

Research Letters

Partial Exchange Transfusion as an Adjunct to the Treatment of Severe Falciparum Malaria in Children

Exchange transfusion has been recommended as an adjunct to the treatment of severe *Falciparum* malaria, although there is no well designed clinical trial to prove its efficacy. Our review of literature reveals that, with the exception of three cases^{1,2} the published case reports are confined almost exclusively to the adult population and large volumes of blood have been used in most cases.²⁻⁴ The amount of compatible blood required for total exchange is rarely available in areas endemic for malaria and the risks of the procedure including transfusion-related infections are high. Moreover, the parasite count falls dramatically over time, the steepest decline occurring early in the procedure.^{5,6} This is the rationale for using partial exchange transfusion. There is only one isolated case report of partial exchange from India.⁷ We therefore decided to determine the efficacy of partial exchange transfusion as an adjunct to the treatment of severe *Falciparum* malaria in children.

Partial exchange transfusion was performed on all children with severe *Falciparum* malaria, as defined by the World Health Organization,⁸ admitted to St John's Medical College Hospital between December 1997 and September 1998. A total of 20 malaria cases were admitted during this period, of which 5 (25 per cent) had severe *Falciparum* malaria.

Vascular access was established through a radial artery cannula and a peripheral venous cannula in four out of five subjects. Vascular access was established through a femoral cannula in the other subject. The partial exchange was done by sequentially withdrawing and infusing 20 ml of blood. The volume of

blood used was 40 ml/kg and the total volume of blood used varied from 500 to 900 ml. Vital signs were monitored closely throughout the procedure. Parasitaemia was estimated pre-exchange and immediately post-exchange. All five children were administered quinine pre- and post-exchange.

The children were between 3 and 8 years of age. The duration of symptoms prior to admission varied from 3 to 20 days and two children were in altered sensorium on admission. The time gap between admission and commencement of the exchange varied from 8 to 12 h (Table 1).

Four of the five children had pre-exchange hyperparasitaemia ranging from 6 to 90 per cent and the other child had a parasitaemia of 2.1 per cent. There was a significant decrease in parasitaemia following partial exchange ranging from 5 to 88 per cent among the children who showed hyperparasitaemia. Patients with hyperparasitaemia are at increased risk of developing all the dangerous manifestations of *Falciparum* malaria. The risk is roughly proportional to the parasitaemia⁹ and significant mortality occurs despite appropriate parenteral antimalarial chemotherapy and general supportive care.⁵ The child with a parasitaemia of 2.1 per cent was in altered sensorium on admission and the neurological status of the child improved progressively during the procedure and immediately post-exchange. This indicates that rapid reduction in parasite load is not the sole beneficial effect of exchange transfusion. The procedure was well tolerated by all the children. All five children survived and were discharged within 10 days.

The procedure of exchange transfusion still remains controversial and its exact technique has been poorly described.³ The minimum volume for effective exchange has not been defined. The volume of blood used in our study was 40 ml/kg (half volume exchange).

We conclude that, partial exchange transfusion is a useful adjunct to the treatment of severe *Falciparum*

TABLE 1
Clinical profile of five cases of severe Falciparum malaria who underwent partial exchange transfusion

	Case 1	Case 2	Case 3	Case 4	Case 5
Age (years)	3	7	8	7	4
Weight (kg)	12	19	22	15	18
Sensorium	Irritable	Coma	Irritable	Irritable	Coma
Seizures	-	+	-	-	-
Jaundice	+	-	+	-	+
Hb (gm/dl)	8.3	11.1	8.9	4.5	4.9
Thrombocytopenia	+	+	+	+	+
Parasitaemia (%)					
pre-exchange	90	2.1	70	15	6
post-exchange	1.5	1.2	8	6	1
Volume of blood (ml)	500	800	900	600	720

malaria in children. Further assessment of the efficacy and feasibility of this technique is warranted.

