Iron status of Libyan infants with urinary tract infection

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مستوى الحديد لدى الرضّع الليبيين المصابين بعدوى في المسالك البولية

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خلاصة: تم قياس مستوى الحديد بالمصل، والمدى الكامل لاستيعاب الحديد في الدم ومستوى التشبع بالترانسفيرين، وذلك في خمسة وأربعين رضيعا، كان من بينهم تسعة عشر مصابا بعدوى بالمسالك البولية تم التحقق منها بعد فحص عيّنة من البول سُحبت من المثانة بالبزل من فوق العانة. وكانت نتيجة الفحص إيجابية. أما المجموعة الشاهدة فتكوّنت من 26 رضيعا صحيحا معافى جاءت نتائج فحصهم سلبية. وكانت القِيَم الوسطى لمستوى الحديد والتشبُّع بالترانسفيرين أقل بدرجة جوهرية في الرضّع المصابين بعدوى المسالك البولية عنها في المجموعة الشاهدة (P<0.01 وP<0.001 على التوالي)، وخصوصا إذا كانت الجراثيم المستزرعة هي الإشريكية القولونية (P<0.01 وP<0.02). أما المدى الكامل لاستيعاب الحديد في الدم فقد كان في حدود النطاق الطبيعي. ونستنتج من تلك النتائج أن عوز الحديد ليس عاملا رئيسيا في إحداث عدوى المسالك البولية في الرضّع الليبيين.

ABSTRACT Serum iron, serum total iron binding capacity and tranferrin saturation levels were measured in 45 infants, of whom 19 had urinary tract infections confirmed by positive suprapubic aspiration. The control group comprised 26 healthy infants with negative results. Mean serum iron and transferrin saturation values were significantly lower in infants with urinary tract infection compared with the control group ($P < 0.01$ and $P < 0.001$ respectively), especially if the cultured organism was *Escherichia coli* ($P < 0.01$, $P < 0.02$). Total iron binding capacity was within the normal range. We conclude that iron deficiency is not a major factor in the etiopathogenesis of urinary tract infection in Libyan infants.

Le bilan en fer des nourrissons libyens ayant une infection des voies urinaires

RESUME Le fer sérique, la capacité totale de fixation du fer sérique et les niveaux de saturation de la transferrine ont été mesurés chez 45 nourrissons dont 19 avaient une infection des voies urinaires confirmée par aspiration sous-pubienne. Le groupe de témoins était composé de 26 nourrissons en bonne santé ayant des résultats négatifs. Les valeurs moyennes du fer sérique et de la saturation de la transferrine étaient considérablement plus faibles chez les enfants ayant une infection des voies urinaires que chez ceux du groupe des témoins ($P < 0,01$ et $P < 0,001$ respectivement), tout particulièrement si le micro-organisme mis en culture était *Escheria coli* ($P < 0,01$, $P < 0,02$). La capacité totale de fixation du fer se situait dans les valeurs normales. Nous en concluons que la carence martiale n'est pas un facteur majeur dans l'étiopathogénie des infections des voies urinaires chez les nourrissons libyens.

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Introduction

Nutrition is a critical determinant of immunocompetence and of risk of infectious illness. This is mainly attributed to impaired immune response, cell mediated secretory response and antibody affinity.

It is now recognized that deficiencies in single nutrients impair immune responses [*1*]. Iron, apart from its well known functions connected with transporting haemoglobin, storage (myoglobin), and utilizing oxygen for respiration (cytochrome, cytochrome oxidase), also plays a critical role in host–pathogen interactions; it is essential for microbial growth as well as for immune function [*2–5*].

There is growing evidence of a relationship between enhanced susceptibility to infection and iron deficiency [*6*] and overload [*7,8*]. Iron deficiency has far-reaching consequences for systemic functions, apart from the easily recognized and treated iron deficiency anaemia. The non-haematological manifestations of iron deficiency have been overlooked. Iron deficiency is associated with changes in cellular function, in growth motor development, behaviour and cognitive function [*9–12*].

Iron deficiency is thought to be relatively common among Libyan infants and children. Its relation to urinary tract infection in infancy has not been studied. Therefore, in this study we measured serum iron (SI) and serum total iron binding capacity (STIBC), and calculated the transferrin saturation (TS) concentrations in a group of Libyan infants with or without urinary tract infection.

