Nutritional koilonychia in 32 Iraqi subjects

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Koilonychia is taught to medical students as a sign of iron deficiency anaemia.1-2 Koilonychia literally means “hollow nails” (Greek), i.e. spooning. However, flattening of nails is accepted as an early stage of koilonychia; thinning and softening of nails is commonly associated.3-6 In developed well-nourished communities, koilonychia is rare,7 although it is reported occasionally in association with non-nutritional deficiency states,7-10 as a familial condition11-13 and in association with several skin diseases.14 Reports of as few as two cases8,9,13 stand as testimony of its rarity. However, in malnourished communities, nutritional koilonychia is not rare. Thus in rural Tanzania, the prevalence of “nutritional” koilonychia was reported to be 18.1% in 1996.15 In Iraq, while under the embargo of the U.N. Security Council, koilonychia was not uncommon. A study conducted in Mosul in 1998 stated an 8% prevalence rate of koilonychia in apparently normal adults and 29 percent among hyperthyroid patients,16 in whom anaemia was not evident but there was no confirmatory laboratory evidence. Admittedly, the association of koilonychia with chronic iron deficiency anaemia is unquestionable. The older generation of clinicians recalls severely anaemic farmers who displayed spooning of the nails due to ankylostomiasis; some enjoyed dropping water in such nails, which settles without falling off. However, the aetiological relation of koilonychia to iron deficiency has been questioned since 1959 and clippings of koilonychia nails contained reduced amounts of cystine as compared with normals.17 In fact, koilonychia has even been reported in haemochromatosis.6 We aimed to assess the validity of the long-held and still-held association of koilonychia with iron deficiency and test for any relationship between koilonychia and the state of body proteins.

Patients and methods

The study was begun in January 1999 with an initial intention to confine it to hyperthyroid patients because of the expected high prevalence of koilonychia.16 On facing a lack of such patients in the Thyroid Clinic of the Oncology and Nuclear Medicine Hospital (ONMH) because kits for thyroid function tests (T3; T4; TSH) were not available to attract patients, and being then tied by a time limit for conducting the study, we sought medical inpatients with koilonychia at Ibn Seena Teaching Hospital. By April 1999 kits for T3, T4 and TSH became available and the study was shifted to the Thyroid Clinic of ONMH. By mid-July 1999, enrollment of patients had to be terminated.

Each patient was evaluated clinically and investigations were conducted that were thought worthwhile and were available. The age, gender, marital status, and number of offspring and family members were recorded. For females, breast-feeding and menstrual history were sought. Among the non-hyperthyroid patients, diagnosis of the main illness was recorded. The duration of the hyperthyroidism was recorded for patients with this disease. Included patients had either flat, thin and soft nails (mild koilonychia), or mildly concave nails (moderate koilonychia), or frank concavity (severe koilonychia), a classification that largely conforms with similar studies.1,6 Koilonychia was sought in both fingers and toes. Patients with not less than 5 of the 20 nails involved were included. The skin fold thickness at the knuckle of the middle finger on the dorsum of each hand was examined by Holtain calliper; the mean of the two readings was taken as the knuckle skin fold thickness (KSFT).

Five mL of venous blood were obtained from each patient between 9-11 a.m. Four mL were put in a bland tube to clot and serum was removed for estimating serum iron, total iron binding capacity, total serum proteins and serum albumin. The remaining 1 mL was put in a tube containing potassium ethylene diamine tetra-acetate for estimating the
haemoglobin level and packed cell volume. The total serum protein level was estimated by the biuret method and albumin by the bromo-cresol-green method. The serum iron and total iron binding capacity were estimated by a colourimetric method. All the reagents used were from Randox Laboratories Ltd., Ardmore, Diamond Road, Crumlin, Co Antrim, UK. A haemoglobin level signifying anaemia was taken as less than 115 g/L for women and less than 130 g/L for men.  

The normal serum iron was taken as 9–27 μmol/L and the normal percent saturation of transferrin as 20–45%. An iron deficiency that causes anaemia requires a serum level of less than 5.4 μmol/L, and a transferrin saturation of less than 10%. A serum albumin of less than 35 g/L was considered hypoalbuminaemia and a total serum protein level less than 60 g/L as hypoproteinaemia.

