Study Of N-Acetyl-β-D-Glucosaminidase In Elderly Patients With Iron Deficiency Anaemia

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Citation

S Zaki, N Hamed, H Elwakil, A Ketat. *Study Of N-Acetyl-β-D-Glucosaminidase In Elderly Patients With Iron Deficiency Anaemia*. The Internet Journal of Hematology. 2008 Volume 5 Number 2.

Abstract

Mean urinary levels of N-acetyl-β-D-glucosaminidase (NAG) in non smoker elderly iron deficiency anaemia patients ≥ 65 years (4.97^a±0.83 U/L) were significantly higher than in controls (2.17± 0.79 U/L) with higher mean values observed with increasing age (>70 years) (6.59^a ±1.59 U/L). No statistically significant difference was observed between mean urinary NAG values in males (19 patients) (5.54 ± 1.43 U/L) and females (11 patients) (6.19 ± 1.57 U/L). In elderly iron deficiency anaemia patients of both age groups, urinary NAG values showed statistically significant negative correlation with haemoglobin levels (p=0.006 and <0.001 for patients ≥ 65 – 70 years and patients >70 years respectively) and were positively correlated with age (p<0.001 and <0.001 for patients ≥ 65 – 70 years and patients >70 years respectively). No correlation was detected between urinary NAG and haemoglobin values in either males or females (p=0.064 for males and p=0.821 for females).

INTRODUCTION

The prevalence of anaemia in elderly patients ranges from 2.9% to 61% in men and from 3.3% to 41% in women. Higher rates of anaemia are found in hospitalized patients than in community dwellers, as well as in the oldest patients (Health Incorporated, 2001) (Kikuchi et al, 2001).

Anaemia in elderly was defined as a haemoglobin concentration <13 g/dl for men and <12 g/dl for women. The same values suggested by the World Health Organization for younger adults (World Health Organization,1968). Nutritional deficiency was present in one third, with more than half of them deficient in iron, either alone or in combination with folate or B_{12}. Anaemia of chronic illness or chronic renal disease or both was present in one third and unexplained anaemia was present in one third (Guralnik et al, 2004) (Ferrucci et al, 2007).

Anaemia in older persons reflects poor health and increased vulnerability to adverse outcomes (Health Incorporated, 2001). Untreated geriatric anaemia has been associated with increased mortality, increased prevalence of various comorbid conditions and decreased function (Kikuchi et al, 2001). 12.5% of persons aged 71 years and older who were anaemic at baseline spent more hospital stay and were hospitalized more frequently. Furthermore, anaemia is a risk factor for delirium in hospitalized older patients (Steensma et al, 2007).

Urinary N-Acetyl-β-D-glucosaminidase (NAG) is a high molecular weight lysosomal enzyme that shows high activity in renal proximal tubular cells. It is usually not filtered in the glomerulus and its increased levels in urine reflect proximal tubular dysfunction of the kidney. NAG remains stable in urine and can be determined easily (Kalahasthi et al, 2007).

The present study was undertaken to investigate urinary NAG as an index of renal tubular function in asymptomatic non smoker iron deficiency anaemia patients above 65 years of age and compare it with non anaemic persons of matched age and sex.

MATERIALS AND METHODS

Two groups of asymptomatic non smoker elderly iron deficiency anaemia patients were studied. Group Ia consisted of 15 iron deficiency anaemia patients ≥ 65 – 70 years of age while group Ib consisted of 15 iron deficiency anaemia patients > 70 years. Nineteen patients were males and 11 were females. These patients were diagnosed during routine check up. History of reflux oesophagitis and / or peptic ulcer disease was obtained in the majority of these cases at a certain point of their life. Patients with known comorbid conditions and patients with creatinine clearance below 70 ml/min were excluded from the study. An equal number of age and sex matched subjects formed the control group (group II). Blood samples were analysed for complete blood count (Dacie et al, 1995), red blood cell indices (Dacie et al,

1995), serum iron, total iron binding capacity (TIBC) (Tookey, 1970), serum ferritin (White et al,1986), hepatic and renal function tests and a test for the presence of occult blood in stool (Blebea et al, 1985).Urine samples were analysed for estimation of urinary NAG activity by spectrophotometry (Maruhn, 1976). The statistical analysis of the data was done as in SPSS (version 9 for Windows). The means were compared using ANOVA test. The x^2-test was used to compare the sex frequency distribution of patients and control group subjects. Correlation between the different studied variables and urinary NAG was evaluated with Pearson's correlation (r). Probability of $P < 0.01$ and $P<0.05$ were described as highly significant (at 1% level) and significant (at 5% level) respectively.

