Sero-epidemiological study of outbreak of measles among children in Diyala - 2009

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Abstract:

Measles is a serious infectious disease in children. Despite reaching global measles vaccination coverage of 80% of individuals, measles virus remains the fifth leading cause of death and the most common cause of vaccine-preventable death in children under 5 years of age.

This article aimed to assess the sero-epidemiological characteristics of the outbreak of measles among children in Diyala province in 2009.

This study was done during the outbreak of measles in Diyala provinc (spring and summer of 2009) in Al-Batool hospital of Pediatrics and Gynecology in Baquba city during a 2-month period from first of April 2009 to first of June 2009. A sample of 103 pediatrics patients presented with clinically suspected measles was studied by thorough history and physical examination with a determination of immunoglobulin M antibodies in serum by enzyme-linked immunosorbent assay testing for measles.

There was 58.3% (66 out of 103) positive blood samples for immunoglobulin M of measles in children with clinically evident measles. The present study showed that there was no significant difference in the distribution of children with measles positive by immunoglobulin M according to their age, sex, residency, mothers′ previous vaccination status and previous measles. On the other hand, the study revealed that the distribution of immunoglobulin M positive measles cases was significantly higher ($p<0.05$) among unvaccinated children, and in children with low and medium economic status.

It was concluded that the single serum assay of immunoglobulin M antibodies by enzyme-linked immunosorbent assay testing has medium sensitivity in the diagnosis of measles in children, and there is an increasing susceptibility of infection with measles for infant less than one year of age and for children with poor family economic status.

Key words: Measles, IgM, serology, **Children, Diyala**

Introduction:

Measles (rubeola) is caused by a single-stranded RNA paramyxovirus with one antigenic type and humans are the only natural host[1].It is a serious infection characterized by high fever, an enanthem, cough, coryza, conjunctivitis, and a prominent exanthem. After an incubation period of 8–12 days, the prodromal phase begins with a mild fever followed by the onset of conjunctivitis with photophobia, coryza, a prominent cough and increasing fever[2].

Despite reaching global measles vaccination coverage of 80% of individuals, measles virus (MV) remains the fifth leading cause of death and the most common cause of vaccine-preventable death in children under 5 years of age[3].

Countries in the Eastern Mediterranean Region (EMR) reduced the number of measles-related deaths by approximately 75% from 2000 to 2007. However, large measles outbreaks continue to occur throughout the region, suggesting that much work remains to eliminate measles in the EMR[4-7].

Despite almost universal use of measles vaccines in recent decades, epidemics of the disease continue to occur. Understanding the role of primary vaccine failure (failure to seroconvert after vaccination) and secondary vaccine failures (waning immunity after seroconversion) in measles epidemics is important for the evaluation of measles control programs in developing countries[8].

The pathogenicity of MV is intimately linked to the immune status of the infected individual. Measles is typically a self-limiting disease; however, individuals who are immunocompromised[9,10], and malnourished[11-12] are at increased risk for severe measles.

During 1997-1998 in EMR, the number of cases reported increased by 58% from previous outbreak; outbreaks were reported in Iran, Syria, Morocco, and Saudi Arabia[13]. In our country an outbreak of measles had occurred at the same period[14].

The aim of the present study is to identify the sero-epidemiological characteristics of measles pediatrics cases admitted to Al-Batool hospital of Pediatrics and Gynecology in Baquba city (April-June 2009) and to determine the presence of associations between certain studied variables and measles IgM positivity.

Subjects and method:

This study was done during the outbreak of measles in Diyala provinc (spring and summer of 2009) in Al-Batool hospital of Pediatrics and Gynecology in Baquba city during a 2-month period from first of April 2009 to first of June 2009. A sample of 103 pediatrics patients presented with clinically suspected measles was studied by thorough history (including sex, age, weight, address, previous vaccination status, mothers′ previous vaccination status and history of previous measles infection, history of contact, family size and economic status of the family) and careful

physical examination for signs, symptoms, and complications of measles. A determination of immunoglobulin M (IgM) antibodies by enzyme- linked immunosorbent assay (ELISA) testing for measles for 103 patient was done in the central laboratory of health in Baquba to prove recent infection. Data were statistically analyzed by chi square test.

