Abscess infections and malnutrition – a cross-sectional study of polydrug addicts in Oslo, Norway

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#### Abstract

**Background:** Injection drug use and malnutrition are widespread among polydrug addicts in Oslo, Norway, but little is known about the frequency of abscess infections and possible relations to malnutrition.

**Objectives:** To assess the prevalence of abscess infections, and differences in nutritional status between drug addicts with or without abscess infections.

**Design**: A cross-sectional study of 195 polydrug addicts encompassing interview of demographics, dietary recall, anthropometric measurements and biochemical analyses. All respondents were under the influence of illicit drugs and were not participating in any drug treatment or rehabilitation program at the time of investigation.

**Results:** Abscess infections were reported by 25% of the respondents, 19% of the men and 33% of the women (P=0.025). Underweight (BMI<18.5 kg/m<sup>2</sup>) was significantly more prevalent in the abscess infected than in the non-abscess infected group (P=0.001). The abscess infected addicts reported fewer meals, lower intakes of fruits and vegetables, lower energy percentage (E%) from protein and higher E% from sugar. They also had lower total intakes of vitamins D,  $B_1$ ,  $B_6$ ,  $B_{12}$ , folic acid and vitamin C than the non-abscess infected group.

The two groups differed significantly with respect to S-C-peptide (P = 0.042) and B-HbA1c (P = 0.012), and the prevalence of hyperhomocysteinemia ( $P - tHCY > 15 \mu mol/l$ ) was 73% in the abscess infected group and 41% in the non-abscess infected group (P = 0.001). The concentrations of S-25-hydroxy-vitamin  $D_3$  was very low.

**Conclusion:** The prevalence of abscess infections was 25% among the examined polydrug addicts. Dietary, anthropometric and biochemical assessment indicated a relation between abscess infections and malnutrition.

Key words: Abscess infections, Nutrients, Vitamin C, Malnutrition, Drug injection.

### Introduction

Polydrug addicts in Oslo, Norway, who often live their lives on the margins of our affluent society, are exposed to food insecurity and unstable living conditions [1, 2]. Injection of drugs is common [3] and frequently causes bacterial infections as abscesses, that may result in serious morbidity and costly medical care [4, 5]. The occurrence of abscess infections has been related to hepatitis infections, HIV/AIDS, intramuscular injections and the reuse and sharing of syringes, female gender, recent imprisonment, involvement in the sex trade and frequent cocaine use [6, 7].

Drugs of abuse are immunosuppressive [8], making the drug addicts more susceptible to infections. Evidence suggests also that inflammation plays a role in depression [9-11]. Symptoms of depression are widespread in populations of drug addicts [12].

Populations of drug addicts may suffer from malnutrition due to poor and unstable access to food [13] and/or choice of food with low nutrient density [1, 2, 14]. Few meals and a poor food choice among drug addicts have been associated with weight loss; low body mass index (BMI<18.5 kg/m²), protein-energy malnutrition and micronutrient deficiencies [15, 16], all factors known to cause immunodeficiency [17, 18].

It is known that malnutrition generally suppresses the body's immune function, diminishes response to therapies, and promotes co-morbidities [18]. Moreover, infections and fever increase nutritional needs, probably making drug addicts more prone to developing and maintaining abscess infections [19]. Insufficient nutrition may be assessed by low nutrient intakes, underweight (BMI<18,5 kg/m²), and aberrant biochemical parameters in the blood, serum or plasma.

This paper is part of a cross-sectional study of drug addicts in Oslo where we previously have studied living conditions [1], and access to food and food choice [2]. Here the possible relation between abscess infection and malnutrition was addressed.

### Materials and methods

## Study design

This paper is part of a cross-sectional study of polydrug addicts in Oslo encompassing a dietary assessment, anthropometric measurements, a medical examination, biochemical

analyses and personal interviews using of a pre-coded questionnaire. The study was approved by the Norwegian Regional Committee for Medical Ethics, and the data were collected in accordance with the Helsinki Declaration [20], from November 2001 to April 2003. Personal data storage was supervised by the Norwegian Social Science Data Service (NSD). Each respondent gave his/her written consent. To validate the individual reported intakes of drugs in the previous 24 hours, blood samples from the first 25 respondents were subjected to biochemical analyses to identify the consumed substances. Analyses showed 98% agreement with the types of substances reported [1]. This implies that the respondents were able to give valid information concerning drug use.