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References

1. Rudnitsky G, Miller KD, Padua T, Stull TL. Continuous infusion quinine gluconate for treating children with severe *Plasmodium falciparum* malaria. *J Infect Dis* 1987; 155: 1040–43.
2. Miller KD, Greenberg AE, Campbell CC. Treatment of severe malaria in the United States with a continuous infusion of quinine gluconate and exchange transfusion. *N Engl J Med* 1989; 321: 65–70.
3. Phillips P, Nantel S, Benny WB. Exchange transfusions as an adjunct to the treatment of severe *Falciparum* malaria: case report and review. *Rev Infect Dis* 1990; 12: 1100–8.
4. Saddler M, Barry M, Ternouth I, Emmanuel J. Treatment of severe malaria by exchange transfusion. *N Engl J Med* 1990; 322: 58.
5. Vanden Ende J, Moorkens G, Van Gompel A, *et al.* Twelve patients with severe malaria treated with partial exchange transfusions: comparison between mathematically predicted and observed effect on parasitaemia. *Trop Geogr Med* 1994; 46: 340–45.
6. Wilkinson RJ, Brown JL, Pasvol G, Chiodini PL, Davidson RN. Severe *Falciparum* malaria: predicting the effect of exchange transfusion. *Q J Med* 1994; 87: 553–57.
7. Aquinas SR, Ross C, Vincent J, Sridhar C. Partial exchange transfusion in the treatment of severe *Falciparum* malaria. *Natl Med J India* 1996; 9: 163–65.
8. World Health Organization Malaria Action Programme. Severe and complicated malaria. *Trans R Soc Trop Med Hyg* 1986; 80 (Suppl): 3–50.
9. Field JW. Blood examination and prognosis in acute *Falciparum* malaria. *Trans R Soc Trop Med Hyg* 1949; 43: 33–48.

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HIV Seroprevalence by ELISA in High Risk Indian Children and Their Presentation

Considering that most of the HIV in children occurs through vertical transmission and approximately 1 per cent of the pregnant women in Bombay are seropositive,¹ we studied the seroprevalence of HIV in high-risk group children, by expanding the World Health Organization (WHO) high-risk criteria.² A total of 47 children fulfilled the WHO high-risk criteria² and 11 more were included after expanding the criteria by adding grade IV protein-energy malnutrition and disseminated tuberculosis as cardinal findings. Tuberculosis of two or more organs was taken as disseminated tuberculosis. All the children were screened for HIV seroprevalence by

ELISA, as well as the parents of the children found seropositive. A repeat ELISA by another kit was done in all positive patients. Informed consent was taken for testing. The clinical presentations of the children were documented and all of them were investigated for the presence of tuberculosis, as well as bacterial and fungal infections (see Table 1).

Of the 58 who fulfilled the expanded high risk criteria 10 (17.24 per cent) were positive for HIV. Six (12.76 per cent) out of 47 were positive for HIV according to WHO criteria. Although the difference between these two prevalence values was not significant ($p = 0.64$) there was a 5 per cent increase in detection of positive cases. It is interesting to note that after expanding the WHO criteria for high risk, four children, two of them with disseminated tuberculosis and two with grade IV malnutrition, were tested positive. *Mycobacterium tuberculosis* from sputum and lymph node biopsy in two children, *Candida albicans* from oral thrush and urine, *Salmonella typhi* and *Staphylococcus aureus* from blood, and *Acinobacter* sp. from subcutaneous abscess were the isolates in the ELISA-positive children.

Children are caught in the HIV epidemic as innocent bystanders. Most of the studies for the seroprevalence of HIV have been carried out on adults in the developing countries, except for two published reports.^{1,3} Most of the children in the present study were below the age of 3 years, which is comparable to the other published studies.

In our study, vertical transmission was 90 per cent, 71.4 per cent in Bombay. In Nigeria, blood transfusion was the major route (47.6 per cent) and vertical transmission accounted for 20.6 per cent. Blood transfusion as a mode of HIV transmission was noted in 14.3 per cent in Bombay. Grade IV malnutrition, chronic diarrhoea, generalized lymphadenopathy were the main features. Nineteen per cent of the Nigerian children had skin manifestations which was not noted in our study. In a Zambian study, HIV seroprevalence was found to be 37 per cent among the children with tuberculosis as compared to 11 per cent among those without tuberculosis.⁴ This study endorses our view of using disseminated tuberculosis as an isolated cardinal sign for including children under the high-risk category.