Serological analysis:

Blood samples (2.5 ml) were obtained from the 103 children and sera were collected and frozen at –20°C until serological analysis. Measles IgM antibodies were determined by ELISA (bioactive diagnostica. Product number (103 determinations).

Test procedure:

The sera were diluted 1/101 and mixed well, then 100ul of undiluted control sera and diluted samples pipetted in duplicate into respective wells of the microtiter strips (except the well for the blank), the plate was covered and incubated for one hour at room temperature. Wells then emptied by aspiration and unbound sera were removed by three cycle of washing, then 100ul of anti-IgG-HRP conjugate was added into each well, then plate was covered and incubated for 30 minutes at room temperature, then unreacted HRP-Abs were washed by 3 cycles of washing by ready to use washing solution. Then, 100ul of ready to use substrate (TMB) was added into each well, then plate was covered and incubated for 15 minutes at room temperature in the dark, then 100ul of 1M H_2So_4 (stopping reagents) to stop substrate reaction and after thoroughly mixing the color was stable for 30 minutes and the absorbance was measured at 450nm using an ELISA reader.

The low positive control served as the cut-off value and when the absorbance of the subject sample was more than 10% above the cut-off value, the result regarded as positive and the absorbance more than 10% below the cut-off value, the result regarded as negative, results in between that could not clearly be defined and they were regarded as questionable. The higher optical density (OD), the higher levels of anti- immunoglobulins are present. The mean cutoff value was calculated through the OD which was 0.638. Any OD reading higher than this OD reading by 10% was considered as positive, any OD reading below by 10% was considered as negative (according to the manufacturer instruction).

Results

This study revealed that from the total number of 103 blood samples obtained from children with clinically evident measles, 66 were positive for IgM of measles, which represents about 58.3 % of the total.

The study showed that there was no significant difference in the distribution of children with measles positive by IgM assay according to their age and sex as shown in table (1).

Table (1) : Distribution of children with measles positive for Ig M assay according to their age and sex.

Age by year	Female	Male	Total	
			No.	%
<1	16	13	29	43.4
1-2	10	5	15	22.7
3-4	7	6	13	19.7
≥ 5	2	7	9	13.7
Total	35	31	66	100

df = 3, calculated $X^2 = 4.8$, tabulated $X^2 = 7.85$, $p > 0.05$ [NS]

There was statistically insignificant difference in the distribution of measles positive patients by IgM assay according to residency, table (2).

Table (2) : Association of IgM positivity and residency in study patients.

Residency	Positve IgM		Negative IgM		Total
	No.	%	No.	%	No.
Rural	36	54.5	17	45.9	53
Urban	30	45.5	20	54.1	50
Total	66	100	37	100	103

df = 1, calculated $X^2 = 0.519$, tabulated $X^2 = 3.841$, $p > 0.05$ [NS]

The study revealed that the main clinical presentations of measles positive by IgM were skin rash (95%), fever (94), bronchitis (74%), conjunctivitis (68%), and diarrhea (46.9) respectively, as in table (3).

Table (3) : The clinical presentations of measles positive for IgM assay among the studied group.

Clinical presentation	No.	%
Skin rash	63	95
Fever	62	94
Bronchitis	49	74
Conjunctivitis	45	68
Diarrhea	31	46.5
Pneumonia	15	22.7
Koplik spot	12	18.2
Vomiting	4	6
Meningitis	1	1.5

The study revealed that positive IgM assay for measles was significantly more among children who did not receive previous vaccination than those who received vaccination ($p < 0.05$).Table (4).

Table (4) : Association of previous vaccination history and IgM positivity among study cases.

Vaccination history	Positive IgM		Negative IgM		Total
	No.	%	No.	%	
vaccinated	18	27	10	27	28
non-vaccinated	36	55	27	73	63
unknown	12	18	0	0	12
Total	66	100	37	100	103

df = 1, calculated $X^2 = 50.2$, tabulated $X^2 = 3.84$, $p < 0.05$ [S], unknown is neglected.

There was no significant difference between patients (≤9 months of age) whose mothers were previously vaccinated and those whose mothers were not vaccinated to be measles positive by Ig M, table (5).

Table (5) : Association between IgM positivity and maternal measles vaccination history among children (≤ 9 months of age) in study patients.