# Respondents

In total, 400 polydrug addicts were asked to participate; 180 were excluded due to different kind of indispositions, and 220 were recruited for an on the spot examination at 23 different locations: hospices, night shelters, meeting places and on the street. Unforeseen events during the data collection, including clogged veins, resulted in the finally number of 188 respondents that also stated if they presently were suffering from abscess infections or not.

They confirmed orally that they were currently under the influence of illicit drugs.

Examinations were conducted all days, both during the day and at night. Twenty percent of the respondents reported having their own home. The remainder had no fixed abode. Some 10% reported sleeping rough in the preceding month, i.e. on the street, in parks or in multistory car parks. Although the respondents' drug habits varied according to day-to-day access to drugs, heroin and flunitrazepam (Rohypnol illegal drug in Norway from 2004) were the most frequently used, often in combination with amphetamine, cannabis, benzodiazepines or methadone [1].

None of the respondents were participating in a drug addiction treatment programs at the time of the survey.

## Questionnaire

The questionnaire has been described in earlier papers from this study [1, 2] Those who confirmed that they had used ascorbic acid in the past 24 hours when injecting, were asked to estimate the amount of ascorbic acid in mg from models. The respondents were also asked whether they were currently suffering from abscess infections/injection cite infection (not including periodontal abscesses) and how often they visited medical care centers during the

preceding three months. When relevant, what type of disease or medical condition that had occasioned their visits were asked about. Access to food and if they lately had experienced longer lasting periods of depression were as well included in the questionnaire.

### **Dietary assessment**

One 24-hour dietary recall was used to assess food intake [1, 2].

## **Anthropometric measurements**

Body Mass Index (BMI-kg/m²) was calculated using WHO's standardized methods for measuring height and weight [21]. Mid upper arm circumference (MUAC) was measured at the mid-point between the acromion and the olecranon using a non- stretch tape measure. MUAC corresponding to underweight was defined as MUAC<23.2 cm for men and MUAC<23.0 cm for women [22].

## **Biochemical analyses**

One physician and three biomedical laboratory technicians collected blood from the drug addicts by venipuncture. S-C-peptide, Pyridoxal-5'-phosphate in serum (S-vitamin B<sub>6</sub>) and ascorbic acid in serum (S-vitamin C) were analyzed at the Department of Medical Biochemistry, Oslo University Hospital Aker [2].

Vitamin D as 25-hydroxy-vitamin D<sub>3</sub> was analyzed from serum samples. The assay was performed by AS Vitas (Oslo, Norway: <a href="www.vitas.no">www.vitas.no</a>) using an HP 1100 liquid chromatograph (Agilent Technologies, Palo Alta, CA, USA).

B-HbA1c (glycocated hemoglobin) was analyzed by means of an immune turbidometric assay on a Hitachi 917 analyser (Roche). S-vitamin B<sub>12</sub> (serum cobalamin), S-folate, P-tHCY (plasma-total-homocysteine) were analyzed by means of routine immunoassays performed using a Centaur analytical instrument (Bayer AG, now Siemens AG). Anti-HCV (antibody reaction against hepatitis C virus) was analyzed by means of an immunoassay on an Architect i2000SR (Abbott), following the vendor's instructions. Serum methylmalonic acid (S-MMA) was analyzed using an in-house chromatographic method (LC/MS-MS). S-CRP, antibodies against HIV and Helicobacter pylori were anayzed at Fürst Medical Laboratories in Oslo, Norway, accredited/certified in accordance with NS-EN ISO/IEC 17025.

Drug detection in blood was carried out at the Norwegian Institute of Public Health, Department of Forensic Toxicology and Drug Abuse.

### **Statistics**

Fisher's exact test was used on MUAC, to see if there was a difference in prevalence of abscess infections between those who did or did not want to bare their arms. Pearson's Chi-Square test was applied to check if the abscess infected respondents were more exposed to longer lasting periods of depression than the non-abscess respondents. The correlation between P-tHCY and S-Folate was calculated using Spearman's test. Hyperhomocysteinemia (HHcy) was categorized as P-tHCY above 15 µmol/l. One male respondent with a P-tHcy value of 263.7µmol/l was excluded from the analyses. Eleven respondents reported no food intake in the past 24 hours, five with abscess infection, and were not included in the calculation of food and nutrient intake. Men and women were included in the same analyses, since no gender difference were observed between the abscess infected and the non-abscess infection groups for any variables except MUAC. Serum concentrations of vitamins may be affected by elevated concentrations of CRP [23]. Therefore, calculations were performed for P-tHCY, S-B<sub>12</sub>, S-Folate and S-B<sub>6</sub> where the corresponding concentrations for respondents with S-CRP>10mg/l were removed. With use of Bonferroni corrections a p-value less than or equal to 0.0025 were considered significant in an attempt to account for multiple comparisons. All statistical analyses were performed using SPSS, version 20.00 (SPSS, Inc. Chicago, IL, USA).