The epidemiological features for a paediatric HIV vary from country to country. Compulsory HIV screening of blood for transfusion has been adopted as a policy in some of the developing countries in the last few years. Many children receive multiple pricks with non-sterile needles in most of the developing countries. In the urban areas of developing countries, poor and destitute children are subjected to drug and sexual abuse. In the wake of our observation of increased HIV seroprevalence rates by expanding the standard criteria and the above mentioned socio-cultural factors, there is a need to redefine the WHO criteria in respect of the geographic areas. We feel

TABLE 1
Clinical profile of screened and seropositive children

	Screened children (n = 58)	ELISA positive (n = 10)
Age (years)		
1.5-3	20	6 (60%)
3-6	23	2
>6	15	2
Sex		
M	31	8 (80%)
F	27	2
Transmission		
Vertical		9
Secondary		1
Clinical presentation		
Chronic diarrhoea	21 (36.2%)	6 (60%)
Progressive weight loss	10 (17.24%)	1 (10%)
Persistent fever	10 (17.24%)	1 (10%)
Generalized lymphadenopathy	8 (13.79%)	2 (20%)
Grade IV protein-energy malnutrition	12 (20.68%)	6 (60%)
Hepato splenomegaly	4 (6.89%)	1 (10%)
Disseminated tuberculosis	9 (15.51%)	2 (20%)
Recurrent respiratory infection	12 (20.68%)	1 (10%)
Candidiasis	2 (3.44%)	2 (20%)

that the following are risk groups which should be included in HIV screening programmes: grade IV protein-energy malnutrition; disseminated tuberculosis; children who received blood transfusions before mandatory HIV screening for donors was introduced; children of professional sex workers; children staying in foster homes, and destitute and street children. More studies are needed to confirm our observations.

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References

1. Merchant RH, Shorff RC. HIV seroprevalence in disseminated tuberculosis and chorionic diarrhoea. *Ind Pediatr* 1998; 35: 883-87.
2. Tindyebwa D, Marum L. Diagnosing HIV. *AIDS Action* 1995; 27: 4-5.
3. Emodi IJ, Okafor GO. Clinical manifestation of HIV infection in children at Enugu Nigeria. *J Trop Pediatr* 1998; 44: 73-6.
4. Quinn TC, Mann JM, Curan JW. AIDS in Africa, an epidemiological paradigm. *Science* 1996; 234: 955-63.

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Serum Interleukin-2 and Interleukin-6 Levels in Zinc Deficiency

It has been well established that several trace elements have an essential role in metabolic pathways and immune cell function.¹ However, there have been very few data about the effects of micronutrients on the production of interleukins.²⁻⁶

Zinc is a micronutrient, which plays an important role in growth and many physiological functions including the regulation of some lymphocyte functions such as mitogenesis, antibody synthesis, activation of T lymphocytes and natural killer (NK) cells.^{4,5,7,8} Zinc deficiency reduces the number of CD₃/CD₂₅ cells bearing the interleukin-2 (IL-2) receptor on their surface, and hence leads to a decrease in the production of IL-2. Zinc may be essentially required for IL-2 mediated T-cell activation.^{6,9}

In this study, we aimed to investigate the effect of zinc on the production of interleukin-2 and interleukin-6 (IL-6) in zinc-deficient children by determining the levels of these interleukins before and after zinc supplementation.

Twelve children between the ages of 6 months and 3 years were included in the study (mean age 16.16 ± 7.82 months) and 10 healthy children with similar ages comprised the control group (mean age 22.60 ± 10.89 months). Patients were considered zinc deficient if their plasma zinc levels were below 70 µg/dl, which was estimated to be 2 SD below the control