RESULTS AND DISCUSSION

Haemoglobin value was significantly lower in elderly anaemic patients of both age groups ($10.74^a \pm 0.99$ g/dl) for those ≥ 65 years and $11.37^a \pm 0.86$ g/dl for those >70 years than controls (13.92 ± 0.92 g/dl) with non significant difference between groups Ia and Ib. Haemoglobin values in apparently healthy elderly people are generally lower than those in younger adults and differences between males and females in haemoglobin concentration that are seen in younger adults are lessened with aging as stated by Nilsson-Ehle et al.(1989). In the opinion of Penninx et al. (2003) and Artz et al. (2003) the elderly should not be presumed to have a lower “normal” range for fear of missing a serious underlying disorder.

Steensma et al. (2007) observed that anaemia has been associated with increased frailty, poorer exercise performance, diminished cognitive function, risk of developing dementia, decreased mobility, increased risk of recurrent falls, lower bone and skeletal muscle density and an increased rate of major depression in older than 65 years. However, little data is available about renal function in elderly patients with iron deficiency anaemia.

Mean urinary NAG levels were significantly higher in iron deficiency anaemia patients of both age groups. $4.97^a \pm 0.83$ U/L for those ≥ 65 years and $6.59^a \pm 1.59$ U/L for those >70 years than controls (2.17± 0.79 U/L) ($p<0.001$) with significantly higher mean values observed in patients over 70 years than in those ≥ 65 – 70 years. The selection of NAG specifically as a marker of renal tubular dysfunction in this study was based on results of Moriguchi et al. (2003) study which showed that β_1-microglobulin, β_2-microglobulin and retinol binding protein were not affected in women with iron deficiency anaemia of subclinical degree. Furthermore, a study done by Ozçay et al. (2003) on children with iron deficiency anaemia and impaired renal tubular function showed that haemoglobin levels were not correlated with fractional excretion of sodium.

No statistically significant difference was observed between iron deficiency anaemia males (19 patients) and females (11 patients) regarding urinary NAG values ($p=0.46$). No significant correlation was detected between urinary NAG and haemoglobin values in either males or females ($p=0.064$ for males and $p=0.821$ for females). Similarly, Moriguchi et al, 2003 demonstrated that urinary NAG was not affected in women with iron deficiency anaemia of sub-clinical degree.

The correlation between urinary NAG versus age and haemoglobin values in group Ia patients (≥65 – 70 years) and group Ib patients (>70 years) are represented by figures 1, 2 and figures 3, 4 respectively. There was a statistically significant negative correlation between urinary NAG and haemoglobin values ($p=0.006$ and <0.001 for groups Ia and Ib respectively) and a statistically significant positive correlation between urinary NAG and age ($p<0.001$ and <0.001 for groups Ia and Ib respectively) in elderly patients of both age groups. Ozçay et al, 2003 in a study done on children with iron deficiency anaemia showed that haemoglobin levels were significantly negatively correlated with urinary NAG/creatinine ratio. Also, there was significantly higher mean urinary NAG/creatinine ratio in patients than in controls denoting impaired renal tubular function even in children with iron deficiency anaemia.

In the current study, creatinine-corrected values were not used. Moriguchi et al. (2003) recommended the use of the uncorrected, observed values of the markers rather than the traditional creatinine-corrected values when comparison covers people of a wide range of ages. No significant correlation was present between urinary NAG versus serum iron, TIBC or serum ferritin (r=-0.136, 0.328 and -0.070 at p=0.63, 0.232 and 0.805 respectively for group Ia) and (r=-0.229, -0.333 and 0.107 at p=0.414, 0.225 and 0.704 respectively for group Ib).

