BENHA MEDICAL JOURNAL bmj
Print ISSN 1110-208X.
Online ISSN 2357-0016

Assessment of Serum Amyloid A in Healthy Children

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Received: 17 July 2024
Accepted: 24 August 2024

Abstract:

Background: Serum amyloid A (SAA) is a major conserved and sensitive acute phase protein that is highly expressed in response to inflammation and tissue injury. High levels of SAA are associated with several chronic inflammatory diseases, and may also be a potential biomarker of several malignancies. This work aimed to to assess SAA level in apparently healthy children. **Methods:** This cross-sectional study was carried out on 85 healthy children, aged 8-11 years old, from outpatient clinic of benha university hospital and c. All included children were subjected to detailed history taking, general examination, local examination and investigations including C-reactive protein (CRP) and SAA. **Results:** There was no statistical difference in the level of serum amyloid A regarding their sex but there was statistical difference in the level of serum amyloid A regarding their age, increasing significantly in older children. There was a significant positive correlation between serum Amyloid A and age, also there was a significant positive correlation between SAA and both BMI, and CRP level . **Conclusions**: The mean SSA among healthy children were 2.2±0.7. It wasn't differ by sex, but increase gradually with age. There was a significant positive correlation between SSA and (age, BMI and CRP).

Keywords: Serum Amyloid A level; Healthy; Children.

Introduction

Serum amyloid A (SAA) is acute phase protein that is highly expressed in response to inflammation and tissue injury. In humans, several isoforms have been identified. SAA is present in the blood of healthy subjects at generally quite low levels, but during the acute-phase response (APR), SAA hepatic production leads to remarkable increased serum values within the initial 24 hs with very lower levels after the acute phase [1]. SAA exerts also immunological activity by activating immune cells and inducing cytokines and chemokines [2].

High levels of SAA are associated with several chronic inflammatory diseases, and may also be a potential biomarker of several malignancies. However, the exact role of SAA in physiologic and pathologic settings is only partially understood [3].

In younger children, the differential diagnosis between infectious or noninfectious processes is particularly difficult because a detailed description of the symptoms cannot be obtained. Also, there is the possibility that the symptoms of bacterial infection may be hidden by what appears to be a viral infection, which is a cause of concern to the general practitioner because rapid, accurate intervention is required in such cases [4].

A set of laboratory tests is usually requested because a single test is not sufficiently sensitive or specific to make a diagnosis or to assess the severity of the signs and symptoms [5]. The tests that are usually requested include a complete blood count with a differential white blood cell (WBC) count, erythrocyte sedimentation rate (ESR), urine and/or blood cultures and CRP. CRP is a member of the pentraxin superfamily, whereas SAA belongs to the apolipoprotein family. Both are synthesized by the liver in response to stimuli by various cytokines [6]. ELISA was expected to measure low levels of SAA because of its high sensitivity; however, no widely accepted cutoff was defined for some commercially available immunoassays [2].

The aim of this work was to assess serum amyloid a level in apparently healthy children.

Patients and Methods

This cross-sectional study was carried out on 85 healthy children, aged 8-11 years old, from school and conducted at Benha University Hospitals during the period from March 2023 to December 2023.

Informed written consent was obtained from all participants' parents. The study was done after approval from the Ethics Committee on research of Faculty of Medicine, Benha University
(MS 23-1-2023)

Exclusion criteria were inflammatory disorders, ongoing infections, obesity and use of any medication.

All included children were subjected to detailed history taking including (age, sex, residence, family history, perinatal history, history of previous surgery or history of systemic diseases), general examination (including assessment of vital signs and anthropometric measurements), local examination of all body systems included (cardiovascular system, respiratory system, abdomen, central nervous system and musculoskeletal system).

Investigations:

C-reactive protein was measured by scattering immunoturbidimetry (Beckman Coulter AU5800). SAA was detected and quantified with a commercial solid phase sandwich enzyme-linked immunosorbent assay (human SAA ELISA kit, IBL International GmbH, Germany) used on automated analyzer (immunomat, SERION diagnostic, Alifax, Italy) according to the manufacturer's protocol.

