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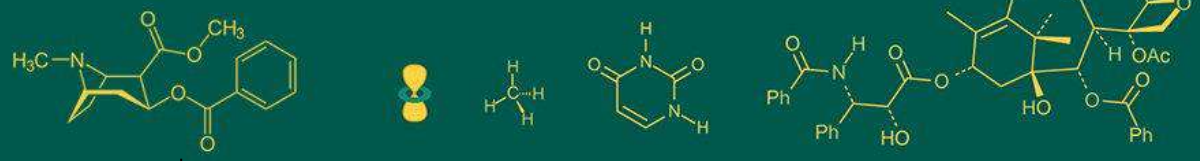

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Prealbumin variation in neonatal bacterial infections

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Abstract
As a malnutrition biomarker, prealbumin or transthyretin (TTR), can detect and reflect various clinical circumstances. In newborns, real malnutrition is rare, and the nutritional situation is relatively constant in the absence of pathologies. However, the management of neonatal bacterial infections remains a major problem due to the non-specificity of clinical signs and diagnostic laboratory markers. This study was conducted in this context to study the variation of prealbumin in neonatal infections.
This is a prospective cross-sectional study carried out at the department of pediatric of the Diamniadio children's hospital in 2016. This includes subjects aged between 0 and 28 days admitted for neonatal infection according to clinical and anamnestic criteria. Prealbumin assay was carried out using the immuno-turbidimetry technique with the A15 automate of Biosystems®. In 50 newborns, bacterial neonatal infection was confirmed in 24% of the population. Prealbumin concentration of newborns with isolated germs (179.08±108.87 mg / L) is lower compared to the group where no germ was isolated (199.41±108.87 mg / L) but without significant difference. However, Gram-negative infection was responsible for a greater decrease in prealbumin.
It is therefore important to include the dosage of prealbumin in the monitoring of neonatal bacterial infections to prevent complications.

Keywords: prealbumin, neonatal bacterial infection, under nutrition

Introduction
Prealbumin also called transthyretin (TTR) is known as a biochemical marker that reflects the nutritional status of patients. It is a plasma protein mainly synthesized by the liver. Its half-life ranges from 2 to 4 days [1].
Small amounts of TTR are also synthesized by the choroid plexus [2], pancreas and retina, but they probably do not affect serum protein concentration [3]. As per its characteristics, it is a protein marker of interest in the biological diagnosis of early malnutrition [4]. It is quickly lowered during acute attacks such as those resulting from trauma, surgery, and especially bacterial infections [5] in favor of many inflammatory proteins.
The interaction between nutritional status and infections has been studied extensively [6, 7].
In intensive care units, the combination of low concentrations of TTR and albumin can help identify patients at high risk of developing sepsis [8].
In newborns, the levels of transthyretin may be affected by several factors such as gestational age, inflammation, infection, and surgery [9]. Though all pathologies can be accompanied by malnutrition, extreme ages are mostly affected due to physiological peculiarities, especially in newborns.
Malnutrition is often unknown in hospitals and more specifically in pediatrics [10]. When combined with other markers, variation in prealbumin concentration can help understand the severity of a disease [2] and the change in the nutritional status of a patient, which may result in the increasing of the length of hospitalization [11].
Early recognition of malnutrition is necessary in the prevention of sepsis, morbidity, as well as mortality [11] from a possible related disease. Thus, TTR may have the potential to detect and reflect various types of clinical circumstances as a biomarker [12] such as in systemic inflammatory response syndrome (SIRS) where its synthesis is reduced in favor of acute phase proteins [13]. In this study, our objective was to assess concentrations of the plasma

prealbumin and to analyze whether these plasma concentrations can predict neonatal infection.

Type of study

This is a prospective cross-sectional study carried out in newborns of consenting parents admitted to the pediatric department of the Diamniadio Children's Hospital for neonatal infection in 2016.

