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Research Article

Measurement of the Complement Protein C3 Levels in Children Suffering from Recurrent Infections at Khartoum State, Sudan

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Abstract

Recurrent moderate or major bacterial infections, autoimmune diseases, or episodes of angioedema-a painless but frequently spectacular swelling beneath the skin or in the bowels that can be excruciatingly painful-are clinical indicators of potential complement deficits. The clinical issues that patients with complement deficits face are dependent on how the particular complement protein functions normally. The study was conducted to determine the complement C3 deficiency among children suffering from recurrent infections. The study includes both sexes: 49 (54%) male and 41 (46%) female. The level of complement C3 deficiency in the age group (> 2.5, 2.6 - 5, 5.1 - 7.5, 7.6 - 10) years showed 17%, 17%, 42%, and 25%, respectively. The study found that both deficient and low levels were (7%), the normal range was (36%), the high level was (37%), and the very high level was (14%). The relationship between the age group and the level of complement C3 was insignificant. According to residents, 67% of Khartoum North yields the highest rate of complement C3 deficiency than 33% of Khartoum. The study concluded that there is a relationship between complement C3 deficiency and recurrent infection, and early diagnosis is important to decrease the risk of acquiring severe infections during childhood.

Keywords: *Complement Protein C3; Children; Recurrent Infection*

Introduction

Almost all organisms have basic defense mechanisms called host defense systems. Higher species, in particular, have developed multiple complex levels of defense that provide protection against invaders and preserve barrier function. A robust defense response is generated by a combination of innate and adaptive immunology, coagulation and contact mechanisms, pattern recognition molecules (PRMs), and antimicrobial peptides. An essential component of this group is performed mediators of defense, which enable an instantaneous response to insults like injury and infection. This is in contrast to adaptive immune responses, which must develop over time and are specific to a given pathogen [1,2]. Several crystallographic structures of C3 have been determined, revealing that this protein contains 13 domains. In humans, C3 is predominantly synthesized by liver hepatocytes and, to some degree, by epidermis keratinocytes [3-8]. It has been

demonstrated that Factor H and Complement Component 3 interact. Deficiencies in C3 cause generic infections, which typically result in the newborn's death. An essential component of the natural defense against common infections is the complement system. Complement activation leads to robust and efficient proteolytic cascades, which terminate in opsonization and lysis of the pathogen and generate the classical inflammatory response by producing potent proinflammatory molecules. An essential function of C3 is to activate the complement system [8-12]. Its activation is required for classical, alternative, and lectin complement activation pathways, is a protein of the immune system [13,14]. However, more recently, observations that connect complement activation to adaptive immune responses have broadened the importance of complement in the immune response. It is now appreciated that complement is a functional bridge between innate and adaptive immune responses that allows an integrated host defense against pathogenic challenges. As such, a study of its functions provides insight into the molecular underpinnings of host-pathogen interactions as well as the organization and orchestration of the host immune response. This review attempts to summarize the roles complement plays in innate and adaptive immune responses and the consequences of these interactions on host defense. One of the main innate immune system effector systems, the complement system is an extensive and essential part of innate immunity. Discovered in 1896 by Bordet as a heat-labile component of serum, it was so named for its ability to 'complement' the antibacterial properties of antibodies in the heat-stabilized fraction of serum. It is now appreciated that complement is a complex network of plasma and membrane-associated serum proteins that can elicit highly efficient and tightly regulated inflammatory and cytolytic immune responses to infectious organisms (bacteria, viruses, and parasites), tissue damaged by physical, chemical, or neoplastic insults, and other surfaces identified as 'nonself'. For many years following its discovery, complement was believed to play only a role in innate immune responses and to have no effect on adaptive immune responses. This was similar to the general belief that innate immunity was limited to immune functions involving the prevention and confinement of infection while adaptive immunity supplied the effectors needed to eradicate the infection. Since the 1970s, there has been a significant increase in the amount of research that shows how the adaptive and innate wings of immunity interact. This is because it was questioned if it was possible to distinguish between the two arms of immunity and their respective purposes. In a similar vein, complement's capacity to drive strong innate immune responses as well as interact with and impact T- and B-cell biology and adaptive responses has gained recognition. A system of over thirty proteins called complement is found in plasma and on the surfaces of cells. It makes up more than 3 g/L and more than 15% of the globular fraction of plasma [15].

