Clinical Profiles and Outcome of Children Admitted with Measles During 2009 Outbreak

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ABSTRACT:

BACKGROUND:

Measles is a highly contagious acute viral infection. It is a common cause of morbidity and mortality constituting half of vaccine preventable diseases.

OBJECTIVE:

The study was designed to describe the demographic, vaccination status, clinical profiles, and outcome of children admitted with measles during outbreak.

PATIENTS AND METHODS:

A cross sectional hospital based study was conducted on 137 children admitted with measles in Children Welfare Teaching Hospital/Medical City /Baghdad during the outbreak of measles in the period from 1st January- 31st May 2009. Patients below the age of 14 years who were clinically diagnosed as cases of measles were treated and followed.

RESULTS:

The median age was 17 months with a range of 3 months-14 years. Male /female ratio of 1.14:1. 86.86 % patients were admitted in March. Sixty eight (49.63%) children were not vaccinated. Twenty four (55.81%) children of vaccinated group had one dose of measles vaccine only and 19(44.19%) children had two doses. Complications of measles were detected in 120(87.59%) of patients. The most frequent complication of measles was pneumonia which was encountered in 72(52.55%) cases. Gastroenteritis was recorded in 44(32.12%) of patients. Six patients (4.38%) died after developing complications in the form of pneumonia in five and encephalitis in one. Forty four (32.12%) cases were malnourished and majority of them 26 (59 %) cases were in the >15 months age group. Two thirds of deaths were among malnourished children. The case fatality was 4.38%.

CONCLUSION:

One third of measles infections occurred before the age of 9 months. Half of measles cases were not vaccinated. The majority of the complicated cases had occurred in the unvaccinated children. Pneumonia was found to be the most frequent complication of measles that necessitated admission. Young age, pneumonia, malnutrition, immune deficiency and non-vaccination status were significant factors related to mortality.

KEYWORDS: measles, outbreak, children, baghdad.

INTRODUCTION:

Measles is a highly contagious, acute viral infection. It is characterized by fever with a distinct exanthem, pathognomonic enanthem (Koplik's spots), accompanied by the classic triad of cough, coryza and conjunctivitis. [1] In developing countries, measles is most common in infants 1 to 2 years of age and is often seen in those less than 9 months old. [2] Measles is extremely rare under the age of 3-4 months, because of protective maternal antibody. In large cities and towns, measles is most likely to occur in infants and preschool children, but in rural and less crowded urban areas the principal incidence is between the ages of 5 and 10 years.[3] In temperate areas, measles disease occurs primarily in late winter and spring. [4] Measles transmission is primarily person to person via large respiratory droplets, following contact with large droplets or by direct transfer of infectious secretions, such as saliva on hands or toys. Face-to-face contact is not necessary because viable virus may be suspended in air up to 1 hour after a source case leaves a room. [5] Measles may be transmitted

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from 4 days before to 4 days after rash onset. The incidence of measles declined dramatically following the introduction of the measles vaccine 1963. The attack rate fell from 313 cases/100,000 population in 1956-60 to 1.3 cases /100,000 in 1982-88. The current rate is <1 case/1,000,000 population. Risk factors for measles infection include; children with immunodeficiency, infants who lose passive antibody prior to the age of routine immunization, people who are not naturally immune or adequately immunized. Risk factors of severe complications and death include: overcrowding, children younger than 5 years of age, malnutrition, underlying immunodeficiency, vitamin A deficiency. Sites of involvement of complications of measles include the middle ear, the respiratory tract, the gastrointestinal tract, and the central nervous system, eyes and skin.[4] Measles-related mortality occurs in 0.1-0.3% of reported and most often due to respiratory and neurologic complications.[2] WHO and UNICEF are collaborating to reduce global measles death by 90% by 2010. The strategy includes; strong routine immunization for children by their first birthday, a second opportunity for measles immunization through mass vaccination campaigns, to ensure that all children receive at least one dose, effective surveillance in all countries to quickly recognize and respond to measles outbreaks, better treatment of measles cases to include vitamin A supplements, antibiotics if needed, and supportive care that prevents complications. [6]

AIMS OF THE STUDY:

The study aimed to describe the demographic characteristics, clinical presentations, complications and outcome of children admitted with measles, and to evaluate the impact of measles vaccine on susceptibility and outcome of measles and the possible risk factors associated with mortality in measles cases during outbreak.