Blood samples were collected from peripheral veins under sterlized condition, blood samples were collected with a 20 G straight needle directly into BD Vacutainer® plastic serum collection tubes (becton, dickinson and company, NJ USA), and the samples were then

centrifuged at 2500 g for 15 min at room temperature within 1 h of collection and the sera stored at −20°c until used .

Sample size:

Sample size was calculated using G power sample size calculator version 3.1.9.4 based on Carbone et al. [2] the mean serum SAA of the studied group was 71.7 ± 80.8 ng/ml. Study power 95 % and alpha error probability 0.05. The minimal calculated sample size is 16 patients and increased to 85 patients.

Statistical analysis:

Statistical analysis was done by SPSS v28 (IBM Inc., Armonk, NY, USA). Quantitative variables were presented as mean and standard deviation (SD) and compared between the two groups utilizing ANOVA (F) test. Qualitative variables were presented as frequency and percentage (%) and were analysed utilizing the Chi-square test. A two tailed P value < 0.05 was considered statistically significant. Pearson correlation was done to estimate the degree of correlation between two quantitative variables.

Results

This study included 42 (49.4%) males and 43 (50.6%) females; their mean age was 9.5±1.2 years and the mean body mass index in the studied group was 18.9±2.4 Kg/m^2. Table 1- Figure 1

The mean C-reactive protein in the studied group was 3.3±1.4 mg/dl and the mean serum amyloid A in the studied group was 2.2±0.7 mg/L. Table 2- Figure 2

There was no statistical difference in the level of serum amyloid A regarding their sex but there was statistical difference in the level of serum amyloid A regarding their age, increasing significantly in older children.Table 3- Figure 3

There was significant positive correlation between serum Amyloid A and age, also was significant positive correlations between serum Amyloid A and both BMI, and CRP. Table 4- Figure 4

Table 1: Socio demographic data and body mass index of the studied group

		N=85	%
Sex	**Male**	42	49.4%
	Female	43	50.6%
Age (years)		9.5±1.2	
Body mass index (Kg/m^2)		18.9 ± 2.4	

Data presented as mean ± SD of frequency (%).

Table 2: C- reactive protein and serum amyloid A of the studied group

	N=85
C- reactive protein (mg/dl)	3.3±1.4
Serum Amyloid A (mg/L)	2.2±0.7

Data presented as mean ± SD of frequency (%).

Table 3: Serum Amyloid A according to sex and age groups in the studied group

		Serum Amyloid A (mg/L)	P value
Sex	**Male**	2.3±0.7	0.37
	Female	2.2±0.7	
Age (years)	**8**	1.53±0.17	**<0.001***
	9	1.78±0.26	
	10	2.65±0.47	
	11	3±0.31	

Data presented as mean ± SD, *: statistically significant as P value <0.05.

Table 4: Correlation between serum Amyloid A and (age, body mass index and C- reactive protein) in the studied group

	Serum Amyloid A (mg/L)	
	r	**P value**
Age (years)	0.867	**<0.001***
BMI	0.365	**0.001***
CRP	0.245	0.024*

BMI: body mass index, CRP: C- reactive protein, r: Correlation coefficent, *: statistically significant as P value <0.05.