Figure 1

Table 1: Mean ± SD. of the values of the clinical data of the studied groups.

Parameter	Elderly patients		Controls (Group II) (n=15)
	≥65-70 years (Group Ia) (n=15)	>70 years (Group Ib) (n=15)	
Age (years)	69.13[a] ± 1.25	73.67 ± 2.26	71.4 ± 4.69
Sex			
Males	9	10	6
Females	6	5	9

Superscript (a) denotes there is existence difference between two means
Significant value ($p \leq 0.01$) indicates highly significant at 1% level

Figure 2

Table 2: Mean ± SD. of the values of the laboratory data of the studied groups.

Parameter	Elderly persons		Controls (Group II) (n=15)
	>65-70 years (Group Ia) (n=15)	>70 years (Group Ib) (n=15)	
Haemoglobin (g/dl)	10.74[a] ±0.99	11.37[a]±0.86	13.92 ± 0.92
Serum iron (µg/dl)	43.53[a] ± 11.45	42.4 ± 10.75	73.66 ± 6.98
TIBC (µg/dl)	478.73[a] ±39.48	456.33 ±29.39	377.2 ± 36.24
Serum ferritin (ng/ml)	18.6[a] ± 7.56	19.87 ± 8.98	134.8 ± 18.89
Urinary NAG (U/L)	4.97[a]±0.83	6.59[a] ±1.59	2.17 ± 0.79

TIBC = Total iron binding capacity NAG = N-acetyl-β-D-glucosaminidase Superscript (a) denotes there is existence difference between two means
Significant value ($p \leq 0.01$) indicates highly significant at 1% level

Figure 3

Table 3: Comparison of the Mean ± SD. of the values of urinary N-acetyl-β-D-glucosaminidase (U/L) in the different age groups according to sex.

Group	Males	Females
Controls (n=15) M:F=6:9	2.25 ± 0.73	2.12 ± 0.86
Patients ≥ 65-70 years (n=15) M:F=9:6	4.87 ± 1.03	5.12 ± 0.42
Patients > 70 years (n=15) M:F=10:5	6.14 ± 1.52	7.49 ± 1.45
Patients ≥65-70 years and >70 years (n=30) M:F=19:11	5.54 ± 1.43	6.19 ± 1.57

Correlation between urinary N-acetyl-β-D-glucosaminidase versus age and haemoglobin values in group Ia (≥65 - 70 years) (figures 1 and 2).

Figure 4

Figure 1: correlation between urinary NAG (U/L) and age (years)

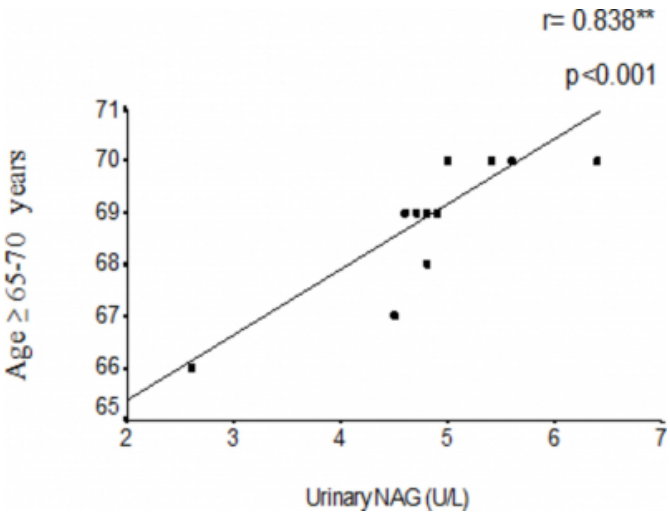


Figure 5

Figure 2: correlation between urinary NAG (U/L) and haemoglobin (g/dl)Correlation between urinary N-acetyl-β-D-glucosaminidase versus age and haemoglobin values in group Ib (>70 years) (figures 3 and 4).