- **Study population**

Patients aged between 0 and 28 days, hospitalized in the neonatology unit of the pediatric department for a suspected neonatal infection according to clinical-anamnestic criteria were included in this study.

- **Sampling**

Samples are taken at the hospitalization Unit by qualified personnel on a dry tube and on a blood culture bag.

- **Determination of prealbumin**

The A15 auto analyzer by Biosystems® was used. The prealbumin assay was made from serum using the immuno-turbidimetry technique with the reagent from Biosystems®. An internal quality control was carried out to validate the results.

- **Principle**

The presence of prealbumin in the sample precipitates in the presence of anti-human prealbumin antibodies. The light s attering generated by the antigen-antibody complexes was proportional to the prealbumin concentration and can be quantified by turbidimetry.

- **Statistical analysis**

Statistical analysis was performed using SPSS version 20 software. The statistical analysis methods used are Fisher's F tests and KHI-DEUX test. A p> 0.05 is considered significant.

Results

Table 1: Distribution of the population according to the prealbumin values

Normal prealbumin	Number	Percentage
NO	15	30%
YES	35	70%
Total	50	100%

70% of patients had normal prealbumin (n = 35) versus 15% with abnormal prealbumin (n = 15). With a p-value = 0.010.

Table 2: Variation of prealbumin depending on the type of infection and isolated germs

Type of infection	Number	Prealbumin (mg/L)	p-value
INNP	38	186,43±80,62	0,26
INNT	12	219,08±105,93	
Group I	12	179,08±80,44	0,33
Group II	38	199,41±108,87	

The mean level of prealbumin in patients with early neonatal infection (INNP) was 186.43 mg / L with a standard deviation±80.620 mg / L and extremes ranging from [61 - 418] mg / L while the mean level of prealbumin in patients with late neonatal infection was 219.08 mg / L with a standard deviation±105.934 mg / L and extremes ranging from [103 - 410] mg / L. Studying the difference gave a p-value of 0.26 greater than 0.05. Group I patients where bacterial infection was confirmed with isolation of a germ had a lower prealbumin concentration (179.08±80.44 mg / L) than those in group II (199.41±108, 87) where infection was not confirmed but without significant difference.

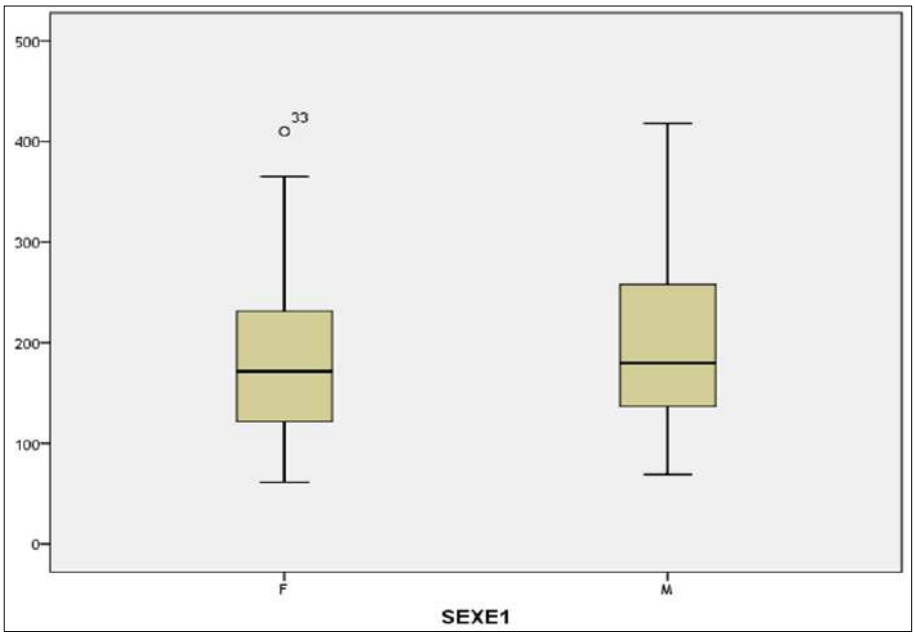

Fig 1: Variation of the mean prealbumin according to sex

The mean level of prealbumin in female patients was 187.71 with a standard deviation ±90.221 while the mean level of prealbumin in male patients was 200.88 with a standard deviation ±165.36 (figure 1).

