Prediction of allergic diseases by measurement total IgE in umbilical cord blood levels: A 8 -year follow up study

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Abstract

Allergic diseases in children have increased significantly in recent years and now affect up to 35% of children. This study aimed to investigate the total IgE level in newborn's umbilical cord blood and its association with the development of allergic diseases during 8 years.

Methods: In cross-sectional study included 500 infants who were born in the obstetrics department at Tishreen and Al-Assad University Hospitals during the period 2007-2015. Questionnaires were administered after the birth of the infant included gender, gestational age, birth weight, mode and season of delivery, smoking during pregnancy, family history of the allergic diseases, and umbilical cord blood was obtained for measurement of total immunoglobulin E (IgE) levels. We followed the newborns for eight years through clinical examination to investigate the development of allergic diseases.

Results: Of 500 newborns, 214 (42.8%) were classified as having high total immunoglobulin E in umbilical cord blood. We followed 143 of 214 newborns for 8 years. There was an allergic family history in 51.7% of newborns. During the following period, the allergic diseases developed in 76.22% of the children with high total immunoglobulin E in umbilical cord blood. Allergic symptoms in children varied between nasal allergy in 19.6% of children, skin allergy (Eczema and urticarial)in 25.2% of children, childhood asthma in 31.5% of children. The rate of development of allergic symptoms in the presence of two factors (family history and high total immunoglobulin E in umbilical cord blood) was 51.7%.

Conclusion: We found a high Prevalence of allergic diseases in children with high total immunoglobulin E in umbilical cord blood. The Current study could be used as a preventative strategy to reduce the risk of allergic diseases by predictive of subsequent

Introduction

Allergic diseases represent an increasingly important public health problem worldwide in recent years **[1].** Allergic diseases result from the interaction between genetic and environmental factors to produce high levels of immunoglobulin E (IgE), which can activate the immune system **[2].** Accordingly, there is a great interest in the initial prevention of allergic diseases. Early prenatal diagnosis is the first essential step towards prevention and better treatment **[3].** IgE in cord blood is thought to be a product of the fetus and is secreted by the fetus by the 11^{th} week of gestation which does not typically cross the placental barrier **[4].** The role of cord blood IgE levels in predicting the development of allergic diseases has been widely discussed in a few decades ago, and it has been proposed as a valuable tool for identifying neonates with a high risk of developing the allergic disease in later life**[5-6].** However, there are also various studies on the accuracy of umbilical cord blood in predicting childhood allergy**[7]**

ThE current study aimed to investigate the total IgE level in umbilical cord blood of newborns in Lattakia, Syria to specify the association between this level and development of allergic disease during 8 years following up.

Materials And Methods

A cross-sectional retrospective study included 500 cord blood samples from neonates of mothers who were referred to Al-Assad Hospital of Lattakia, Syria for delivery between 2007 and 2015. Exclusion criteria included severe co-morbidity, e.g. congenital defects, perinatal trauma, intracranial hemorrhage, other life-threatening conditions in the perinatal period neonates. A self-administered questionnaire was distributed to the study participants and was completed by them. Data was collected by recording the following information: demographic information (gender, gestational age, birth weight, number of previous pregnancies, mode and season of delivery, smoking during pregnancy etc..), family history of allergy (asthma, allergic rhinitis, atopic dermatitis, urticarial, food allergy, and drug allergy). The total IgE level in umbilical cord blood samples was analyzed using an immune radiometric assay technique and classified according to the value 0.5 IU/ml into normal and high value **[7].**

We followed up on the possibility of neonates for 8 years through clinical examination of the development of any of the allergic diseases (recurrent wheezing, allergic rhinitis, atopic dermatitis, urticarial). Parents provided informed consent for umbilical cord blood sampling and the sharing of this research. All data were analyzed using the Statistical Package for Social Sciences (SPSS Version 16).

Descriptive data are reported as mean ± standard deviation or number (percentage) as appropriate. Depending on the nature of each variable, a special Colmogrove Smirnov test, non-parametric tests, the conjugation coefficient test was used. Results were considered statistically significant with a p-value<5%.

Results

The study included 500 neonates, 238(47,6%) were male and 262(52.4%) were female. Cesarean section pattern was predominant in 310(62%) children, gestational age more than 37 in 472(94.4%), the birth weight more than 2500 in 456(91.2%).

The most common season of delivery was winter in 258(51.6%) children, and the positive family story was in 246(49.2%) children. Smoking during pregnancy was in 306(61.2%) children**.** The frequency of high total IgE was 214(42.8%). Comparison between high and normal total IgE in umbilical cord blood groups; family history of allergic diseases, smoking in pregnancy, and season of delivery was significantly higher in high total IgE in umbilical cord blood group (p-value=0.00011), (p-value=0.00012), (p-value=0.00005) respectively.