Subjects and methods

The study was carried out at the paediatric department of Al-Kadra Teaching Hospital, Tripoli from January to July 1993. Informed consent was obtained from parents before starting the study. The study involved 45 Libyan infants living in Tripoli, of whom 26 with no evidence of urinary tract infection acted as the control group.

Excluded from the study were infants younger than 4 weeks or older than 12 months, very sick or seriously ill infants, and infants with a history of prematurity, evidence of anaemia or those receiving iron supplements. Also excluded were those whose urine samples had been collected in bags.

A dietary history was taken from the mothers and their feeding was classified as breast only, bottle only, combined breast/bottle, or weaned (i.e. semi-solid foods introduced). Urine samples were collected by suprapubic aspiration, after which the samples were immediately cultured using standard culture media.

A blood sample was collected from each infant in a plain tube. The serum was separated and analysed for iron and serum total iron binding capacity (μg/L), within a week of the sample being taken. Analysis was by spectrophotometry using Raichem reagents (Raichem, San Diego, California). Transferrin saturation was calculated using the equation: $TS = (SI/STIBC) \times 100$ (%).

The mean was calculated for each group of infants: values are presented in the tables as mean ± standard error of the mean ($s_{\bar{x}}$). The Student *t*-test was used to test the significance of the difference between the means.

Results

In all, 19 infants were diagnosed as having urinary tract infection by positive urinary suprapubic aspiration. No colony count was required. Overall, 15 of the 19 infants

(78.9%) with urinary tract infection were aged between 1 month and 6 months. Of these, males had double the incidence of urinary tract infection (10 of the 15) compared to females (5 of the 15). The commonest organism isolated was *Escherichia coli* in 12 of the 19 infants (63.1%). *Klebsiella* spp. was prevalent in infants 6 months or under and *Proteus* spp. was isolated from males only. The majority of infants were bottle- and breastfed. Approximately 50% had been weaned (Table 1).

In the infants with urinary tract infection, serum iron concentrations were significantly lower than those of the control group ($P < 0.01$), especially if the organism was *E. coli* ($P < 0.001$) (Tables 2 and 3). Transferrin saturation concentrations were also significantly lower than in the control group ($P < 0.001$), especially if the organism was *E. coli* ($P < 0.001$) or *Proteus* spp. ($P < 0.05$) (Tables 2 and 3).

In patients with urinary tract infection, serum iron and transferrin saturation concentrations were significantly low, both in infants aged 1–6 months ($P < 0.05$, $P < 0.01$ respectively) and in infants aged 6–12

Table 1 **Relationship between urinary tract infection and the type of feeding**

Variable	Control (n = 26)		Infants with UTI							
			Escherichia coli (n = 12)		*Klebsiella* spp. (n = 4)		*Proteus* spp. (n = 3)		Total (n = 19)	
	M	F	M	F	M	F	M	F	M	F
Age (months)										
1–6	11	8	5	4	3	1	2	0	10	5
>6	3	4	0	3	0	0	1	0	1	3
Feeding mode										
Breast alone	3	0	0	0	0	0	1	0	1	0
Bottle alone	0	1	1	0	1	1	0	0	2	1
Both	11	11	4	7	2	0	2	0	8	7
Weaned	6	5	1	3	0	0	2	0	3	3

UTI = urinary tract infection M = male F = female

Table 2 **Serum iron, serum total iron binding capacity and transferrin saturation in a group of Libyan infants**

Measurand	Control (n = 26)	UTI (n = 19)	P-value
Serum iron (µg/L)	110.2 ± 13.8	67.6 ± 7.7	< 0.01
Serum total iron binding capacity (µg/L)	308.3 ± 18.6	315.5 ± 13.3	Non-significant
Transferrin saturation (%)	37.0 ± 3.5	21.9 ± 2.5	< 0.001

Values are presented as mean ± $s_{\bar{x}}$
UTI = urinary tract infection

Table 3 **Relationship between serum iron, serum total iron binding capacity and transferrin saturation in a group of Libyan infants according to organism type**