#### **Results**

Abscess infections were reported by 47 respondents (25%), 19% of the men and 33% of the women (P=0.025). Regular use of heroin and flunitrazepam/Rohypnol was more frequent in the abscess infected group (P=0.012). The abscess infected drug addicts injected larger amounts of ascorbic acid (to dissolve the heroin during the heating process before injection) than the non-abscess infected group (P=0.003) (Table I). Use of other drugs did not differ between the two groups; neither did injection sites, frequency of drug injection, imprisonment, sex trade involvement or number of overdoses (data not shown in tables). The abscess infected reported longer lasting periods of depression than the non-abscess infected (P=0.018). Moreover, the abscess infected respondents requested medical treatment three times more frequently than the non-abscess infected (21% and 6% respectively, P=0.005). Most of these visits (60%) were requests for treatment of abscess infections (data not shown

in tables). There was no difference between these groups regarding completed education. Number of eating events during the past 24 hours, intake of fruits, juice and vegetables, energy percent (E%) from protein, and the diets density of fiber were lower in the abscess infected group than in the non-abscess infected group, while E% from added sugar was significantly higher in the abscess infected group (Table II). Intake of alcohol was similar in both groups. Intake of vitamins and minerals generally fell below recommended intakes. The abscess infected group had a significant lower intake of most vitamins and zinc and selenium.

Underweight (BMI<18.5 kg/m<sup>2</sup>) and energy malnutrition (MUAC<23.2 cm for males and 20.0 cm for females) were more prevalent in the abscess infected group than in the non-abscess infected group (Table III).

Fifty-one percent of the abscess infected did not want to bare their arms for MUAC measurements, this was significantly different from the non-abscess infected group where 35% refused (P=0.008).

The concentration of the acute inflammation marker S-CRP was more frequent above the reference value (S-CRP>10 mg/l) in the abscess infected group, than in the non-abscess infected group. The concentrations of S-MMA (measure of vitamin  $B_{12}$  activity) was higher, while S- $B_{12}$  and S- $B_6$ , when S-CRP<10 mg/l, were both significantly lower in the abscess infected than in the non-abscess infected group (Table III). The concentrations of S-Folate correlated with P-tHCY (Spearman's rho, r=-0.502, P<0.001), but S-Folate was not different, while P-tHCY concentrations were significantly different between the two groups, as were B-HbA1c and S-C-peptide (Table III). The concentrations of S-25-hydroxy-vitamin  $D_3$  was generally very low, and significantly lower in the abscess infected group (Table III). S-vitamin C concentrations were highest in the abscess infected group, but did not reach statistical significance (Table III).

### **Discussion**

In this study we found that the 47 respondents who reported abscess infections, probably were more exposed to drug abuse and depressions than the non-abscess infected. Furthermore, they reported fewer meals, had lower intakes of fruits and vegetables, and their diet had a lower E% from protein and a higher E% from sugar than the diet of the non-abscess infected respondents. The abscess infected also had lower intakes of most of the vitamins and zinc and

selenium than the non-abscess infected. They suffered significantly more often from underweight (BMI<18.5 and MUAC< references) and the inflammation marker S-CRP was frequently more often above references (S-CRP>10 mg/l) than in the non-abscess infected group (P=0.040). Further the abscess infected group had significantly higher concentrations of S-C-peptide (P=0.042), B-HbA1c (P=0.012) and P-tHCY (P<0.001), and significantly lower concentration of S-25-hydroxy-vitamin  $D_3$  (P=0.021).

More frequent drug abuse may be due to self-medication trying to relieve pain from the abscesses. Self-medication/abuse of analgesics and self-injections of morphine for pain relief has been reported among patients suffering from tooth ache [24]. A side effect of the more frequent use of drugs like heroin is that the drug addicts become even more susceptible to infections due to the possible immune suppressive effect of the drugs [8]. Their more frequent reported periods of depressions further support that the abscess infected addicts probably were more exposed to infections than the non-abscess infected [9-11].