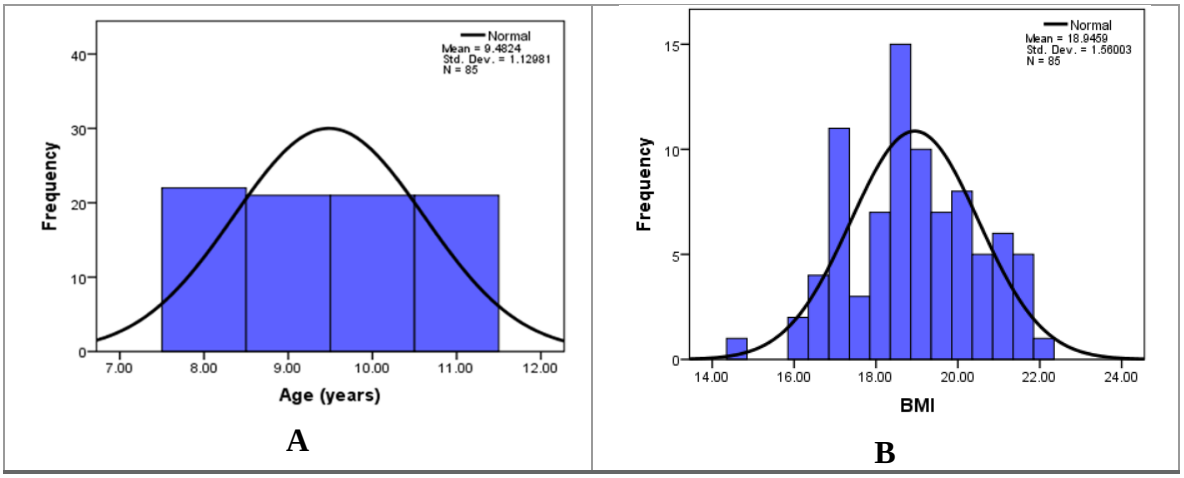

Figure 1: A: Age distribution in the studied group, B: Distribution of body mass index values in the studied group

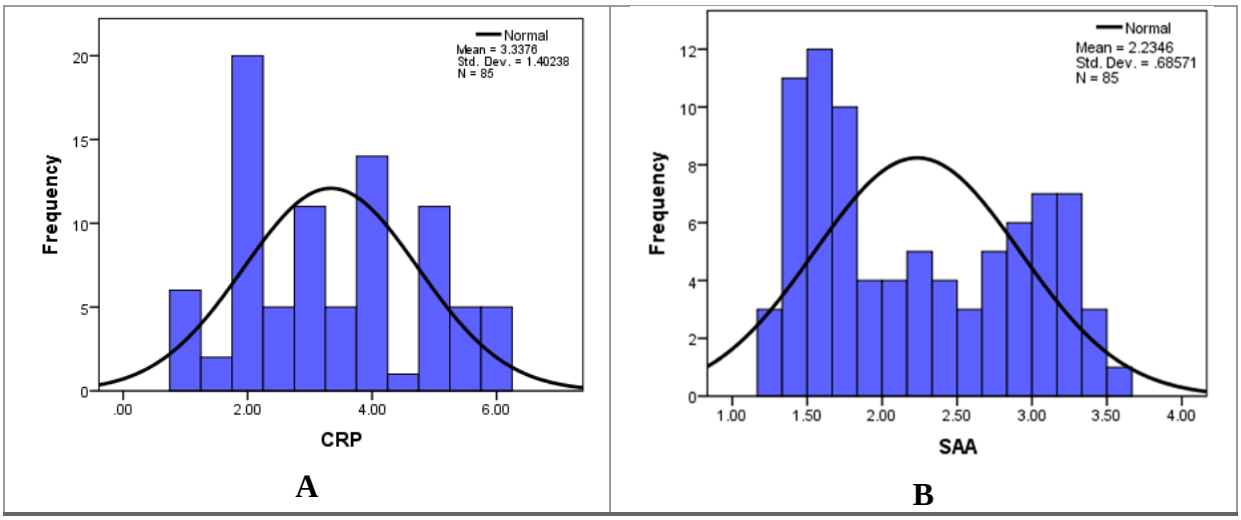

Figure 2: A: Distribution of C- reactive protein values in the studied group, B: Distribution of serum amyloid A values in the studied group