Table 3: Variation of the mean prealbumin according to the type of germs isolated

Isolated germs	numbers	Pre-albumin (mg / L)	p-value
Enterobacteriaceae	3	145,67	
Non-fermentation	2	129,50	0,8
Staphylococci	6	176,33	
Streptococci	3	214,00	

Prealbumin was lower for subjects infected with bacilli, non-fermentative bacteria and enterobacteria, compared to cocci, but without a significant difference.

Discussion

In our population consisting of 50 newborns, 70% had normal prealbumin values (Table I) with a significant difference (p = 0.01). In newborns, real malnutrition was rare [14]. At birth, plasma TTR concentrations were approximately two-thirds of those measured in healthy mothers, and then increase linearly as the infant grows [5]. Based on the type of infection, particularly in the case of early neonatal infection (INNP) which occurs between D0 and D7 and late neonatal infection (INNT) which occurs between D8 and D28, no significant difference was observed (Table II). However, subjects with an NNRT had higher prealbumin values. This comparison also corresponds to the study of the variation of prealbumin as a function of age, which was therefore not significant.

The result was contradictory with the one of Johnson [15] who demonstrated that prealbumin varied with age. Jono's multicenter study [12] also demonstrated variation with age for both sexes. This contradiction may be related to the size and age difference between our populations and theirs. Also regarding sex, the difference was not significant with a p-value equal to 0.83 between an average prealbumin equal to 200.88±86.05 mg / L in males and 187, 71±90.22 mg / L for female subjects (Figure 1). According to Ingenbleek [16], the difference based on sex was apparent because of androgenic hormones on anabolic processes. Similarly, Aliyazıcıoğlu [17] noted a difference according to gender for a determination of prealbumin in the umbilical cord. As per his findings, the levels of gonadotropins in the umbilical cord were significantly higher in men than in women. This explains the differences found in relation to our results.

Moreover, the evaluation of prealbumin based on the isolation of germs allowed us to obtain an average of 179.08±108.87 mg / L for group I and of 199.41±108.87 mg / L for group II (Table IV). The average of the prealbumin concentration of the group where a germ was isolated was lower compared to the group where no germ was isolated but without significance with a p-value equal to 0.33 well above 0.05. However, no difference was observed that may depend on the type of germs isolated. Subjects infected with Gram negative bacilli had lower prealbumin concentrations (Table III). This is because bacteria in this group can express pathogenicity factors that allow them to overcome various obstacles in the body's specific and non-specific defenses. They can then directly access the targeted tissues or allow toxins to diffuse therein, which could lead to temporary or permanent cellular alterations [18]. Non-fermenting *Pseudomonas aeruginosa* for example, is very pathogenic in subjects with impaired means of defense.

As evidenced by the study by Cynober *et al*. [19] which reported that burns with sepsis had very low serum TTR levels compared to those who did not. He concluded that low serum TTR levels seemed to predict fatal outcomes for patients. Bernstein's study [13] also demonstrated among hospitalized patients that the TTR was lower in patients with Systemic Inflammatory Response Syndrome with an increased white blood cell count of over 12,000 / µl, and procalcitonin (PCT) of more than 2.0 pg / ml.

Conclusion

Our results highlighted normal values for most of our targeted population. The group with a confirmed bacterial neonatal infection had a lower average prealbumin concentration whereas neonates infected with Gram-negative bacilli had lower TTR concentrations, probably related to their virulence.

Authors' Declaration

The authors declare having no conflict of interest in related to this article.

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