The frequency of abscess infections in the present sample was comparable to the 29% frequency reported for injection drug users in Colorado, USA in 2010 [5]. Injection frequency, puncture site and the prevalence of other infections, such as hepatitis C and Helicobacter pylori have been found to be associated with abscess infections in other studies [6, 7]. This was not confirmed in this study, possibly indicating that other factors were more important for abscess formation in this sample.

The poorer dietary intake among the abscess infected was probably due to heavier involvement in drug abuse. Other studies have reported that heroin suppresses appetite [25], and heroin addicts develop a special preference for sweet taste resulting in a high sugar intake through sweet food items with a poor nutrient density [26]. This seems to apply also for out respondents. A high intake of added sugar will displace other, more nutritious foods, such as fruits, vegetables and cereals, which explain the low dietary density of fiber the low intakes of folic acid and vitamin C in the abscess infected group.

A higher infectious rate also increases nutritional needs, and insufficient dietary intakes promote malnutrition and co-morbidities, suppress immune function and diminish response to therapies [5].

The anthropometric measurements BMI and MUAC both below reference values indicated that the abscess infected was more exposed to underweight. In an earlier paper from this investigation 64% of the drug addicts reported not to be content with their food accessibility, and the food they bought themselves was less nutritious dense than the food they got from providers [2]. We also published that a lower number of meals was associated with decreasing BMI [1]. These earlier results imply that the drug addicts most likely could improve their nutritional status if healthy food was made more accessible to them.

The biochemical parameters B-HbA1c, S-C-peptide and P-tHCY more frequently exceeded the reference values in the abscess infected respondents compared to the non-abscess infected, indicating higher metabolic stress probably caused by insulin resistance due to a low grade inflammation reaction, heavier drug abuse and higher E% from sugar in the diet [27, 28].

Higher concentrations of P-tHCY found in the sub-population with S-CRP<10 mg/l, may relate to the lower energy intake from protein, vitamin B<sub>6</sub>, B<sub>12</sub> (a consequence of low intake of food of animal origin) and folate. It may be speculated that the relatively high S-B<sub>12</sub> in the abscess infected respondents, in spite of the low dietary intakes of B<sub>12</sub>, may be a consequence of the low intakes and low concentrations of B<sub>6</sub>, inhibiting the metabolism of B<sub>12</sub> and homocysteine [29]. Elevated P-tHCY has been shown to promote inflammatory processes, and probably further hampering the recovery from abscess infections [30].

The drug addicts' low S-vitamin  $D_3$  suggests limited sun exposure, making food the main source of vitamin D. The significantly lower S-vitamin  $D_3$  in the abscess infected respondents is alarming, since the vitamin D is crucial in the body's fight against infections. Vitamin D insufficiency may lead to dysregulation of human immune responses and are maybe an underlying cause of infectious disease and immunological disorders [31].

The abscess infected respondents had lower intake of ascorbic acid from the food than the non-abscess infected, an intake so low that a scorbutic state was to expect. However, their blood ascorbic acid concentrations were satisfactory (Table III), probably due to the ascorbic acid used to dissolve the heroin before injection. Vitamin C also plays an important role in the immune system [17], and the respondents may have suffered even more health-related complications from drug abuse without the injection supply of vitamin C. The resulting blood concentration was expected to be much higher from daily use of 300-1000 mg ascorbic acid,

but the vitamin activity were maybe reduced during the heating process and probably also by the respondents heavy cigarette smoking habit.

The self-reported occurrence of abscess infections may be biased by recollection problems of the drug addicts, but self-reported occurrence of abscess infections has also been reported in earlier studies [4]. A significantly higher number of drug addicts among the abscess infected did not want to bare their arms for MUAC measurements, possibly due to pain or feeling embarrassed.

In a study by Kerr et al., abscess infected respondents visited medical care centers more frequently [32]. This agrees with the results of our study, where abscess infected addicts reported a higher frequency of consultations at medical health services. This indicates that self-reported occurrence of abscess infection is reliable due to the pain that accompanies abscesses. The fact that the drug addicts also were studied in their own environment probably makes the abscess recollection relevant to their actual life situation.