Previous mothers′ vaccination	Positive IgM		Negative IgM		Total	
	No.	%	No.	%	No.	%
vaccinated	14	73.7	5	26.3	19	100
Non-vaccinated	5	71.4	2	28.6	7	100
Total	19	73.1	7	26.9	26	100

df = 1, p > 0.05 [NS], unknown is neglected

Table (6) shows no significant difference between patients (≤9 months of age) whose mothers have had previous attack of measles and those whose mothers declared no such history by IgM positivity.

Table (6) : Association between IgM positivity and maternal previous history of measles attack among children (≤ 9 months of age) in study patients.

Mothers′ previous infection	Positive IgM		Negative IgM		Total	
	No.	%	No.	%	No.	%
yes	6	60	4	40	10	100
no	16	16.5	10	38.5	26	100
Total	22	61.1	14	38.9	36	100

df = 1, p > 0.05 [NS], unknown is neglected

Table (7) indicates no significant difference between patients with measles positive by IgM who had positive history of family contact with measles and those who had no such history.

Table (7) : Association between IgM positivity and previous history of contact with a measles case among the family in study patients.

Family contact	Positive IgM		Negative IgM		Total
	No.	%	No.	%	No.
Yes	34	51.5	21	56.7	55
No	32	48.5	16	43.3	48
Total	66	100	37	100	103

df = 1, calculated $X^2 = 0.441$, tabulated $X^2 = 3.841$, p > 0.05 [NS]

Finaly, the study showed that the distribution of measles positive by IgM was significantly more ($p<0.05$) in patients with low economic status than those with moderate or good economic status as shown in table (8).

Table (8) : Association between IgM positivity and the economic status in the studied group.

Economic status	Positive IgM		Negative IgM		Total
	No.	%	No.	%	No.
Low	46	65	25	35	71
Moderate + good	20	62.5	12	37.5	32
Total	66	64.1	37	35.9	103

df = 1, calculated $X^2 = 3.859$, tabulated $X^2 = 3.841$, $p < 0.05$ [S]

Discussion

This study was conducted during the last outbreak of measles in Diyala province which represents an important medical event in this area, and possibly in other areas of Iraq, that may reflect the different aspects of general child′s health including primary health care services, vaccination programs, and other social services.

This study revealed that about 58.3% of blood samples of children with clinically evident measles was measles IgM positive. Other studies revel variable higher rate[15-17]. The apparently significant negative or questionable levels of measles IgM can be attributed to either early sampling of blood, children malnutrition and decreased immunity, or to a less extent due to wrong diagnosis or laboratory errors. However, taking these factors in mind, assays of IgM of measles with careful clinical history and physical examination largely improve the accuracy of diagnosis especially in sporadic cases. This accuracy can be further improved by further blood sampling in questionable levels and possibly by other investigations.

This study find no significant differences in measles distribution according to the sex and the different age groups of patients, which can be explained by the general shortage of the medical services and vaccination programs; and the general malnutrition and overcrowding which affect both sexes and multiple age groups. Most importantly, the increasing incidence of measles attacks below one year of age may reflect lacking immunity against measles in infants as a consequence of absence or failure of vaccination[8] in their mothers.

Measles attacks confirmed by IgM assay were found to be significantly more in previously unvaccinated children than the vaccinated. This reflects the vital importance of vaccination in

disease prevention as a known medical fact[18-20] especially in our society which require further vaccination coverage and further social education about the great benefits of vaccination.

The present study revealed that there was no significant difference, regarding measles positive IgM cases, between children (≤9 month of age) whose mothers were previously vaccinated against or have had an attack of measles and those whose mothers were not vaccinated or gave no history of such attack. These findings can be explained by a possible weaning infants′ passive immunity[21], maternal vaccination failure[8], maternal malnutrition or immunodeficiency, and a possible defects in information taking by history only without medical records.

The present study showed no significant association between IgM positivity and the presence or absence of history of contact with a measles case within the family. This is possibly due to that many patients might not yet develop high positive titers of IgM, or they had questionable titers, with a possible improper history given by the followers.

Finaly, the study showed that measles IgM positive cases was significantly more ($p<0.05$) among patients whose family was classified as a low economic status family (according to income by ID and family size) than those with moderate or good economic status. This finding may be attributed to the better care, nutrition, vaccination coverage, and less crowding in the second group.