Materials and Methods

Study design

This is a clinical-based descriptive study to detect complement protein C3 deficiency.

Study area

This study took place in Sharg El Nile Hospital. That located in Khartoum, Khartoum North, Sudan.

Study population

Recurrent infection children attending Khartoum state.

Sampling technique

It is a convenient sampling technique. Ninety patients with recurrent infections were accepted to participate in this study.

Inclusion criteria

Patients diagnosed with recurrent infections attending Sharg El Nile Hospital were included in this study. Patients who were between 3 months and 10 years old were included in this study.

Exclusion criteria

Recurrent infection patients aged less than 3 months and above 10 years were excluded.

Tools for data collection

Primary data were collected from recurrent infection patients by using a questionnaire taken by the investigator. The questionnaire was specifically designed for participants to obtain the research objectives written in the English language. The questions related to demographic data. Secondary data were obtained from the serum of recurrent infection patients. Data of complement C3 were detected by nephelometric immunoassay [MISPA-i2].

Sample collection

Under aseptic conditions, 5 ml of venous blood was collected in a plain container by venue puncture using a holder device from each participant. Then samples were left to clot, and the serum was separated by centrifugation and kept at 20 degrees Celsius until use.

Sample processing techniques

The serum was thawing at room temperature and detected for complement component C3 using nephelometric immunoassay.

Principles of a nephelometric immunoassay

The serum sample reacts with specific antibodies for human complement protein C3 and causes a change in absorbance that is directly proportional to the concentration of protein C3 in the sample.

Ethical consideration

Permission was sought from the administration of Sharge Alnile Hospital to conduct data collection for this particular study. Furthermore, informed verbal consent was also obtained from patients who were participating in this research before interviewing them. The participation of the participants was voluntary. Participants were guaranteed that the information provided would be kept confidential and solely used for this study.

Data analysis and presentation

The data was analyzed using the computer statistical program Statistical Package of Social Sciences (SPSS) version 22, which used the chi-square test and was presented using a suitable method. Then a chi-square test was used to get the correlation for significance, and the p-value was considered significant when it was < 0.05.

Results

This study was conducted from March to June 2018, to determine the frequency of complement protein C3 deficiency among children suffering from recurrent infection. A total of 90 participants were involved in this study, blood samples were collected from each, and serum was separated by centrifugation and preserved at -20°C until tested. The enrolled study targets were patients situated in Khartoum and Khartoum North with age groups of 3 months to 10 years. Most of the study group 29 (32%) were aged between 3 months and 2.5 years (Table 1), and most of them were male 49 (54%) (Table 2). The majority of the participants were from Khartoum North 51 (57%) (Table 3). Complement protein C3 deficiency was found in 14% of the study group (Table 4). The participants in the age group 5.1 - 7.5 years showed the highest rate of complement C3 deficiency (16%) (Table 5). According to gender, the female group showed a slightly high rate of complement C3 deficiency (7%) (Table 6). The participants from Khartoum North showed a higher frequency of complement C3 deficiency (8%) (Table 7). In the relationship between age and the level of complement C3 deficiency, the highest rate of complement C3 deficiency was seen between 5 and 7.5 years old (42%), However, the association between age and complement C3 deficiency was statistically insignificant (P value = 0.288) (Table 8). The relationship between the gender factor and the level of complement C3 deficiency showed similar statistically significant findings (50%) (P value = 0.017) (Table 9). The relationship between the location and the level of complement C3 deficiency was statistically insignificant (P value = 0.385) (Table 10).

Age	Frequency	Percent
Less than 2.5 years	29	32%
2.6 - 5 years	17	19%
5.1 - 7.5 years	25	28%
7.6 - 10 years	19	21%
Total	90	100%

Table 1: *Frequency of study group according to age.*

Sex	Frequency	Percent
Male	49	54%
Female	41	46%
Total	90	100%

Table 2: *Frequency of study group according to sex.*

Residence	Frequency	Percent
Khartoum	39	43%
Khartoum north	51	57%
Total	90	100

Table 3: *Frequency of study group according to residence.*

Complement C3	Frequency	Percent
Very low	6	7%
Low	6	7%
Normal	32	36%
High	33	37%
Very high	13	14%
Total	90	100%