In the present cross-sectional study, a snap-shot of the polydrug addicts' nutritional status was assessed by collecting data on dietary habits, anthropometric measurements and biochemical analyses, methods that together are considers to improve validity of the nutritional assessment [33]. .

### Conclusion

Abscess infections were reported by 25% of the drug addicts. Those who were infected had a higher prevalence of malnutrition, as indicated by dietary intakes, underweight and aberrant biochemical analyses. The metabolic stress from drug intake, inflammatory processes and poor dietary intakes, probably made the abscess infected even more susceptible to infections and pain, and heavier drug abuse as pain relieving self-medication.

Further research should focus on how to improve the nutritional status of malnourished drug addicts through a diet that is adequate from a sensory and nutritional perspective. The diet should preferably include food supplements and a special attention should be given to improve the accessibility of the food.

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Table I Demographics, drug habits and infections among abscess infected and non-abscess infected polydrug addicts in Oslo, Norway.

		N	Abscess	N	Non-abscess	P-
			infected		infected	values
Age years*		47	36.9 (7.7)	141	35.1 (7.6)	0.181*
Age at drug debut years†		47	13 (12.0 ,15.0)	141	14 (12.0 , 17.0)	0.044†
Years in school†		47	11.0 (9.0, 13.0)	141	11.0 (9.0, 12.0)	0.617†
Years drug injection*		47	15.3 (8.9)	141	14.5 (9.0)	0.593*
Ascorbic acid injected last 24 h	mg†	26	1000 (250, 1100)	56	300 (100, 575)	0.003†
Injecting regularly	%	47	94	144	85	0.116‡
Heroin on regular basis	%	47	94	144	77	0.012‡
Amphetamine on regular basis	%	47	45	145	46	0.890‡
Flunitrazepam on regular basis	%	47	83	144	63	0.009‡
Benzodiazepines	%	47	30	146	30	0.965‡
Hashish/cannabis	%	47	51	144	47 <sup>§</sup>	0.647‡
Institutionalized $\geq$ 14 days the						
previous 12 months	%	47	34	146	43	0.201†
Hepatitis C infected (HCV)	%	39	92	126	83	0.137‡
Hepatitis A infected (HAV)	%	17	41	74	49	0.740‡
Helicobacter pylori positive	%	33	36	113	35	0.844‡

<sup>\*</sup> Mean (SD), Students' t-test (parametric)
† Median (P25, P75), Mann-Whitney U-test (non-parametric)
‡ Pearson's Chi-squared test (categorical)
§ Gender difference in use of hashish: Male 54 %, Female 34 %, P=0.027

Table II Food accessibility and dietary intake for abscess infected and non-abscess infected polydrug addicts in Oslo, Norway.

		Abscess	Non-abscess	P-	NNR†
		infected	infected	values	
		N=47	N=141		
Limited access to food %		75	62	0.10	-
Number of meals last 24 hours*		2 (1, 3)	3 (2, 4)	0.01	4 - 5
Fruit, juice and vegetables g*		0 (0, 106)	40 (0, 299)	0.003	>500
Carbohydrate (E %)*		63 (51,77)	57 (48, 69)	0.17	55 - 60
Sugar	(E %)*	35 (19, 49)	23(12, 34)	0.01	≤ 10
Protein	(E %)*	9 (6, 12)	11 (8, 15)	0.02	10 - 15
Fat	(E %)*	22 (10, 36)	29 (18, 37)	0.13	25 - 30
Fiber	g/ MJ*	1.0 (0.4, 1.5)	1.3 (0.7, 2.1)	0.01	3
Vitamin A	$\mu g^*$	189 (2, 546)	371(126, 765)	0.03	700
Vitamin D	μg*	0.15 (0.0, 1.6)	1.0 (0.1, 2.8)	0.01	7.5
Vitamin E	mg*	2 (0, 7)	4(2,9)	0.02	8
Vitamin B <sub>12</sub>	$\mu g^*$	0.95 (0.0, 3.2)	2.4 (1.1, 4.5)	0.01	2.0
Folic acid	μg*	65 (83, 137)	113 (50, 189)	< 0.001	300
Vitamin B <sub>6</sub>	mg*	0.4 (0.1, 0.91)	0.7(0.3, 1.3)	0.01	1.6
Vitamin B <sub>1</sub>	mg*	0.4 (0.1, 1.11)	0.8 (0.4, 1.5)	0.01	1.5
Vitamin C	mg*	3 (0, 35)	15 (1, 84)	0.00	75
Copper	mg*	0.6 (0.2, 1.0)	0.7 (0.4, 1.3)	0.12	2
Zink	mg*	3.8 (0.7, 7.3)	6.6 (2.6, 9.6)	0.02	15
Selenium	μg*	10 (0, 27)	18 (8, 34)	0.03	40/50‡
Iron	mg*	4.1(1.0, 8.5)	5.7 (2.3, 9.6)	0.97	15/10‡