Measurand	Control (n = 26)	*Escherichia coli* (n = 12)	*Klebsiella* spp. (n = 4)	*Proteus* spp. (n = 3)
Serum iron (µg/L)	110.2 ± 13.8	59.2 ± 8.2[a]	84.0 ± 18.4[b]	79.0 ± 29.1[b]
Serum total iron binding capacity (µg/L)	308.3 ± 18.6	314.6 ± 19.6[b]	306.7 ± 17.5[b]	330.7 ± 30.4[b]
Transferrin saturation (%)	37.0 ± 3.5	19.7 ± 2.9[a]	28.0 ± 6.7[b]	22.9 ±6.5[c]

[a]*P < 0.001 versus control group*
[b]*Non-significant*
[c]*P < 0.05 versus control group*
Values are presented as mean ± $s_{\bar{x}}$

Table 4 **Serum iron, serum total iron binding capacity and transferrin saturation in Libyan infants aged 1–6 months**

Measurand	Control (n = 19)	UTI (n = 15)	*P*-value
Serum iron (µg/L)	112.9 ± 18.3	73.9 ± 8.7	< 0.05
Serum total iron binding capacity (µg/L)	298.3 ± 19.6	3101.1 ± 15.4	Non-significant
Transferrin saturation (%)	38.1 ± 4.4	24.3 ± 2.8	< 0.01

Values are presented as mean ± $s_{\bar{x}}$
UTI = urinary tract infection

months ($P < 0.01$, $P < 0.001$) (Tables 4 and 5). Concentrations were especially low in male infants aged 1–6 months ($P < 0.01$, $P < 0.02$) (Table 6). No significant differences were observed between female infants aged 1–6 months and the control group. Serum total iron binding capacity for all the infants was within the normal range (< 400 µg/L).

Discussion

Iron is an essential nutrient for the growth of most pathogenic microorganisms. However, *in vivo*, iron is complexed with host proteins such as transferrin in the blood and lactoferrin in secretions [*13*]. Successful competition for iron by potential pathogens is essential to establish infection. The role of various types of microbial iron-acquisition systems in host–pathogen interactions depends on the nature of the infection and the location of the pathogen within the host [*11*]. Restricted availability of free iron in the host, so-called "nutritional immunity", plays a key role in non-specific defence strategies against potential pathogens [*13,14*].

Table 5 **Serum iron, serum total iron binding capacity and transferrin saturation in Libyan infants aged 6–12 months**

Measurand	Control ($n = 7$)	UTI ($n = 4$)	*P*-value
Serum iron (μg/L)	102.7 ± 14.5	43.7 ± 11.7	< 0.01
Serum total iron binding capacity (μg/L)	335.6 ± 45.6	335.5 ± 27.9	Non-significant
Transferrin saturation (%)	33.9 ± 5.2	13.1 ± 3.3	< 0.001

Values are presented as mean ± $s_{\bar{x}}$
UTI = urinary tract infection

Table 6 **Serum iron, serum total iron binding capacity and transferrin saturation in male infants aged 1–6 months**

Measurand	Control ($n = 11$)	UTI ($n = 10$)	*P*-value
Serum iron (μg/L)	95.8 ± 12.5	69.7 ± 10.0	< 0.01
Serum total iron binding capacity (μg/L)	268.6 ± 23.6	319.4 ± 20.4	Non-significant
Transferrin saturation (%)	39.1 ± 6.9	22.4 ± 3.0	< 0.02

Values are presented as mean ± $s_{\bar{x}}$
UTI = Urinary tract infection

Serum iron and transferrin saturation were low in infants with urinary tract infection. These findings are consistent with those for adults with urinary tract infection [*15*], and for children with viral infections such as mumps or chickenpox [*16*]. However, compared to findings for adults with chronic viral hepatitis [*17*], our results showed significant differences, especially if the organism was *E. coli*, which is known to be iron-dependent, and occurred in male infants aged 1–6 months. The latter observation is difficult to explain on a dietary basis alone and requires further elucidation.

The overall serum total iron binding capacity in all infants was within the normal range. This indicates that the infants were not iron-deficient and iron deficiency was unlikely to be a contributory factor in the pathogenesis of urinary tract infection in Libyan infants. The low serum iron in our study reflects sequestration of iron into the reticuloendothelial system, so that free iron was not available to the invading bacteria [*18,19*]. This iron-withholding mechanism seems to be an important host defence against bacterial infection.

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