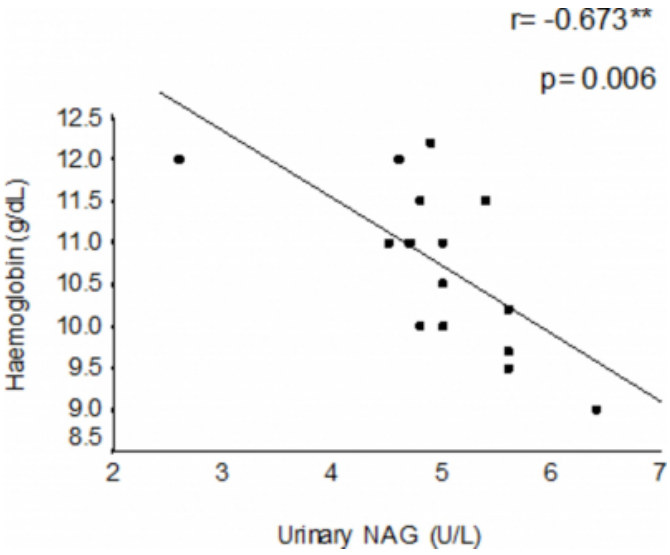


Figure 6

Figure 3: correlation between urinary NAG (U/L) and age (years)

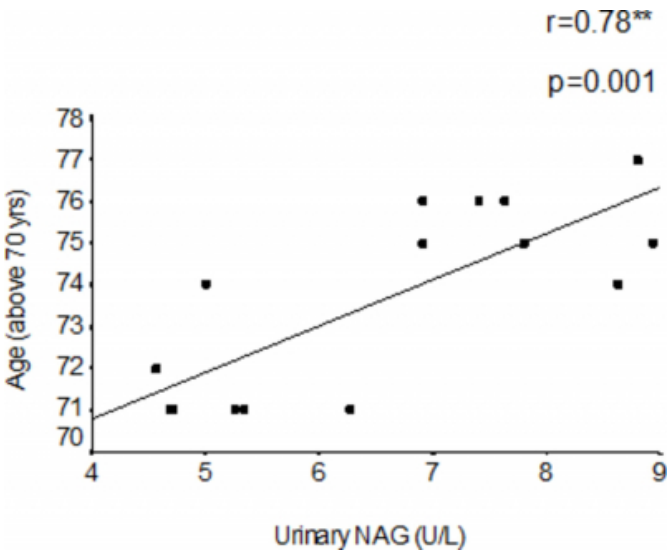
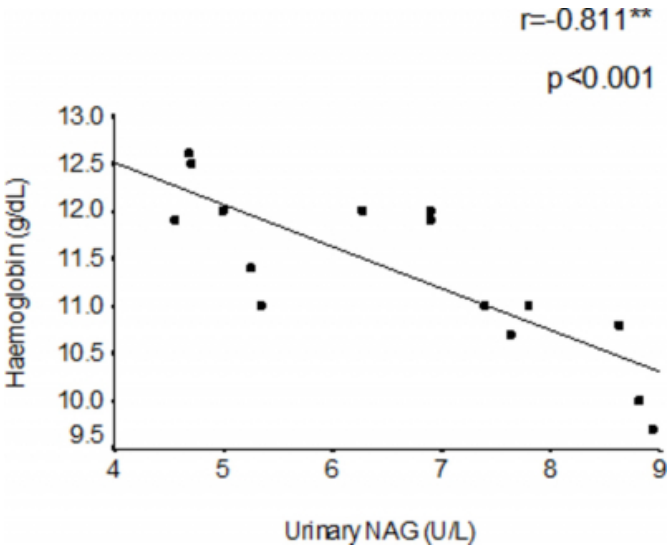


Figure 7

Figure 4: correlation between urinary NAG (U/L) and haemoglobin (g/dl)



CONCLUSIONS

From the above results it can be concluded that in elderly patients, iron deficiency anaemia, even when asymptomatic, may be a contributing factor for the development of impaired renal tubular function. Thus, anaemia in the elderly should not be considered a normal consequence of aging; it should be early diagnosed and treated even if no clinical disease is immediately apparent.