<sup>\*</sup> Median (P25, P75)

<sup>†</sup> Nordic Nutritional Recommendations ‡Reference values: Female/Male

**Table III** Indicators of nutritional and metabolic disturbances in abscess infected and non-abscess infected polydrug addicts in Oslo, Norway.

Parameters	N	Abscess	N	Non-abscess	P-	Reference
		infected		infected	values†	values‡
BMI (kg/m <sup>2</sup> )*	47	20.4 (17.8, 22.8)	141	22.0 (20.3, 24.6)	0.002	20 – 25
BMI <18.5 %*	47	26	141	8	0.001	< 18.5
MUAC cm **	24	24.5 SD 3.6	105	26.8 SD 3.1	0.002**	<23.2/23.0
MUAC< ref. cm %	24	42	105	14	0.002	< 23.2/23.0
S-CRP mg/l*	40	11.0 (7.0, 34.3)	128	9.0 (5.0, 18.0)	0.110	< 10
S-CRP > 10 %	40	53	128	44	0.040	-
B-HbA1c %*	39	6.0 (5.7, 6.1)	131	5.7 (5.5, 5.9)	0.012	<6%
B-HbA1c > 6% %	39	26	131	12	0.035	< 6%
S-C peptide pmol/l*	33	1419 (1010, 1757)	115	1072 (722, 1551)	0.042	<1400
S-C peptide >1400 pmol/1 %	33	55	115	30	0.029	<1400
P-tHCY >15 μmol/l %	37	73	121	43	0.001	-
P-tHCY μmol/l*	37	17.6 (14.3, 21.9)	121	13.8(11.2, 17.3)	0.000	5-15
P-tHCY, CRP<10 mg/l*	16	17.0 (13.2, 21.9)	60	13.8 (11.2, 16.9)	0.055	5-15
S-MMA μmol/l*	32	0.21 (80.14,0.29)	108	0.17 (0.13, 0.21)	0.015	< 0.30
S-MMA, CRP<10 mg/l*	17	0.23 (0.20, 0.30)	52	0.16 (0.12, 0.22)	0.004	< 0.30
S-Vitamin B <sub>12</sub> pmol/l*	41	290 (240, 400)	130	310 (260, 390)	0.209	170-650
S-B <sub>12</sub> , CRP<10 mg/l*	19	260 (220, 300)	64	330 (263,410)	0.006	170-650
S-Folate nmol/l*	40	9.6 (7.2, 12.8)	128	11.0 (8.0, 14.6)	0.238	> 5.7
S-Folate, CRP<10 mg/l*	18	1.0 (7.4, 12.5)	64	10.9 (8.4, 15.8)	0.324	> 5.7
S-Vitamin B <sub>6</sub> nmol/l*	17	17.0 (11.0, 24.5)	77	19.5 (16.0, 28.8)	0.233	≥ 25
S-B <sub>6</sub> , CRP<10 mg/l*	8	16.6 (9.8, 19.8)	32	21.0 (18.0,35.8)	0.021	≥ 25
S-25-Hyrox-vitamin D <sub>3</sub> nmol/l*	37	27.0 (15.0, 38.0)	116	35.0 (21.3, 52.8)	0.021	50-150
S-Ascorbic acid µmol/l*	6	62 (24, 124)	32	55 (43, 67)	0.603	45-92

<sup>\*</sup> Median (P25, P75) and %, \*\*Mean SD, Student's *t*-test

<sup>†</sup>P-values: BMI<ref and MUAC< ref: Persons Chi-square test; other Mann-Whitney U-test (non-parametric).

<sup>‡</sup> Reference values for biochemical parameters at time of investigation (Fürst Medical Laboratories, Oslo, Norway); and reference values for S-B6/S-C-peptide: Nutritional/Hormone Laboratory, Dept of Medical Biochemistry, Oslo University Hospital, Aker.

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