The present study concluded that the single assay of IgM antibodies by ELISA testing has medium sensitivity in the diagnosis of measles, there is increasing susceptibility of infant less than one year of age for infection with measles and that the incidence of measles infection in children is inversely related to the economic status of the family.

The study recommend doing second IgM antibody testing by ELISA with negative or questionable result or using other method for diagnosis as polymeras chain reaction (PCR), improvement of maternal vaccination, and improvement of the economic status of the poor families.

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دراسة مصلية ـ وبائية لتفشي مرض الحصبة لدى الأطفال في محافظة ديالى – ٢٠٠٩

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تمهيد: يعتبرمرض الحصبة من الامراض المعدية المهمة لدى الاطفال. يمثل فايروس الحصبة السبب الرئيسى الخامس لدى الاطفال وذلك بالرغم من وصول النسبة العالمية للتلقيح ضد المرض الى حوالي ٨٠% من عدد السكان. بالاضافة الى ذلك يمثل هذا المرض السبب الأشهر للوفيات التي يمكن منع حدوثها بواسطة برامج التلقيح لدى الأطفال بعمر اقل من ٥ سنوات.

الأهداف: تحديد الصفات المصلية والوبائية لتفشي مرض الحصبة لدى الاطفال في محافظة ديالى – ٢٠٠٩.

الأشخاص وطرق العمل: اجريت هذه الدراسة اثناء تفشي مرض الحصبة في محافظة ديالى وذلك في مستشفى البتول للولادة والأطفال في مدينة بعقوبة ولمدة شهرين للفترة الممتدة من الأول من نيسان ٢٠٠٩ ولغاية الاول من حزيران ٢٠٠٩. وتمثلت عينة الدراسة ب ١٠٣ اطفال كانوا يعانون من أعراض سريرية تحتمل اصابتهم بمرض الحصبة، حيث تمت دراسة كل حالة بأستحصال التاريخ المرضي والفحص السريري الكاملين، بالأضافة الى الفحص المختبري للاجسام المضادة ل (اميونوكلوبيولين نوع M) في امصال المشاركين في الدراسة وذلك باستخدام فحص (الايزا – ELISA).

النتائج: اظهرت هذه الدراسة ان النتائج الموجبة لفحص الاجسام المضادة ل (اميونوكلوبيولين نوع M) شكلت مانسبته ٥٨.٣% (٦٦ من ١٠٣) من المجموع الكلي لامصال الاطفال الذين يعانون من اعراض تحتمل اصابتهم بالحصبة. وأظهرت الدراسة ايظا عدم وجود تباين مهم لمعدل انتشار الحصبة ذات النتيجة الموجبة لفحص الاجسام المضادة ل(اميونوكلوبيولين نوع M) حسب عمر الطفل وجنس الطفل ومحل السكن، وكذلك حسب التاريخ المرضي للامهات فيما يتعلق با لحالة التلقيحية السابقة او الاصابة السابقة بالمرض. ومن جهة اخرى، أظهرت الدراسة بان معدل انتشار الحصبة ذات النتيجة الموجبة لفحص الاجسام المضادة ل(اميونوكلوبيولين نوع M) لدى الاطفال الذين لم يتلقوالتلقيح المسبق ضد المرض هو اعلى بصورة مهمة ($p<0.05$) منه لدى الاطفال الذين تلقوا التلقيح، وكذلك وجد بان ذلك المعدل هو اعلى لدى الاطفال ذوي العائلات المتدنية والمتوسطة الحالة الاقتصادية منه لدى الاطفال ذوي العائلات ذات الحالة الاقتصادية الجيدة.

الاستنتاج: ان الفحص المختبري المفرد للاجسام المضادة ل (اميونوكلوبيولين نوع M) في الدم باستخدام فحص (الايزا – ELISA) يمتلك حساسية متوسطة القوة في تشخيص مرض الحصبة، وان هناك امكانية متزايدة للرضع دون عمر السنة وللاطفال ذوي العائلات ذات الحالة الاقتصادية المتدنية للاصابة بمرض الحصبة.

الكلمات المفتاحية: الحصبة، فحص الاجسام المضادة ل(اميونوكلوبيولين نوع M)، الاطفال، ديالى