ACKNOWLEDGEMENT

The authors are thankful to Professor Mona Gamal, Professor of Microbiology & Immunology for her aid.

References

r-0. Artz, A.S., Fergusson, D. and Drinka, P.J. (2004). Mechanisms of unexplained anaemia in the nursing home, J Am Geriatr Soc, 52: 423 -426.
r-1. Blebea, J. and Mcpherson, R.A. (1985). False positive guaiac testing with iodine, Arch Pathol Lab Med, 109: 437 - 440.
r-2. Dacie, J.V. and Lewis, S.M. (1995). Practical Haematology, 8th ed., Edinburgh, London, Melbourne: Churcill Livingstone, pp. 49 - 85, 143 - 74.
r-3. Ferrucci, L., Guralnik, J.M.and Bandinell, S. (2007). Unexplained anaemia in older persons is characterised by low erythropoietin and low levels of pro-inflammatory markers, Br J Haematol,136: 849 - 853.
r-4. Guralnik, J.M., Eisenstaedt, R,S,, Ferrucci, L., Klein, H.G. and Woodman, R.C. (2004).Prevalence of anaemia in persons 65 years and older in the United States: Evidence for a high rate of unexplained anaemia, Blood, 104: 2263 - 2268.
r-5. Health Incorporated. (2001). The prevalence and impact of anaemia: a systematic review of the published medical literature, Zynx Health Incorporated; Los Angeles, CA, 109.
r-6. Kalahasthi, R.B., Rajmohan, H.R., Rajan, B.K. and Karuna Kumar, M. (2007). Urinary N-acetyl-beta-D-glucosaminidase and its isoenzymes A & B in workers exposed to cadmium at cadmium plating, Journal of Occupational Medicine and Toxicology, 2: 5 - 9.
r-7. Kikuchi, M., Inagaki, T. and Shinagawa, N. (2001).Five-year survival of older people with anaemia: variation with haemoglobin concentration, J Am Geriatr Soc, 49: 1226 -122 8.
r-8. Maruhn, D. (1976). Rapid colorimetric assay of B-galactosidase and N-acetyl-β-glucosaminidase in human urine, Clinica Chimica Acta,73: 453 - 461.
r-9. Moriguchi, J., Ezaki, T., Tsukahara, T., Furuki, K., Fukui, Y., Okamoto, S., Ukai, H., Sakurai, H,, Shimbo, S. and Ikeda, M. (2003). Comparative evaluation of four urinary tubular dysfunction markers, with special references to the effects of aging and correction for creatinine concentration, Toxicol Lett, 143 (3): 279 –290.
r-10. Nilsson-Ehle, H., Jagenburg, R. and Landahl, S. (1989). Decline of blood haemoglobin in the aged: a longitudinal study of an urban Swedish population from age 70 to 81, Br J Haematol, 71: 437 - 441.
r-11. Ozçay,F., Derbent, M., Aldemir, D., Türkoğlu, S., Baskin, E., Ozbek, N. and Saatçi, U. (2003). Effect of iron deficiency anaemia on renal tubular function in childhood, Pediatr Nephrol, 18 (3): 254 - 256.
r-12. Penninx, B.W., Guralnik, J.M. and Onder, G (2003). Anaemia and decline in physical performance among older persons, Am J Med, 115: 104 -108.
r-13. Steensma, D.P. and Tefferi, A. (2007).Anaemia in the elderly: how should we define it, when does it matter and what can be done? Mayo Clin Proc, 82 (8): 958 - 966.
r-14. Tookey, L.L. (1970).Determination of serum iron. Anal Chem, 42: 779.
r-15. White, D., Kramer, D., Johnson, G., Dick, F. and Hamilton H. (1986). Human ferritin enzyme immunoassay for quantitative determination of ferritin concentration in human serum, J Clin Pathol; 72; 346.
r-16. World Health Organization. (1968). Nutritional anaemias: report of a WHO scientific group. Technical Report Series No. 405. Geneva: World Health Organization,

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