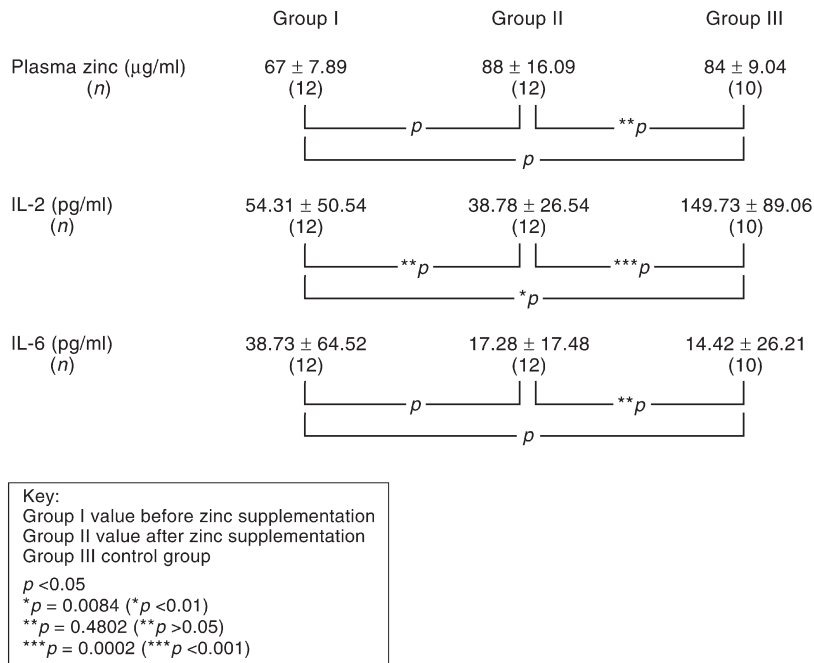


FIG. 1. Characteristics of patients (mean ± SD).

group's values. Plasma zinc levels were measured by using previously described methods.¹⁰

The serum IL-2 and IL-6 concentrations were measured by an enzyme-linked immunoabsorbent assay (Endogen, Boston, MA, USA).

The children in the test group received 2 mg/kg/day elemental zinc in the form of zinc sulphate syrup for 3 months. At the end of zinc supplementation all the parameters were studied again.

Data were analysed by using SPSS software (Statistical Package for the Social Sciences, SPSS Inc., Chicago, IL). Wilcoxon matched-pairs signed rank and Mann-Whitney *U*-Wilcoxon ranks sum *W* tests were used to test for significance of results. Statistical significance was established at $p < 0.01$.

The mean values in patients are given in Fig. 1. Although we had found a significantly lower level of IL-2 in the zinc-deficient group compared with the control group, after zinc supplementation their levels still remained lower than in the control group. The amount and the duration of the zinc supplementation in our study might have been inadequate to normalize the serum IL-2 levels, even when it seemed to be adequate to normalize plasma zinc levels.

Prasad¹¹ observed decreased serum thymulin activity, decreased production of IL-2, decreased NK cell activity, decreased production of TNF- α and increased production of IL-1 β and IL-6 in the

experimental human model during the zinc depletion phase.

Grüngreiff, *et al.*¹² examined the effect of zinc supplementation in patients with chronic liver disease with reduced serum zinc levels. They found decreased concentrations of elevated cytokine (IL-6 and IL-10).

In our study IL-6 levels were found to be significantly higher in the zinc-deficient group compared with the control group, which became normal in response to zinc supplementation, suggesting the effect of zinc on the production of IL-6.

In conclusion zinc deficiency may seem to influence the production of some cytokines but we have little information about its physiopathology.

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References

1. Bendich A, Chandra RK (eds) Micronutrients and Immune Functions. New York Academy of Sciences, New York, 1990.
2. Sipahi T, Akar N, Eğin Y, Cin Ş. Serum interleukin-2 and