There were no significant differences between the two groups regarding the gender, gestational age, birth weight, mode of delivery **(table I)**

We followed up 143 neonates of 214 neonates with high total IgE for 8 years. During follow up, we noticed that allergic diseases developed in 109(76.22%) children from 143 with high total IgE in umbilical cord blood with significant correlation (p-value $\leq$0.001). Allergic symptoms in children varied between

nasal allergy in 19.6% of children, skin allergy (Eczema and urticarial)in 25.2% of children, childhood asthma in 31.5% of children **(Table II).**

There was a family history of allergic diseases in 74 (51.7%) children from 143 children. The family history was positive for allergic diseases prevalent in first-degree relatives 63(44.1%). Allergic symptoms in family members varied between nasal allergy 18(12.6%), asthma 15(10.5%), atopic Eczema 5(3.5%), urticarial 4(2.8%), drug and food allergy6(4.2%). The prevalence of more than one allergic symptom was the most common 26(18.2%).

In the current study, there was statistically relationship between the positivity of the family history and the development of allergic diseases later during the follow up (p-value <0.001).

During the follow-up period, we noticed that the development of allergic diseases increased with the presence of two factors together (high total IgE in the umbilical cord and family history of allergic diseases) with a rate of 51.7% and with significant correlation (p-value=0.001)**(Figure 1).**

Table (I): Comparison between high and normal total IgE in umbilical cord blood groups

variables	Total neonates	High IgE in umbilical cord blood	Normal IgE in umbilical cord blood	P-value
Gender				
male (percentage)	238(47.6%)	112(47,06%)	126(52,94%)	0.03
Female (percentage)	262(52.4%)	102(38.93%)	160(61.71%)	
Mode of delivery				
Cesarean delivery	190(38%)	80(42.11%)	110(57.89%)	0.03
vaginal birth	310(62%)	134(43.23%)	176(56.77%)	
Gestation age				
>37 gestation week	472(94.4%)	204(43.23%)	268(56.77%)	0.6
< 37 gestation week	28(5.6%)	10(35.72%)	18(64.28%)	
Birth weight				0.6
>2500 gram	456(91.2%)	194(42.55%)	262(57.45%)	
<2500 gram	44(8.8%)	10(35.72%)	18(64.28%)	
Smoking during pregnancy				
Yes	306(61.2%)	154(50.32%)	152(49.68%)	0.00012
No	194(38.8%)	60(30.93%)	134(69.07%)	
Family history of allergy				
Yes	246(49.2%)	130(52.84%)	116(47.16%)	0.00011
No	254(50.8%)	84(33.07%)	170(66.73%)	
Season of delivery				
Winter	258(51.6%)	124(48.07%)	134(51.93%)	
Spring	108(21.6%)	52(48.16%)	56(51.85%)	0.00005
Autumn	16(3.2%)	14(87.50%)	2(12.5%)	

Summer	118(23.6%)	24(20.34%)	94(79.66%)

Table (II) : The development of allergic diseases with a family history of allergic disease

		development of allergic diseases			
		nasal allergy	**skin allergy (Eczema and urticarial)**	**childhood asthma**	**No allergic diseases**
family history of allergic disease	**No (percentage)**	3(4.3%)	22(31.9%)	19(27.5%)	25(36.2%)
	Yes (percentage)	33(44.6%)	6(8.1%)	26(35.1%)	9(12.2%)
	Total (percentage)	36(25.2%)	28(19.6%)	45(31.5%)	34(23.8%)

Discussion

In the current study, a high total IgE in the umbilical cord was found in 143(42,8%) of 500 neonates, while it was 56% in Hernández et al study in Mexico 2013 **[8]**.

We could not find any association between neonatal gender and total IgE levels in cord blood. Consistent with our findings, krimi et al 2012 also found that the total IgE level in umbilical cord blood did not association with newborn gender **[9].** These findings are in contrast to Mohammad zadeh et al study in Iran 2019 which found significantly higher levels of total IgE in umbilical cord were seen in male newborns **[10]**. Higher levels of total IgE in male newborns might be related to a higher prevalence of atopy and allergic diseases in boys **[11]**.

In the current study, the delivery method did not significantly influence the total IgE levels in the umbilical cord. That is similar to a Mohammadzadeh et al study in Iran 2019**[10].** In contrast, Petrovičová et al study in that reported the total IgE level in the umbilical cord was higher in newborns born by cesarean section than those born via vaginal birth. These different rates might be due to the low number of samples and vaginal births in current study**[12].**

We found an association between seasonal variation and total IgE levels in umbilical cord blood, with the lowest values in autumn and the highest value in summer. The results of most other studies investigating this topic are in agreement with our findings **[13-14]**. This seasonal variation may indicate the effect of environmental allergens on umbilical cord blood total IgE levels.

In current study, smoking during pregnancy is associated with total high IgE in the umbilical cord. Our results are consistent with the results of several studies **[15-16-17].** On the other hand, our result is contrasted with Vilchis et al study in Mexico **[18]** which found that total IgE umbilical cord blood was not associated with exposure to smoking during pregnancy.

