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## Interest of beta 2-microglobulin determination in chronic hemodialysis patients

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### Abstract

The amylose beta 2-microglobulin ( $\beta 2m$ ) is a common complication of long-term hemodialysis, mainly responsible for osteo-articular manifestations including carpal tunnel syndrome (CTS). With the aim to study the various parameters involved in the increase of and determine the interest of dosage, we conducted a cross-sectional study of 104 chronic hemodialysis patients for more than 6 months. The mean age of patients was 52.82 years with a male predominance (62.5%). 61, 3% of our patients are anuric. They all have intermittent hemodialysis at 12 hours per week using a low permeability membrane in 52% of patients. The average age of dialysis layout is 42, 18 years. The mean duration of hemodialysis was 74 months. The mean serum  $\beta 2m$  is 35, 24 mg / l. regarding complications, there were four confirmed cases of carpal tunnel syndrome and 12 deaths. Our study objectify the parameters involved in the increase of  $\beta 2m$ : The current age, age advanced dialysis layout, lack of urine output, low permeability membrane and extended duration hemodialysis. Increased serum levels of  $\beta 2m$  in our hemodialysis demonstrate the poor treatment of middle molecules. Its reduction can be made by improving the quality of dialysis and will avoid all the complications.

**Keywords:** Chronic Hemodialysis; Beta-2microglobuline; Age; Diuresis; Hemodialysis; Duration of membrane; Type amyloidosis; SCC

### 1. Introduction

Beta-2-microglobulin is a key component of the adaptive immune system. It is a low molecular weight polypeptide that exists in free form and bound to cell membranes (light chain histocompatibility class 1 molecules). Its rate of synthesis normally varies from 2 - 4mg/kg/d with a half-life of 2 to 5 hours. This protein is filtered in the kidney by the glomeruli and reabsorbed by the proximal convoluted tubule. In case of renal insufficiency, the serum level of beta-2-microglobulin increases. Internationally, several studies have identified factors that may influence the modification of beta2-microglobulin in different biological media. In hemodialysis patients, the increase in beta2-microglobulin is affected by multiple additional factors such as the duration of hemodialysis and the type of membrane used for hemofiltration. This elevation is at the origin of several complications in chronic hemodialysis patients, including beta-2-microglobulin amyloidosis, which is responsible for osteoarticular manifestations.

The objective of this work is to determine: - The different parameters involved in the increase of beta2-microglobulin: this study focused on the following factors: the age of dialysis, the presence or absence of diuresis, the duration of hemodialysis and the type of membrane used for hemofiltration. Interest of the determination of beta 2-microglobulin in chronic hemodialysis patients: As a preventive measure, in the detection of complications, especially beta 2-

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microglobulin amyloidosis, the first manifestations of which are essentially osteoarticular. As a prognosis, to evaluate its interest as a factor of morbidity and mortality.

## 2. Material and methods

Monocentric cross-sectional study carried out on 123 patients with renal insufficiency, treated by periodic hemodialysis for more than 6 months at the nephrology hemodialysis center "Atlas". The period extended from January 2020 to July 2020. The census of patients was obtained during a survey conducted by a single physician. The questionnaire consisted of three parts: anthropometric data (age, sex, body mass index, and history), data concerning hemodialysis (age of dialysis initiation, residual diuresis, duration of hemodialysis, and membrane used), and clinical data (joint pain, motor and sensory deficits) and paraclinical data (biological workup and electromyogram). The study of beta2-microglobulin was performed by the immunonephelometric method in the biochemistry department of the Avicenne Military Hospital in Marrakech. Statistical analysis was performed using SPSS version 17 software. The tests used to analyze the parameters influencing beta-2-microglobulin are: the chi2 test for the comparison of percentages and the student t test for the comparison of means. A  $p < 0.03$  is considered as statically significant.

## 3. Results

In our study, 62.5% of our patients were male with a male to female sex ratio of 1.6. Their mean age was  $52.82 \pm 16.1$  with extremes ranging from 16 to 82 years. Diabetic nephropathy is the most frequent cause with 29.8% of cases, followed by chronic glomerulonephritis (16.3%) and vascular nephropathy (15.4%). 61.3% of patients are anuric. Regarding the hemodialysis (HD) data, the mean age of initiation of dialysis is 42.18 and the mean duration of entry into HD was 74 months with extremes of 12 to 228 months. 52% of our patients are hemodialysed by a high permeability membrane. The mean beta-2-microglobulin level was 35.24 mg/l with extremes between 7 and 68 mg/l. Statistically, a significant correlation could be found between the increase in  $\beta_2m$  and the age of hemodialysis initiation ( $p = 0.004$ ). To further detail this relationship, our sample was divided into 2 groups according to the cumulative mean serum  $\beta_2m$  value (Table 1).

Patients with higher  $\beta_2m$  concentration are currently older, with a statistically significant difference.