- interleukin-6 levels in iron deficiency anemia. *J Pediatr Hematol Oncol* 1998; 15: 69–73.
3. Galan P, Thibault H, Preziosi P, Hercberg S. Interleukin-2 production in iron-deficient children. *Biol Trace Elem Res* 1992; 32: 421–26.
 4. Chandra RK, McBean LD. Zinc and immunity. *Nutrition* 1994; 10: 79–80.
 5. Keen CL, Gershwin ME. Zinc deficiency and immune function. *Ann Rev Nutr* 1990; 10: 415–31.
 6. Tanaka Y, Shiozawa S, Morimoto I, Fujita T. Role of zinc in interleukin 2 (IL-2) mediated T-cell activation. *Scand J Immunol* 1990; 31: 547–52.
 7. Aggett PJ. Zinc. *Ann Nestle* 1994; 52: 94–106.
 8. Fernandes G, Nair M, Onoe K, Tanaka T, Floid R, Good RA. Impairment of cell-mediated immunity functions by dietary zinc deficiency in mice. *Proc Natl Acad Sci USA* 1979; 76: 461.
 9. Prasad AS. Discovery of human zinc deficiency and studies in an experimental human model. *Am J Clin Nutr* 1991; 53: 403–12.
 10. Çavdar AO, Arcasoy A, Cin Ş, Babacan E, Gözdaşoğlu S. Geophagia in Turkey: Iron and zinc deficiency, iron and zinc absorption studies and response to treatment with zinc in geophagia cases. In: Prasad AS, Çavdar AO, Brewer GJ, Aggett PJ (eds) *Zinc Deficiency in Human Subjects*. Alan R Liss Inc, New York, 1983; 71–97.
 11. Prasad AS. Zinc and immunity. *J Trace Elem Exp Med* 1995; 8: 108.
 12. Grüngreif K, Reinhold D, Ansoerge S. Effect of zinc on immune cells and cytokines (IL-2, IL-6, IL-10, TGF- β 1) in vitro and in chronic liver disease. *J Trace Elem Exp Med* 1995; 8: 81–82.

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Plasma Zinc Levels in Patients with Iron-Deficiency Anemia

Iron deficiency is the most common single nutrient deficiency in the world. There is a marked variation, being highest in infancy and in patients of low socio-economic status.^{1,2} Zinc is also another important element which has structural and regulatory roles for enzymes, signal transduction pathways, and gene transcription systems. It is considered to be essential for cell division, and for DNA and protein synthesis.³ Causes for insufficient zinc intake during infancy are low zinc content of breastmilk, especially during late lactation, and low content and low bioavailability in consumed food.^{5,6} High prevalence of iron and zinc deficiency were reported in Turkey but, previous reports were based on either iron or zinc deficiency.^{7,8}

The aim of this study was to find out the incidence of zinc deficiency in patients with iron-deficiency anemia.

This study was performed at the Pediatric Hematology Department of Ankara University. One hundred children with the diagnosis of iron-deficiency anemia, between the ages of 6 months and 3 years (median 17.1 ± 8 months), were included. Subjects with recent infection or chronic disease, geophagia and those who had been taking iron or

zinc supplements were excluded. Twenty age- and sex-matched healthy children were taken as the control group. Hemoglobin (Hb), hematocrit, red blood cell count, mean corpuscular volume, and mean corpuscular hemoglobin were measured on a Counter Model T890. Blood smears were evaluated after Wright staining, and serum iron level was assayed spectrophotometrically (Perkin-Elmer Coleman 795 Spectrophotometer). Total iron-binding capacity (TIBC) was measured and the per cent transferrin saturation was calculated by multiplying the ratio of serum to TIBC by 100. Serum ferritin was determined by enzyme-linked immunoabsorbent assay, standardized using the international reference. Plasma zinc levels were measured by atomic absorption spectrophotometry (Perkin-Elmer model 2380), as described previously.⁹

Iron-deficiency anemia was defined according to WHO criteria by combination of abnormal values for the following indicators: hemoglobin below 10 g/dl, serum ferritin level < 12 ng/l, and transferrin saturation < 12 per cent.¹⁰ Patients were considered zinc deficient if their plasma zinc levels were below 70 μ g/dl which was 2 SD below the plasma zinc values in the control group (92.0 ± 10.9 μ g/dl). Subjects were considered zinc deficient if their plasma zinc levels were below 2 SD. The mean values in subjects of hemoglobin, serum iron, transferrin saturation, and serum ferritin levels were 9.38 ± 1.33 g/dl, 18.42 ± 9.14 μ g/dl, 8.55 ± 3.26 per cent, and 6.76 ± 2.18 ng/ml, respectively. Mean plasma zinc levels were found to be 92 ± 10.9 μ g/dl in the control group. In the subject group it was 84.5 ± 19 μ g/dl. Nineteen subjects (19 per cent) were zinc deficient (below 2 SD = 70 μ g/dl). Forty-two subjects had plasma zinc levels below 1 SD (Table 1).

