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MATERIAL SCREENING OF β-THALASSEMIA CARRIER USING DRIED BLOOD SAMPLES COLLECTED ON FILTER PAPER.

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β-thalassemia is an autosomal recessive genetic disease. Because of the high incidence (1-3%) of β-thalassemia carrier in Taiwan, a mass screening program directing to prospective prevention of homozygous β-thalassemia is strongly indicated. Since hemoglobin A_2(HbA_2) is increased in β-thalassemia carrier, a method to determine HbA_2% in the dried blood spots collected on filter paper by microchromatography was developed by our laboratory in 1991. Because hemoglobin E (HbE), the most common hemoglobinpathy in Southeast Asia, can't be differentiated from HbA_2 by the microchromatographic method, a method for analysis of globin chain in dried blood spots by HPLC with reverse phase C4 column was established for differential diagnosis. To detect the HbE mutation (G→A) and the four common Southern Chinese β-thalassemia mutations, namely Codon 17(A→T), 41/42 frameshift (-TCTT-deletion), -28 TATA(A→G), and IVS-II 654 (C→T), with the same dried blood spot screening specimens, a non-radioactive method by analyzing the restriction fragments of the polymerase chain reaction (PCR) amplified DNA was also developed. During 1992, a pilot maternal β-thalassemia carrier screening program was carried out in rural areas (Taitung and Nantou Counties) of Taiwan. 0.5ml venous blood of pregnant women with gestation age no more than 18 weeks was collected and immediately spotted on filter paper by 30 local health Stations, 3 Obstetrics Clinics, and 2 Hospitals. The blood sample was air-dried, sealed in plastic bag, and mailed to our laboratory for analysis. Out of the 2,867 samples screened, 117 cases (3.5%) were positive (HbA_2% > 3.2%). Among the 111 (95%) successfully recalled positive cases, 45 were confirmed to be β-thalassemia carriers and 1 case with 21.1% of HbA_2% was found to be HbE carrier. The HbA_2% values of confirmed β-thalassemia carriers were between 3.4% and 5.4%. The range of MCV and MCH of the β-thalassemia carriers were determined by local referral hospitals and were reported from 60 to 87fl and 18.5 to 31pg, respectively. The incidence of β-thalassemia carrier was estimated to be around 1.7% in Taiwan. 37 cases (82%) of the 45 β-thalassemia carriers were found to have one of the four common Chinese β-thalassemia mutations. 6(13%) Codon 17, 13(29%) IVS-II 654, 10(22%) 41/42 frameshift, and 8(18%) TATA were detected. The mutation analysis were confirmed by allelic specific oligonucleotides probes. The results indicated that the dried blood specimens, which is convenient for sample collection and transportation, could be used for mass maternal β-thalassemia carrier screening program even in the rural areas. The restriction fragments analysis developed in this study presented a fast and non-radioactive method to detect the β-thalassemia mutations and HbE mutations using the same dried blood spot screening specimens and may be applied on amniotic or chorionic villi samples for prenatal diagnosis.

RETYPED FOR PRESENTATION