This study confirms the correlation between high total IgE values in the umbilical cord and further clinical allergy development. Similarly, Lopez et al in Brazil 2001 also found that the high total IgE level in umbilical cord blood Predict the occurrence of allergy in children**[19]**. In contrast, Bergmann et al 1997 Germany reported little importance of total IgE in the umbilical cord as predicting allergies in children **[20].**

Tariq. SM et al 1999 study in British found that family history Predict the occurrence of allergy in children later. This is consistent with current study**[21]**.

We found in current study that the combination of allergic family history and high total IgE in umbilical cord blood plays an important role in predicting the occurrence of allergies in later childhood. That is similar to Tariq. SM et al 1999 study in British which confirmed that the total IgE in umbilical cord blood scan is necessary and required in the event of positive allergic family history **[21].**

Conclusion

The current study demonstrates that serum total IgE may be predictive of subsequent allergy onset, and this becomes more important if associated with a family story.

This may be used as a predictive measure through which prevention can be achieved by emphasizing parental feeding, preventing smoking in the child's environment, and avoiding allergens.

Declarations

- **Acknowledgments:**

We wish to thank the medical officer, doctors in Pediatric department and laboratory assistants in Al-Assad University Hospital laboratory who worked with us in reviewing the patients and doing the laboratory analysis.

- **Conflict of interest statement**:

None declared.

- **Data Availability:**

We can't share patient data due to our hospital's privacy policy, which is concerned with maintaining patient confidentiality and refuses to publish or share data. Also, the informed consent signed by the parents to participate in the study prevents the sharing of information with the non - Study researchers.

- **Statement of Ethics:**

All parents whose children were studied gave informed consent for the sharing of this research. Ethical clearance for this study was obtained from the Ethical Committee of the University of Tishreen Hospital

- **Funding Sources:**

None

- **Author Contributions:**

Prof. Ghazal Deeb developed the research idea and implemented the sample collection process. Literature review, data analysis and reading of final data were performed by all authors

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Figures

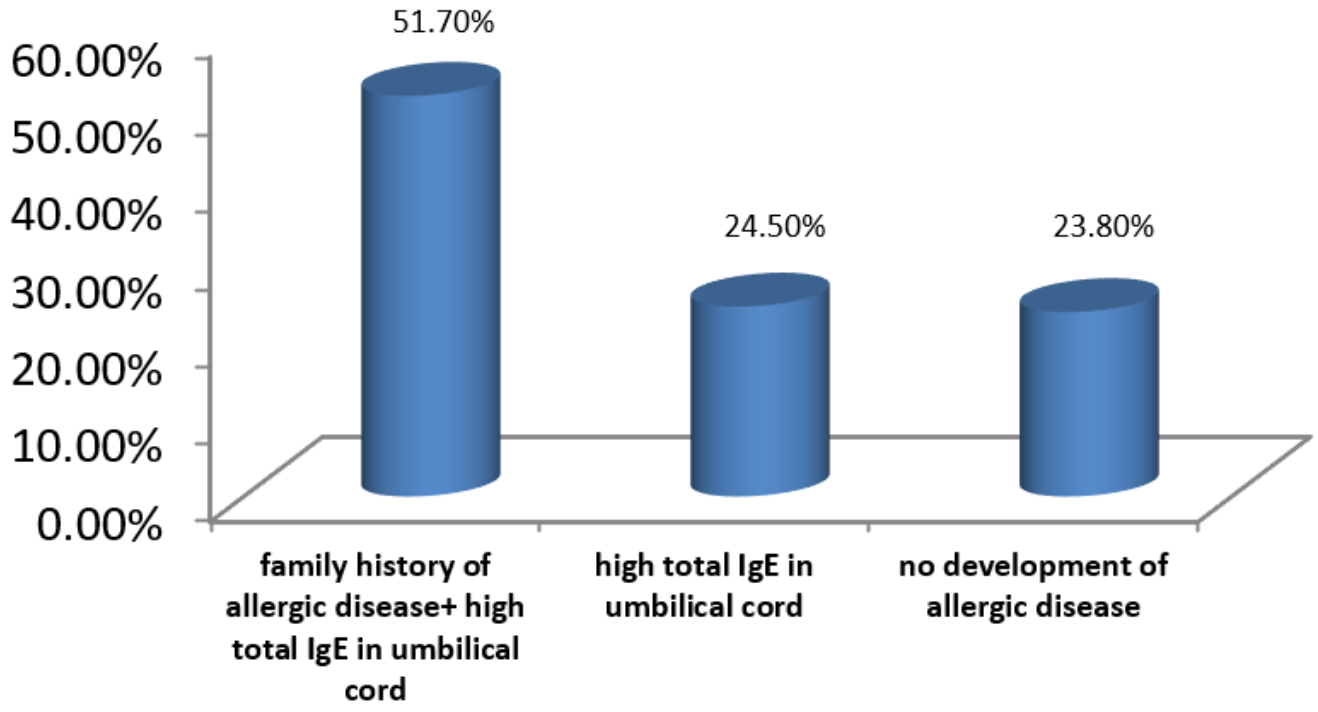

Figure 1

The development of allergic diseases with the presence of factors