Clinical features of zinc deficiency such as anorexia, failure to thrive, increased susceptibility to infection, and impaired immune function, are similar to those of iron deficiency. The common cause of zinc and iron deficiency is probably inadequate dietary intake, as dietary factors appear to play an important role in the pathogenesis of iron and zinc deficiency.^{2,3}

Our results revealed that it is necessary to determine the zinc status of patients diagnosed as suffering from iron-deficiency anemia and zinc

TABLE 1
Distribution of zinc-deficient patients according to 1 or 2 SD

	n	(%)
Plasma Zn: 70–80 mg/dl (1 SD below)	23	(23)
Plasma Zn: 70 mg/dl \downarrow (2 SD below)	19	(19)
Total	42	42

supplementation must be initiated following iron therapy.

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References

1. Lönnerdal B, Dewey KG. Epidemiology of iron deficiency in infants and children. *Ann Nestle* 1995; 53: 1–7.
2. Oski FA. Iron deficiency in infancy and childhood. *N Engl J Med* 1993; 329: 190–93.
3. Aggett PJ. Zinc. *Ann Nestle* 1994; 52: 94–106.
4. Michaelsen KF, Samuelson G, Graham TW, Lönnerdal B. Zinc intake, zinc status and growth in a longitudinal study of healthy Danish infants. *Acta Paediatr* 1994; 83: 1115–21.
5. Sandstead HH. Zinc deficiency. A public health problem? *Am J Dis Child* 1991; 145: 853–59.
6. Chandra RK, McBean LD. Zinc and immunity. *Nutrition* 1994; 10: 79–80.
7. Sözmén M. Ankara kentinde 0–6 yaş çocuklarda kan sayımı değerleri. PhD thesis, 1977.
8. Arcasoy A, Cavdar AO, Babacan E. Decreased iron and zinc absorption in Turkish children with iron deficiency and geophagia. *Acta Haematol* 1978; 60: 76–84.
9. Perkin-Elmer. Determination of zinc in serum. AA-Zn-1. In: *Clinical Methods for Atomic Absorption Spectroscopy*. Perkin-Elmer, Morwalk, Connecticut, 1971.
10. World Health Organization. Control of nutritional anaemia with special reference to iron deficiency, Technical Report no. 580. WHO, Geneva, 1972.

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Helicobacter pylori Seropositivity in Children with Diabetes Mellitus Type 1

There have been reports in recent years of an increased prevalence of dyspepsia in diabetic patients, although the causes underlying this association are poorly understood.^{1–3} The aim of the present study was to evaluate *Helicobacter pylori* serology in children who suffered from insulin-dependent diabetes mellitus (IDDM).

Forty children (mean age 12.84 ± 4.12 years) being followed-up for IDDM for 0.5–6.5 years and 37 age-matched normal healthy children (control group) (mean age 11.08 ± 3.58 years) were included in the study. None of the children from the control group had abdominal pain or other gastrointestinal symptoms. The evaluation of *H. pylori* infection was made by ELISA for anti-*H. pylori* IgG. The children in the patient group were selected randomly from the diabetic patients who had come to the outpatient department for routine control. All of these patients

were questioned for gastrointestinal symptoms, previous gastric or bowel surgery, chronic gastritis and intestinal problems. Patients were screened for diabetic complications; only three of the patients had mild neuropathy.

Comparing the children under and above 10 years of age, it was observed that the percentage of seropositivity increased by age, as also indicated in the literature.^{4–8} The rate of *H. pylori* seropositivity was significantly different ($p < 0.05$) between the diabetics (47.5 per cent) and the controls (18.9 per cent). The reason for this difference has not yet been explained clearly. IDDM is an immunocompromised disorder and diabetic patients are predisposed to develop a persistent infection eventually leading to atrophic gastritis.^{3,9} Frequent visits to hospital could lead to increased exposure to the pathogen, too. Gastroduodenitis was demonstrated by endoscopic examination in only one diabetic patient who had recurrent abdominal pain and dyspepsia. Other diabetic patients with *H. pylori* (Hp) seropositivity did not have such complaints.

There were no statistical differences between Hp (+) and Hp (–) diabetic patients for HbA1c and daily insulin requirement. But the seropositivity percentage was shown to increase with the duration of the illness ($p < 0.05$). None of the possible diabetic complications were related to *H. pylori* seropositivity. Two of the three neuropathic children were seronegative.