As we lacked a figure for the normal KSFT, 20 apparently healthy males and 20 apparently healthy females among our hospital staff were assessed and the average figures were taken as a “normal” representation of the KSFT. The mean±SD was 2.8±0.3 mm for males and 2.6±0.4 mm for females. The mean minus SD was taken as the minimum normal KSFT for the purpose of the study. For statistical evaluation, the unpaired Student’s t-test and Spearman’s Rank coefficient of correlation were used.

Results
The study included 32 patients with koilonychia; 26 women and 6 men, mean age 40.1±10.7. Twenty-two patients were hyperthyroid; 17 females and 5 males. Of the remaining 10 patients, two suffered from chronic renal failure, dilated cardiomyopathy and bronchiectasis. Another patient had asthma, another had liver cirrhosis, another ischaemic heart disease, and another had thyroid cancer. Koilonychia was mild in 3 patients, moderate in 27, and severe in 2 patients. An average of 6.7 fingernails (range, 4 to 7) and 5.5 toenails (range, 2 to 10) were affected; readings were missing for 3 toenails.

Abnormal values were most frequent for serum albumin (78.1%), total serum proteins (43.7%), KSFT (40.6%) and haemoglobin (31.2%). In correlating the number of fingernails with koilonychia (32 pairs), the highest Spearman’s Rank coefficient of correlation ρ was with KSFT ρ=0.35768, P<0.05. The duration of hyperthyroidism was also significantly correlated with koilonychia ρ=0.3978, P<0.05. The other parameters proved not significant.

Our assessment of the nutritional status of the patients showed that in 28 patients, a meal containing meat, mostly not more than 50 grams on average, was eaten at a frequency of once every nine days, yielding about 12 g of animal protein. The average consumption of eggs was about 56 eggs/year, or about one egg weekly, i.e., about 6 grams of animal protein per week. Milk and beans were added to the ration of the Iraqi citizen in January 1999, which improved protein consumption. Although our inquiry about consumption of milk and milk products did not specify whether the time period was before or after January 1999, the effect of the better rations hardly had time to affect the nails, considering the rate of their growth. We developed an impression that patients, notably women, tended to claim their diet was in a better state than it was in reality.

Nineteen of the 26 females were still menstruating, twenty breast fed their babies; of the remaining six, three were childless and three not married. None of the patients was of good socioeconomic status; 16 were poor while 15 were of moderate socioeconomic status. In one patient this was not recorded.

A moderate status meant patients could afford to eat reasonably more than the distributed ration, including some animal protein.

Discussion
Our results did not substantiate the alleged interrelation between anaemia and koilonychia. On excluding the two patients with chronic renal failure and severe anaemia, the prevalence of anaemia among the remaining 30 patients was 26.7%, a figure almost equal to the 25% prevalence of anaemia reported among male and female workers in a local study conducted in 1972. As for iron deficiency, we had no means of estimating serum ferritin; bone marrow iron content (stain) was thought an unacceptable invasive procedure. Thus we relied on serum iron and percent transferrin saturation. A serum iron of less than 5.4 μmol/L (anaemic set point) was encountered in two (6.2%) patients. A transferrin saturation of less than 10% (anaemic set point) was also encountered in two patients. These were too few patients to assess iron deficiency state as a cause for koilonychia. Thus we can state that nutritional koilonychia is unlikely to be aetiologically due to iron deficiency anaemia. The association of koilonychia with haemochromatosis is another indication against ascribing koilonychia to iron deficiency.

The first report that doubted the aetiological relation between iron deficiency anaemia and koilonychia came from Baghdad in 1959. That study showed abnormally low levels of cystine in the clippings...
of koilonychia affected nails. Although cystine is not an essential amino acid, its main source other than diet is the essential amino acid methionine.\textsuperscript{22} The average ration of the Iraqi citizen during the years of the embargo was estimated to contain just the lowest acceptable dietary protein requirements from flour and rice (46 g/day), with milk and beans added in January 1999. In our study, the calculated average consumption of a single patient was hardly more than 2 grams of animal protein per day, which is less than the basic protein requirements for almost all our patients. The hyperthyroid patients, with their high metabolic activity, can develop nutritional deficiency,\textsuperscript{23,24} specifically a protein deficiency state as evidenced by hypoalbuminaemia.\textsuperscript{25,26}