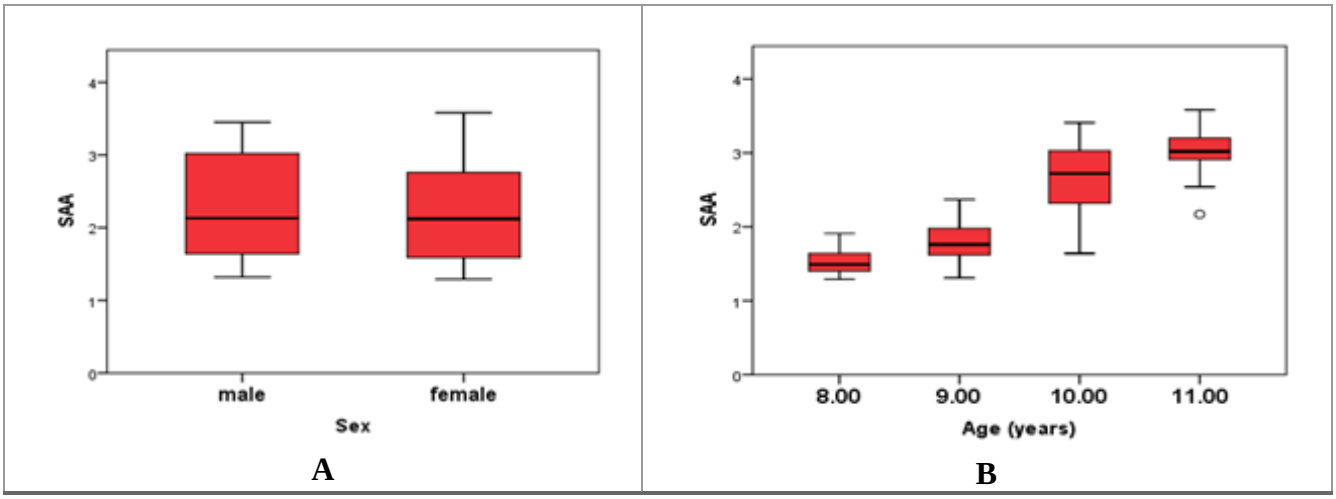

Figure 3: A: Comparison between males and females as regards to serum amyloid A level, B : Serum Amyloid A according to age groups in the studied group