Diabetes in itself is a predisposing factor for *H. pylori* infection in the sense of HLA-associated genetic predisposition and not because of abnormal glycaemic control.⁷ It has been suggested that the HLA-DQA1 gene may contribute to susceptibility or resistance against *H. pylori* infection.¹⁰ *Helicobacter pylori* seropositivity may be the result of the host's immunogenic condition.

Gastric parietal cell autoantibodies (PCA) are found to be more frequent in children and adolescents with IDDM than in a non-diabetic population.¹¹ The authors detected a high association between PCA, *H. pylori* and chronic gastritis in IDDM, suggesting a pathogenic mechanism that increases the presence of PCA in *H. pylori*-infected patients. These findings may be related to our patients who are seropositive, although they have no symptoms.

The association between hyperglycemia and impaired gastric motility has also been investigated.¹² Intermittent attacks of hyperglycemia might lead to duodenogastric reflux of bile and contribute to the subsequent development of peptic dyspepsia. In addition to possible predisposing factors for *H. pylori* infections, mentioned above, impaired gastric motility could also be an etiological factor in diabetic gastric disorders.

In conclusion, in our study, the seropositivity of *H. pylori* was higher in the patient group than in

healthy children. This was not related to any of the diabetic control parameters. It may be suggested that IDDM children who are immunocompromised are more frequently exposed to *H. pylori*. But the real importance of the *H. pylori* infection in diabetic children is still obscure and needs further study.

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References

- Booth IW, Magnay AR. Peptic disease and childhood diabetes. *Lancet* 1993; 341: 868.
- Burghen GA, Murrell LR, Whittington GL, Klyce MK, Burstein S. Acid peptic disease in children with type 1 diabetes mellitus: a complicating relationship. *Am J Dis Child* 1992; 146: 718–22.
- Oldenburg B, Diepersloot RJA, Hoekstra JBL. High seroprevalence of *Helicobacter pylori* in diabetes mellitus patients. *Dig Dis Sci* 1996; 41: 458–61.
- Fioderek SC, Malaty HM, Evans DL, et al. Factors influencing the epidemiology of *Helicobacter pylori* infection in children. *Pediatrics* 1991; 88: 578–82.
- Killbridge PM, Dahms BB, Czinn SJ. *Campylobacter pylori* associated gastritis and peptic ulcer disease in children. *Am J Dis Child* 1988; 142: 1149–52.
- Shetty AK. *Helicobacter pylori* gastritis. *Arch Pediatr Adolesc Med* 1997; 151: 856.
- Poecoco M, Buratti E, Tommasini A, Torre G, Not T. High risk of *Helicobacter pylori* infection associated with cow's milk antibodies in young diabetes. *Acta Paediatr* 1997; 86: 700–3.
- Drumm B, Pérez-Pérez G, Blaser MJ, Sherman PM. Intra-familial clustering of *Helicobacter pylori* infection. *N Engl J Med* 1990; 322: 359–63.
- Winter WE, Chihara T. Autoimmune endocrinopathies. In: Lifshitz F (ed.), *Pediatric Endocrinology*, 3rd edn. Marcel Dekker Inc, New York, 1996; 715–29.
- Azuma T, Konishi J, Tanaka Y, et al. Contribution of HLA-DQA gene to host's response against *Helicobacter pylori*. *Lancet* 1994; 343: 542–43.
- Barrio R, Roldán MB, Alonso M, Cantón R, Camarero C. *Helicobacter pylori* infection with parietal cell antibodies in children and adolescents with insulin dependent diabetes mellitus. *J Ped Endoc Metab* 1997; 10: 511–15.
- Barnett JL, Owyand C. Serum glucose concentration as a modulator of interdigestive gastric motility. *Gastroenterology* 1988; 94: 739–44.