Table 4: *Distribution of complement C3 level in the study group.*

Age	Complement C3 level					Total
	Very low	Low	Normal	High	Very high	
Less than 2.5 years	0	2	11	14	2	29
	(0.0%)	(7%)	(38%)	(48%)	(7%)	(100%)
2.6 - 5 years	0	2	8	3	4	17
	(0.0%)	(12%)	(47%)	(18%)	(23%)	(100%)
5.1 - 7.5 years	4	1	8	8	4	25
	(16%)	(4%)	(32%)	(32%)	(16%)	(100%)
7.6 - 10 years	2	1	5	8	3	19
	(11%)	(5%)	(26%)	(42%)	(16%)	(100%)
Total	6	6	32	33	13	90
	(7%)	(7%)	(35%)	(37%)	(14%)	(100%)

Table 5: *Distribution of complement C3 level according to age.*

P value = 0.288.

Sex	Complement C3 level					Total
	Very low	Low	Normal	High	Very high	
Male	3	3	23	18	2	49
	(6%)	(6%)	(47%)	(37%)	(4%)	(100%)
Female	3	3	9	15	11	41
	(7%)	(7%)	(22%)	(37%)	(27%)	(100%)
Total	6	6	32	33	13	90
	(7%)	(7%)	(36%)	(37%)	(14%)	(100%)

Table 6: *Distribution of complement C3 level according to sex.*

P value = 0.017.

Residence	Complement C3 level					Total
	Very low	Low	Normal	High	Very high	
Khartoum	2	2	12	17	6	39
	(5%)	(5%)	(31%)	(44%)	(15%)	(100%)
Khartoum north	4	4	20	16	7	51
	(8%)	(8%)	(39%)	(31%)	(14%)	(100%)
Total	6	6	32	33	13	90
	(7%)	(7%)	(36%)	(37%)	(14%)	(100%)

Table 7: *Distribution of complement C3 level according to residence.*

P value = 0.385.

Age	Complement C3 level	
	Frequency	Percent
< 2.5 years	2	17%
2.6 - 5 years	2	17%
5.1 - 7.5 years	5	41%
7.6 - 10 years	3	25%
Total	12	100%

Table 8: *Relation between complement C3 level and age.*

Gender	Complement C3 level	
	Frequency	Percent
Male	6	50%
Female	6	50%
Total	12	100%

Table 9: *Relation between complement C3 level and gender.*

Residence	Complement C3 level	
	Frequency	Percent
Khartoum	4	33%
Khartoum north	8	67%
Total	12	100%

Table 10: *Relation between complement C3 level and residence.*

Discussion

Complement component C3 deficiency in children can lead to recurrent infections with severe sequelae and high mortality and morbidity rates. In Sudan, data concerning the role of complement C3 deficiency in relapsing the infection among children could not be found. Early diagnosis of C3 deficiency is necessary to support the treatment and avoid recurrent infections. In my opinion, this study provides information that is considered a primary prevention effort for childhood. The current study focused on the detection of complement C3 deficiency. A total of 90 participants recruited in the present study and their ages were ranged from 3 months to 10 years old, similar to a previous study done by A. S. Grumach., *et al.* concerning Complement Profiles in Neonates of Different Gestational ages (< 34 - > 37) weeks [16], also agreed with another study done by Magdalena Janzi., *et al.* concerning the screening for C3 deficiency in newborns using Microarrays [17]. The present study illustrated that the relation between complement C3 deficiency and age showed that 5.1 - 7.5 years had very low deficiency than the other groups, these findings disagreed with the study of Thomas H., *et al.* about inherited complement component deficiencies in membranoproliferative glomerulonephritis, reported that the patient over a 4-year was in the normal range [18]. Children with recurrent infection in this study showed deficiency in complement C3 level (14%) this agreed with a previous study done by Maimun Syukri., *et al.* about the comparison of serum C3 complement levels between young women with recurrent urinary tract infection and healthy women [19]. However, the *in vivo* significance of these low levels remains unknown.

Conclusion

The study concluded that there was relation between complement C3 deficiency and recurrent infection, and early diagnosis is important to decrease the risk of acquiring severe infections during childhood.

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Conflict of Interest

The author has affirmed that there are no conflicting interests.

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