36	1	1.0
Curaçao, Neth. Antilles	Van der Sar et al (1964)*	121	5	59	6	49	5	1.2
Accra, Ghana	Lewis and Hathorn (1965)	118	12	76	8	22	5	1.6
Pôrto Alegre, Brazil	This communication	672	94	523	11	44	9	1.2
<i>Men + Women</i>								
Chicago, U.S.A.	Naylor et al (1960)	156	11	89	16	40	10	1.6
Ibadan, Nigeria	Gilles et al (1967)	100	6	90	0	4	0	1.0

* These authors did not separate the different abnormal hemoglobin types for this analysis, simply stating that "The abnormal hemoglobin subjects were mostly AS".

double carriers observed does not deviate significantly from expectation. Among male samples, there are slightly less double carriers (ratio of observed/expected generally less than one). In the female samples all ratios have values of one or above but, as stated, the deviations are not significant. The only exception is the result obtained by Naylor et al (1960) which shows more double carriers than expected, but this is a rather selected sample and the authors did not separate the results concerning the AS heterozygotes by sex.

At least four of the populations for which data are available (those of Tanzania, Surinam, Congo and Nigeria) live in regions where malaria is endemic. They do not show any excess of double carriers, as would be expected if the G-6-PDD gene would in some way give additional advantage to these persons. Since there is no difference between the results obtained in populations living in regions with or without malaria, there seem to be no grounds for postulating adaptive interaction between the two polymorphisms. Therefore the rate of decrease of the abnormal genes of these two systems in American non-malarious areas should follow in a general way the curves calculated by Livingstone (1964) for each system separately. The contention of Lewis and Hathorn (1965) and Lewis et al (1966) that the *homozygotes* SS would benefit from the presence of the G-6-PDD condition remains to be tested. But since these homozygotes rarely reproduce, any advantage which they would have would be meaningless from an evolutionary point of view.

Summary

Data are reported about the occurrence of glucose-6-phosphate dehydrogenase deficiency (G-6-PDD) and abnormal hemoglobins in a sample (316 males and 679 females) of the Negroid population of Pôrto Alegre, Brazil. The prevalence of double carriers (AS/G-6-PDD) was that expected from the isolated incidence of both anomalies. A review of the literature shows similar results for 3491 males and 289 females from African and American Negroid groups both from areas with and without malaria. Therefore there seem to exist no grounds for postulating an adaptive interaction between these two polymorphisms.

Acknowledgements

Thanks are due to Mr. Cleuder V. Simões for laboratory help and to Mr. Girley V. Simões for assistance in the analysis of the data. This work has been supported in part by the Rockefeller Foundation, Conselho Nacional de Pesquisas, Conselho de Pesquisas da Universidade Federal do Rio Grande do Sul, and PHS research grants GM-08238 and HE-07430, Division of General Medical Sciences and Heart, Public Health Service, U.S.A.