PATIENTS AND METHODS:

A cross sectional -hospital based- study was conducted on 137 children admitted with measles in CWTH during the outbreak of measles in the period from 1st January- 31st May 2009. Patients below the age of 14 years who were clinically diagnosed as cases of measles were treated and followed. Children with underlying diseases were excluded. Case definition was; "children presenting with fever and a generalized erythematous maculopapular rash spreading from the head down to the extremities, preceded by a prodromal cough, rhinorrhea and conjunctivitis". [7] Information regarding age, sex, residence, date of onset of fever, symptoms at time of admission, complications, vaccination status and number of measles vaccines received, maternal history of measles and vaccination, history of contact with a case of measles within 3 weeks, duration of hospitalization and outcome were reviewed. Children were clinically examined during their stay in the hospital and were closely observed for complications. Weight for age measurements were plotted on National Center for Health Statistics charts. Chest radiographs were taken as indicated. Pneumonia was diagnosed according to WHO criteria "child has pneumonia if he has fast breathing (50 or more breath/minute if the child 2-12months age; 40 or more breath/minute if the child 12months-5 years age) or had chest indrawing", and the presence of pulmonary infiltrate on chest radiograph. [8] The diagnosis of encephalitis was based on the presence of altered degree of consciousness, convulsions, irritability, lethargy, other neurological deficit and lymphocytic pleocytosis in cerebrospinal fluid. Cerebrospinal fluid analysis was done when indicated (suspicion of encephalitis). Liver function test was done to all patients presented with measles and hepatomegaly. Vitamin A was given orally to all children in a dose of 100,000 IU/day for children 6 months to 1 year old and a dose of 200,000 IU/day for children older than 1 year. Duration of stay and outcome were recorded.

RESULTS:

The most frequent age group of children admitted with measles during the outbreak was >15 months which constitute 53.28% of cases. The youngest was 3 months old and the oldest was 14 years, with a median age of 17 months as seen in Figure-1.

Seventy three (53.28%) patients were males and 64(46.72%) were females with a male/female ratio of 1.14:1. One hundred nineteen (86.86 %) patients were admitted in March, April and May as seen in Figuer-2.

Ninety one (66.42%) cases where from urban areas. Forty four (32.12%) cases were malnourished and the majority of them 26 (59.09%) cases were in the >15 months age group as seen in Figure-3.

26Seventy three (53.28%) children had history of contact with a case of measles in the preceding 3 weeks. Forty one (29.93%) children had no history of contact and 23 (16.79%) children had unknown history of contact. Forty three (31.39%) children were vaccinated against measles according to National Iraqi Vaccination Schedule. Sixty eight (49.63%) children were not vaccinated, 26 (18.265) were with unknown vaccination status as seen in table -1.

Twenty four (55.81%) children of vaccinated group had one dose of measles vaccine only and 19(44.19%) children had two doses. Thirty eight (55.88%) of unvaccinated children were not vaccinated because their ages were under 9 months. Vaccinated females constitute 24(55.81%) of vaccinated children. Mothers who were vaccinated against measles constitute 8(5.84%) of the studied cases and mothers who were not vaccinated represented 67(48.90%), while 62(45.26%) mothers had unknown vaccination status. Four (2.92%) mothers had recorded measles infection. All cases had fever, cough and conjunctivitis and maculopapular rash and other signs and symptoms came in decreasing frequency, Koplik's spots was seen in 20 (14.60%), stridor in 8 (5.84%), hepatomegaly 5(3.65%) of patients but jaundice was not detected, splenomegaly 4(2.92%), pallor in 3(2.19%) and lymphadenopathy in 2(1.46%) as seen in table -2.