**Table 1** Increase in  $\beta_2m$  as a function of age at dialysis initiation

	Group 1	Group 2
$\beta_2m$ (mg/l)	$\leq 38.42$	$> 38.42$
Number of patients studied	72	51
Average age of HD onset (years)	39.35	54.89

The mean serum  $\beta_2m$  concentration was significantly higher in anuric patients ( $p = 0.019$ ) (Table 2).

**Table 2** Change in serum  $\beta_2m$  concentration as a function of residual diuresis

Residual diuresis	Number of patients studied	Mean serum concentration of $\beta_2m$ (mg/l)
Present	44	34.18
Absent	79	41.66

The evolution was marked by the appearance of 4 cases of carpal tunnel syndrome confirmed by electromyography and 12 deaths.

## 4. Discussion

The accumulation of beta-2-microglobulin in the extracellular space is a necessary, but probably not sufficient, condition for the occurrence of amyloidosis in dialysis patients. The characteristics of the dialysis membrane, namely its structure;

surface area; permeability and degree of biocompatibility play an important role in the variations of serum beta-2-microglobulin concentration in hemodialysis. Most studies have compared the exclusive or near-exclusive use of low-permeability, low-biocompatibility cellulosic membranes such as cuprophane with high permeability, semi-synthetic non-cellulosic membranes. The majority demonstrated the superiority of synthetic membranes. For the same results, we quote the prospective randomized study of Kuchle which compared 24 hemodialysis patients matched in terms of age and duration of dialysis according to the type of membrane used (cuprophane versus high permeability synthetic polysulfone membrane) [1]. (Table 3).

**Table 3** Role of the dialysis membrane in modifying  $\beta$ -2 m in the literature

Authors, years	Membrane used		Cumulative mean $\beta$ 2m in pre-dialysis
AK Cheung, 2008 [2]	High flow	F80 CT190	33.6 mg/l
	Low flow	F8CA 210	41.5 mg/l
Traut M, 2007 [10]	High flow	Polyamide	21.5 mg/l
	Low flow	Cuprophane	42 mg/l
Jeloka T, 2001 [11]	High flow	Polysulfone	25.5 mg/l
	Low flow	Cuprochane	31.3 mg/l

In our study, patients dialyzed with a high permeability synthetic membrane had significantly more decreased beta-2-microglobulin concentrations compared to the low permeability membrane. The duration of hemodialysis plays an important role in the increase of beta-2-microglobulin [3] as well as in the development of these clinical manifestations [4,5]. The frequency and severity of beta-2-microglobulin amyloidosis and carpal tunnel syndrome are correlated with the years in dialysis and are accelerated after 30 years of treatment [6]. In our study, seven patients with chronic hemodialysis for more than 9 years had clinical manifestations related to the increase in beta-2-microglobulin. Three cases of carpal tunnel syndrome (CTS) were confirmed. Age at start of dialysis is a strong risk factor ( $p < 0.004$ ) for the increase of beta-2-microglobulin and the occurrence of CTS independently of the duration of dialysis and the type of membrane. In our study, the correlation between increased beta-2-microglobulin and advanced age at hemodialysis initiation was striking. Statistically speaking, the elevated serum beta-2-microglobulin level is significantly elevated in our anuric patients. This may be explained by a defect in renal elimination of beta-2-microglobulin in these patients. The highest concentrations of beta-2-microglobulin are reached in oligo-anuric uremic patients [8,9].

Regarding the evolution, 15 of our patients died (14.42%), 3 of whom had a confirmed carpal tunnel syndrome. We could not confirm that beta-2-microglobulin is a prognostic factor of morbidity and mortality in our series for multiple reasons. First, the beta-2-microglobulin assay was not regular, due to the unavailability of its reagent at times, and the serum level of beta-2-microglobulin in 82% of the decedents was lower than the average beta-2-microglobulin level in the study population. Serum beta-2-microglobulin concentration is a prognostic factor for morbidity and mortality in chronic hemodialysis patients, irrespective of the duration of hemodialysis, diabetes, malnutrition or chronic inflammation [3]. The mortality rate is higher in the group with high beta-2-microglobulin level ( $> 32$  mg/l) compared to the second group ( $< 32$  mg/l) ( $p < 0.001$ ).

## 5. Conclusion

In our study, advanced age at dialysis initiation, long duration of hemodialysis and low permeability membrane as well as absence of residual diuresis, seem to be the major parameters for increased beta-2-microglobulin in chronic hemodialysis patients. However, its value as a prognostic factor for mortality and morbidity could not be assessed.

Our interest in the analysis of  $\beta$ 2m in dialysis is related to the fact that it seems to be strongly involved in the complications observed during the long term in the dialysis subject. Among these complications, four dominate in terms

of severity and disability:  $\beta_2$ m amyloidosis responsible for osteoarticular complications (especially SCC), undernutrition, anemia and the development of atherosclerosis aggravated by calcium deposits.

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### **Compliance with ethical standards**

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#### *Disclosure of conflict of interest*

Authors declare that no conflict of interest exist.

#### *Statement of informed consent*

Informed consent was obtained from all individual participants included in the study.

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