References

- GILLES H. M., HENDRICKSE R. G., LINDNER R., REDDY S., ALLAN N. (1967). G-6-PD deficiency, sickling, and malaria in African children in South Western Nigeria. *Lancet*, **1**: 138-140.
- KRAUS A. P., NEELY C. L., CAREY F. T., KRAUS L. M. (1962). Detection of deficient erythrocyte regeneration of reduced triphosphopyridine nucleotide from glucose-6-phosphate. Evaluation of a rapid screening test. *Ann. Intern. Med.*, **56**: 765-773.
- LEWGOY F., SALZANO F. M. (1967). G-6-PD deficiency gene dynamics in a Brazilian population. *A.Ge.Me.Ge.* (In press).
- LEWIS R. A., HATHORN M. (1965). Correlation of S hemoglobin with G-6-PD deficiency and its significance. *Blood*, **26**: 176-180.
- KAY R. W., HATHORN M. (1966). Sickle cell disease and G-6-PD. *Acta Haemat.*, **36**: 399-411.
- LIVINGSTONE F. B. (1964). Aspects of the population dynamics of the abnormal hemoglobin and G-6-PD deficiency genes. *Amer. J. Hum. Genet.*, **16**: 435-450.
- MARTI H. R., SCHOEPF K., GSELL O. R. (1965). Frequency of haemoglobin S and G-6-PD deficiency in Southern Tanzania. *Brit. Med. J.*, **1**: 1476-1477.
- MOTULSKY A. G. (1964). Hereditary red cell traits and malaria. *Amer. J. Trop. Med. Hyg.*, **13**: 147-158.
- VANDEPITTE J., FRASER G. R. (1966). Population genetics studies in Congo. I. G-6-PD deficiency, hemoglobin S, and malaria. *Amer. J. Hum. Genet.*, **18**: 514-537.
- NAYLOR J., ROSENTHAL I., GROSSMAN A., SCHULMAN I., HSIA D. Y. (1960). Activity of G-6-PD in erythrocytes of patients with various abnormal hemoglobins. *Pediatrics*, **26**: 285-292.
- PIK C., LOOS J., JONXIS J. H. P., PRINS H. K. (1965). Hereditary and acquired blood factors in the Negroid population of Surinam. II. The incidence of haemoglobin anomalies and the deficiency of G-6-PD. *Trop. Geogr. Med.*, **1**: 61-68.
- TONDO C. V., SALZANO F. M. (1960). Hemoglobin types of the Caingang Indians of Brazil. *Science*, **132**: 1893-1894.
- — (1962). Abnormal hemoglobins in a Brazilian Negro population. *Amer. J. Hum. Genet.*, **14**: 401-409.
- VAN DER SAR A., SCHOUTEN H., STRUYKER BOUDIER A. M. (1964). G-6-PD deficiency in red cells. Incidence in the Curaçao population, its clinical and genetic aspects. *Enzymologia*, **27**: 289-310.

RIASSUNTO

Sono presentati dati sulla presenza di deficienza di glucosio-6-fosfato deidrogenasi (G-6-PDD) ed emoglobine anormali in un campione (316 uomini e 679 donne) della popolazione negroide di Pôrto Alegre, Brasile. La prevalenza dei portatori doppi (AS/G-6-PDD) era prevista d'accordo con l'incidenza isolata di entrambe le anomalie. Una revisione della letteratura mostra risultati analoghi per 3491 uomini e 289 donne provenienti dai gruppi negroidi africani e americani che vivono in aree con e senza malaria. Non sembra pertanto esistano ragioni sufficienti per formulare una interazione adattativa fra questi due polimorfismi.

RÉSUMÉ

L'on présente des données sur la présence simultanée des déficiences en glucose-6-phosphate deshydrogénase (G-6-PDD) et d'hémoglobines anormales dans un échantillon (316 hommes et 679 femmes) de la population noire de Pôrto Alegre, Brésil. Le pourcentage de conducteurs doubles (AS/G-6-PDD) fut celui espéré en accord avec les pourcentages de chacune des anomalies isolément. Une révision de la littérature montre des résultats semblables pour 3491 hommes et 289 femmes appartenant à des groupes noirs d'Afrique et d'Amérique vivant dans des régions avec ou sans malaria. En conséquence il ne semble pas y avoir de raisons pour postuler une interaction adaptative entre ces deux polymorphismes.

ZUSAMMENFASSUNG

In der folgenden Arbeit bringen Verff. Angaben über die Häufigkeit ungenügender Funktion bei Glukose-6-Phosphat-Deshydrogenase (G-6-PDD) und anormalen Hämoglobinen in Material (316 Männer und 679 Frauen) negroider Bevölkerung aus Pôrto Alegre, Brasilien. In Einklang mit isoliertem Vorkommen beider Anormalitäten, konnte das Überwiegen der Träger des doppelten Faktors (AS/G-6-PDD) erwartet werden. Aus der Revision der Literatur gehen ähnliche Resultate hervor, bei 3491 Männern und 289 Frauen aus negroiden Gruppen Afrikas und Amerikas und aus Gegenden mit und ohne Malaria. Deswegen scheint kein Grund zur Annahme einer Interaktion der Adaptation dieser beiden Polymorphismen vorzuliegen.

Dr. F. M. Salzano: Departamento de Genética, Instituto de Ciências Naturais, Universidade Federal do Rio Grande do Sul, Pôrto Alegre, Brazil.

Drs. F. Lewgoy, C. V. Tondo, F. J. da Rocha: *id.*