Complications of measles were detected in 120 (87.59%) patients, 51.67% of them were ≥ 15 months of age with decreasing frequency in younger than 9 months of age 28.34% and 20% in 9-14 months age group. The most frequent complication was pneumonia which was encountered in (52.55%) cases. Gastroenteritis was recorded in 44(32.12%) of patients while the remaining 17(12.41%) children had no complication and they were admitted because of poor oral intake. Encephalitis was recorded in 1(0.73%) case as seen in table -3.

The mean WBC count of 46 children admitted with measles was (6.39 cells/mm^3 $\pm$3.57 SD).The mean platelets count for 33 children was (312 cells/mm^3 $\pm$ 202.25 SD). Five (3.65%) patients needed RCU admission because of impending respiratory failure.

One hundred thirty one (95.62%) children were discharged well in better conditions and 6(4.38%) died after developing complications in the form of pneumonia in five children and encephalitis in one. The case fatality was 4.38%.

Half of those who died were the >15 months of age, one third deaths were in 9 -14 months of age and one was younger than 9 months. Three patients were males. Two patients were malnourished. Two third (4) of those patients who died were not vaccinated; one of them was under 9 months of age. One patient received only one dose of measles vaccine and one patient with unknown status of vaccination as seen in table -4. Five (83.33%) of those who died had a positive history of contact with a measles case and one had no history of exposure. Maternal history of measles vaccination for 4 (66.67%) patients who died was negative and two (33.33%) was unknown. The majority of deaths were due to respiratory failure as a complication of pneumonia which occurred in 5 (83.33%) patients who died. One patient (16.67%) died due to clinically diagnosed encephalitis. The mean duration of hospitalization of measles cases was 3.372 + 1.93 SD) days. The range was 1-2 days for non-complicated cases and 2 - 28 days for complicated cases.

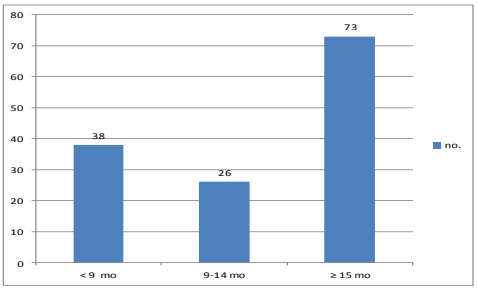

Figure 1: Distribution patients with measles according to age group.

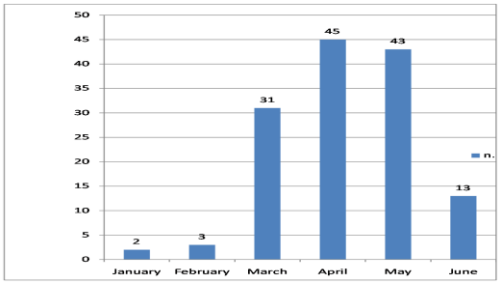

Figure 2: Distribution of children with measles according to months of admission.

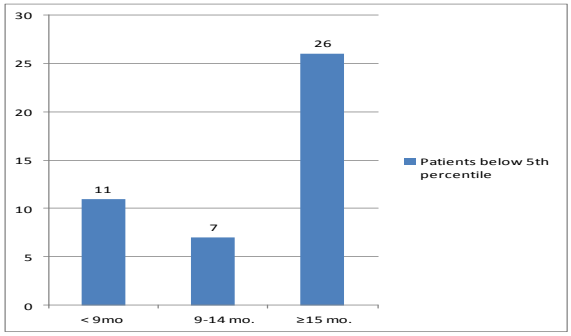

Figure 3: Distribution of malnourished children with measles according to age group.

Table 1: **State of vaccination children with measles according to their age group.**

Age group	Vaccinated No (%)	Unvaccinated No (%)	Unknown No (%)	Total No (%)
< 9 month	0	38 (55.88%)	0	38 (27.28%)
≥ 9 months	43 (31.39%)	30 (44.12%)	26 (18.98%)	99 (72.12 %)
Total	43 (31.39%)	68 (49.63%)	26 (18.98%)	137 (100%)

Table 2: Distribution of children with measles according to clinical features.