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Screening of Hemoglobinopathies in Kahramanmaraş Province (Turkey) Situated in a High Prevalence Area

Sickle-cell anemia and β -thalassemia are the most common genetic disorders in Çukurova, the lowlands between the Taurus mountains and the

Mediterranean sea in southern Turkey. A systematic survey previously carried out in the provinces of Hatay, Adana and İçel showed that the prevalence of the sickle-cell trait was 10.3, 9.3, and 10.5 per cent and that of β -thalassemia carriers was 5.7, 1.8, and 3.3 per cent, respectively. Consequently, premarital screening programs were officially started in these provinces.^{1–4}

We decided to screen the counties and the city of Kahramanmaraş, neighboring the high prevalence areas, to find if they were foci of these diseases. The sample sizes were calculated by EpiInfo 6.0 computer program at 95 per cent confidence level; participation was voluntary. A total of 1491 subjects, (601 males and 890 females aged 6–69 years) were investigated. Blood samples were collected into EDTA and analysed by cell Dyne-1700. Cellulose and agar gel electrophoresis were performed. Hemoglobin A₂ and hemoglobin F levels were determined by microcolumn chromatography and alkali denaturation, respectively, on samples with low MCV. No hemoglobin S was detected in the province.

The β -thalassemia trait was found only in the city of Kahramanmaraş, 0.93 per cent ($n = 751$). Hemoglobin O-Arab was detected for the first time in the province. Two cases of the hemoglobin-D trait were present (0.27 per cent). Overall the prevalence of β -thalassemia was 0.47 per cent. Thus, there seems to be no need to screen couples before marriage in order to detect carriers of hemoglobin disorders in the Kahramanmaraş province.

However, since the population of southern Turkey is at risk for hemoglobinopathies and is mobile, every individual should have knowledge of these disorders. A law passed in 1993 included hemoglobinopathies under primary healthcare status and implemented laboratories in Hatay, Adana, İçel, Muğla and Antalya on the Mediterranean and started premarital screening in these provinces. But the results of premarital screening showed the need for extensive genetic counselling and delivering education to the entire population.

The developed and the developing countries are conscious of the problem, and measures are being taken.⁵ A prevention program was organized in Marseille which depended on education, the detection of carriers, genetic counselling, and prenatal diagnosis.⁶ Education of the public, genetic counselling, screening, and availability of prenatal diagnosis has been in effect in Montreal for 20 years and the incidence of the disease is reported to have fallen by 95 per cent.⁷ Israel has suggested a national screening program for the whole country (population 5.7 million) with the emphasis that healthcare for the homozygous far exceeds the screening programs.⁸

In conclusion, factors such as being on the Mediterranean and the mobile nature of our population, should lead to hemoglobinopathy maps of the

screening surveys in provinces bordering and neighboring the Mediterranean being continued. To obtain effective results from premarital screening, it must be emphasized that education of the public and genetic counselling must go hand in hand with prenatal diagnosis and be readily available.

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References

1. Çavdar AO, Arcasoy A. The incidence of β -thalassemia and abnormal hemoglobins in Turkey. *Acta Haematol* 1971; 45: 313–18.
2. Altay Ç, Yetkin S, Özsoylu S, Kutsal A. Hemoglobin S and some other hemoglobinopathies in Eti-Turks. *Hum Hered* 1978; 28: 56–61.
3. Yüregir GT, Arpacı A, Aksoy K, *et al.* Population at risk for hemoglobinopathies in Çukurova, Türkiye: need for prenatal diagnosis. *Ann Med Sci* 1995; 4: 61–9.

4. Altay Ç, Yılğör E, Beksac S, Gürgey A. Premarital screening of hemoglobinopathies: a pilot study in Turkey. *Hum Hered* 1996; 46: 112–14.
5. Cao A, Saba L, Galanello R, Rosatelli MC. Molecular diagnosis and carrier screening for beta thalassemia. *JAMA* 1997; 278: 1273–77.
6. Lena Russo D, Erny N, Serradimigni F, *et al.* Genetic hemoglobin diseases. Prevention at centers for family planning and education of maternal child protection in Marseille. *Press Med* 1996; 25: 151–53.
7. Mitchell JJ, Capua A, Clow C, Scriver CR. Twenty-year outcome analysis of genetic screening programs for Tay-Sachs and beta thalassemia disease carriers in high schools. *Am J Hum Genet* 1996; 59: 793–98.
8. Ginsberg G, Tulchinsky T, Filon D, Goldforb A, Abramov L, Rachmilowitz EA. Cost benefit analysis of a national thalassemia prevention programme in Israel. *J Med Screen* 1998; 5: 120–26.

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