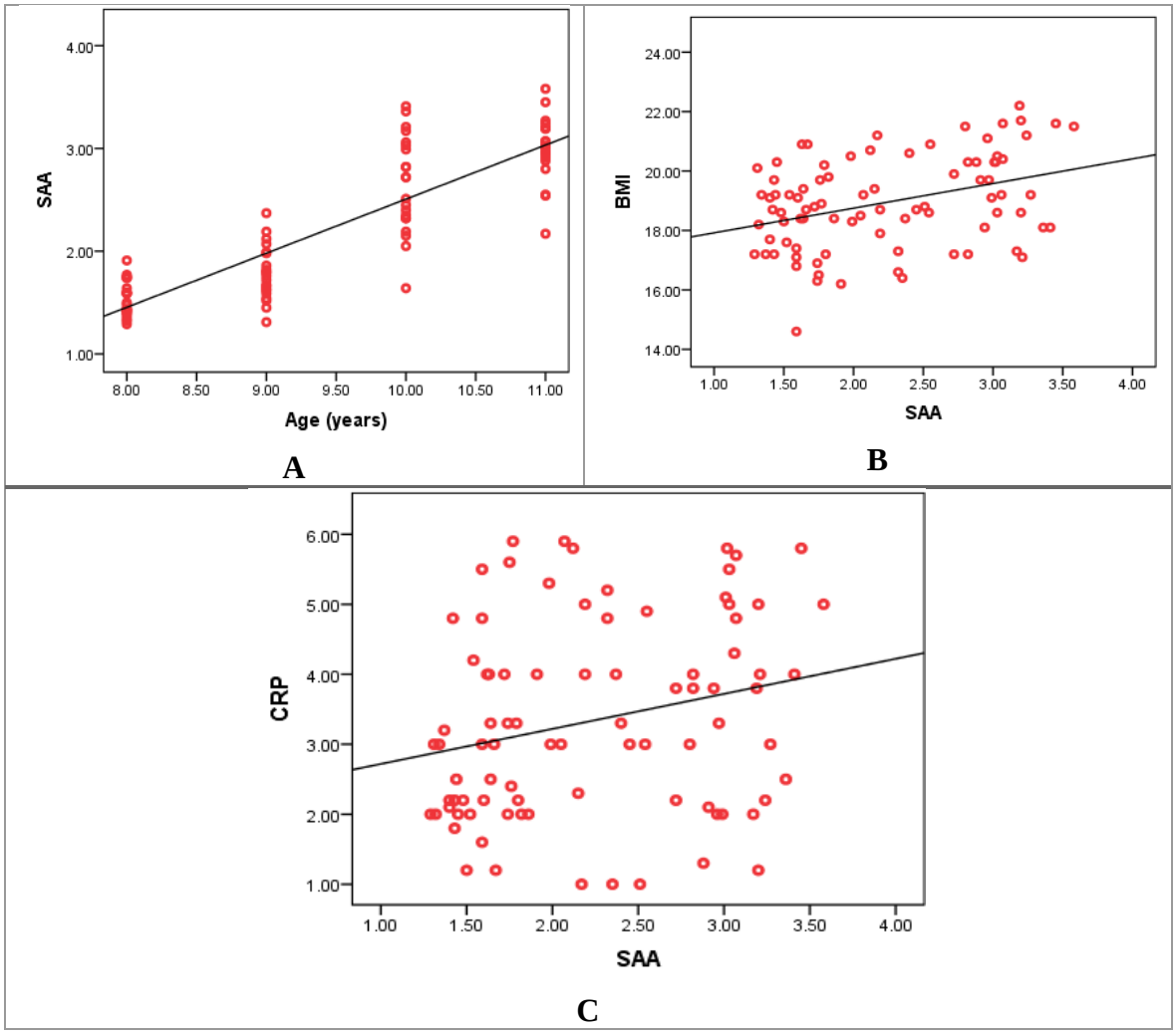

Figure 4: A: Correlation between serum Amyloid A and age, B: Correlation between serum Amyloid A and body mass index, C: Correlation between serum Amyloid A and C- reactive protein in the studied group

Discussion

Our results were in agreement with others [7] who studied serum amyloid A (SAA) in children and adolescents, SAA was assessed by ElISA, they included 100 children (50 males and 50 females), their mean age and BMI z-score of the assessed individuals were 10.82±3.16 years and 1.32±1.62, respectively. The median SAA in children not overweight was 2.8 (range: 1.7-3.7) mg/L.

In the present study, there was no statistical difference in the level of SSA regarding their sex.

Our results were in agreement with other researchers [2] who observed that means of SAA resulted not significantly different between sexes ($p > .05$) when the mean values of males and females were compared.

In the current study, there was statistical difference in the level of serum amyloid A regarding their age, increasing significantly in older children and there was a significant positive correlation between serum amyloid A and age

Our results were in agreement with Barbosa et al., [7] who reported that in the multivariate analysis, age (OR=1.73; 95%CI: 1.16-2.60, p=0.007), was found to be independently associated with increased SAA values.

Our results were not matched with others [2] who observed that no significant association between SAA levels and age was found ($r = 0.05$) in adults.

In the current study, there was a significant positive correlation between SSA and BMI.

In concordance with a previous study [8] which reported in the metaanalysis, that there was a strong association between body mass index and SAA levels was found in the 11 cross-sectional studies. The overall correlation coefficient is 0.230 (95% CI 0.160-0.297, $P < 0.0005$).

In the present study, there was a significant positive correlation between SSA and CRP.

Similarly, Carbone et al., [2] reported a good correlation ($r = 0.49$) between SAA and CRP ($p < .05$) in healthy adults, and others [9], reported that correlation analyses showed that SAA and CRP were positively correlated in the children with familial Mediterranean fever (FMF) ($r = 0.446$, $p = 0.01$).

The correlation between SAA concentration and CRP suggesting a good concordance between the two laboratory parameters. However, because the biosynthesis of SAA and CRP depended by different network of cytokines, the clinical implications of these proteins to the acute-phase response may differ. It has been shown that SAA correlate better than CRP with disease activity in rheumatoid arthritis, spondyloarthritis, inflammatory bowel diseases and viral infections [10].

Conclusions:

Our results showed that the mean serum amyloid A among healthy children were 2.2±0.7. It wasn't differ by sex, but increase gradually with age. There was a significant positive correlation between serum Amyloid A and (age, BMI and CRP).

Further larger studies are need to approve these results, being increasing with age, make it warranted to be assessed in high numbers of each age group, for a better identification of normal range for each age group in children and should assess the normal range of SAA in children according to their BMI.

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To cite this article: Ghada S. Abdelmotaleb , Mohammed A. Elgamal , Amira O. Abd Elghafar , Enas M.Nor Eldeen. Assessment of Serum Amyloid A in Healthy Children. BMFJ 2025;42(1):118-124.