With the above in mind, we decided that an assessment of the state of body proteins was worthwhile. Traditionally, to assess body proteins means assessing serum albumin and fasting plasma amino acids.\textsuperscript{27} As we had no easy way to estimate plasma amino acids, we confined the study to serum albumin; total serum proteins were measured at the same time. We found that 25 (78.1\%) patients had a low serum albumin (less than 35 g/L).\textsuperscript{28} The mean values of haemoglobin, serum iron and percent transferrin saturation of all fell within their normal range, whereas the mean serum albumin was clearly below the minimum normal level. This, we believe, agrees with the view that some sort of protein/amino acid deficiency state does contribute to the development of nutritional koilonychia. Naturally, this does not mean that koilonychia should appear among hypoalbuminaemic patients; leukonychia is the usual condition associated with hypoalbuminaemia. The serum albumin was measured as a parameter of the body content of proteins. In rural Tanzania, likewise, evidence of protein deficiency state (from serum albumin) was found in 3.4\% of a sample that showed an 18.1\% prevalence of koilonychia. This might mean that serum albumin is too crude a method for assessing body proteins. However, it also favours a qualitative protein/amino acid deficiency that is not the same for serum albumin (a globular protein) as for the protein of the nails which is a fibrous protein.\textsuperscript{29} Therefore, we searched for an easily measurable means of assessing structural or “fibrous” proteins. This led us to measure the thickness of a true skin fold without subcutaneous fat as the skin is largely composed of collagen and elastin; both represent fibrous proteins. Our choice was the mid-knuckle skin fold thickness (KSFT) at the dorsum of the hands. Here, thirteen (40.6\%) patients had low KSFT by our method of assessment. Furthermore, KSFT was only significant parameter that correlated with the number of fingernails affected by koilonychia. Among the hyperthyroid patients we also found a positive correlation between the number of fingernails affected and the duration of the disease. We did not include the number of toenails, because they were not recorded in three of the patients. These results confirm that koilonychia strongly parallels thinness of the skin; both are composed of fibrous protein. It also seems that our method of assessing the normality of the KSFT deserves refinement in a wider study. However, a possible confounding factor might have been the chapping of the skin of the dorsum of the hands during the cold dry days of winter time. In our study though, the controls and patients were evaluated at the same time of year.

The significant negative correlation between KSFT and number of fingernails affected by koilonychia points to an amino acid deficiency. Cystine has the sulphydryl linkages between peptide chains that are required for structural proteins. Lack of cystine and/or its progenitor methionine may therefore be responsible for koilonychia, in conformity with the Jalili-Kassab finding of a deficiency of cystine in nails affected by koilonychia.\textsuperscript{17} As for the well known association of koilonychia with iron deficiency anaemia, we think it can be explained on the bases that animal protein, possibly excluding milk and milk products, is a major source of absorbable iron as well as of sulphur containing amino acids, and that cysteine-containing peptides from beef have been found to promote iron absorption.\textsuperscript{29} We may add that the reason koilonychia is found in patients having haemochromatosis might be the loss of blood proteins, including fibrinogen, by the “weekly” venesection recommended for treating the disease, if protein loss is not compensated by sufficient protein in their diet. Finally we must admit that nutritional koilonychia will lag several weeks or even few months after the state of deficiency occurs, taking into consideration the time for the growth of the nail from the nail bed to show koilonychia. Nail growth is stated to be normally at a rate of 0.1 mm/day and is likely to be slower in the malnourished. The higher number of koilonychia affected nails in long-standing hyperthyroidism may be taken as supportive evidence concerning the time of nail growth, including the gradual exhaustion of structural proteins/amino acids by the increased metabolic rate. We suggest that future studies estimate the fasting plasma amino acids levels in patients with koilonychia while on a steady state of nutrition for, say, several months.
In conclusion, our results conform with the Jalili-Kassab concept\(^\text{[7]}\) that a dietary deficiency of proteins, notably the sulphur containing amino acids, is the likely cause of nutritional koilonychia. Iron deficiency as the cause is most unlikely although our results do not deny their association. Koilonychia may serve as evidence of chronic nutritional deficiency in an adult population. Koilonychia has been reported among hyperthyroid patients from U.K. during the second world war when there were dietary restrictions.\(^\text{[8]}\) Thus, koilonychia (and not just onycholysis) may partly reflect the nutritional status of hyperthyroid patients.

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