Clinical features	Number of patients	Percentage
Tachypnea	72	52.55%
Diarrhea and vomiting	44	32.12%
Koplik's spots	20	14.60%
Stridor	8	5.84%
Convulsions	6	4.38%
Hepatomegaly	5	3.65%
Splenomegaly	4	2.92%
Cervical lymphadenopathy	2	1.46%
Disturbance in level of consciences	1	0.73%

Table 3: Distribution of in children with measles according to complications.

Complications of measles	No.	Percentage
Pneumonia	72	52.55%
Gastroenteritis	44	32.12%
Laryngotracheobronchitis	8	5.84%
Febrile convulsion	6	4.38%
Epistaxis	3	2.19%
Encephalitis	1	0.73%

Table 4: Deaths in relation to vaccination status in children with measles.

Vaccination status	No.	Death	%
Vaccinated	43	1	2.32%
Not vaccinated	68	4	5.88%
Unknown	26	1	3.85%
Total	137	6	

DISCUSSION:

This study revealed that males acquired measles infection more frequently than females with M/F ratio 1.14:1, Hirfanoglu et al [9] had reported a male predominance of 2:1. The reason for male predominance may be due to the fact that the vaccinated males (44.19%) were less than vaccinated females (55.81%) in this study. The frequency of children admitted with measles was found to be higher in late winter and spring with a peak in April. This result is in agreement with Abdul Hakeem et al [10], while the peak occurred in March and July in Turkey in Hirfanoglu et al. [9] This may be attributed to the timing of that outbreak in both countries. The median age of measles in current study was found to be 17 months while the median age in Hirfanoglu et al study [9] was 36 months. 27.74% cases of measles in < 9 months age. Since measles may occur at any age if there is no previous immunity; therefore this finding is not unusual and the most probable explanation for measles in this early age could be the waning of transplacental acquired maternal antibodies even before 9 months of age to such low levels that they are unable to afford protection against measles. This is in agreement with Oydeel et al [11] who stated that 58% of infants lose these protective antibodies against measles by 4 months and 97% between 6 and 9 months. In this study a small percentage 2.92% of the patients had maternal history of measles infection and also only 8(5.84%) mothers were vaccinated against measles. These facts may explain the younger age at presentation and youngest age of patients was three months. In the present study 32.12% of children with measles were malnourished. This is in agreement with Ur-Rehman et al[12]who reported 40% as malnourished. Only 53.28 % patients gave a positive history of contact with a case of measles within 3 weeks from presentation. This is in agreement with Hirfanoglu et al [9] who recorded 57% had similar history. The occurrence of measles in patients with no history of exposure may be explained by the fact that an accidental exposure had happened with patients other than family members before the appearance of rash which is an important sign that brings the attention of the family. In spite of the routine administration of measles live attenuated vaccine at the age of 9 months and 15 months according to National Iraqi Vaccination Schedule, it is unfortunate to notice that the percentage of unvaccinated children recorded in this study was high approximately 50%. Ur- Rehman et al [12] recorded that 42.7% were not vaccinated. 27% of children were not vaccinated because they were under the age of vaccination (<9 months) and developed measles infection, this goes with Olusola et al[8] who reported (27.6%). 23.36% of children received only one dose of vaccine and developed measles while in Jahanet al [13] 32.1% received one dose . The occurrence of measles in patients receiving only single dose may happen because it had been shown that seroconversion to measles vaccine is between 70%-90% for a single dose vaccine and 97% with 2 doses. It had been shown that children vaccinated with measles vaccine at 6 and 9 months had a better outcome, compared to single dose of vaccine at 9 months. [14] 8% of children among total admissions had received two doses of measles vaccine this is nearly the same as in Mazin study, (7.65%) [15]. The occurrence of measles in a previously fully vaccinated child may be due to either primary vaccine failure (no immunological stimulation following vaccination) or persistence of maternal measles antibodies beyond 9 months of age must have interfered with seroconversion, improper storage or handling of the vaccine, and administrative procedures. Diversification in measles strains has also being reported to account for the early presentation of measles and occurrence of measles in vaccinated children [16, 17]. It has been associated with the potential risk of an epidemic. [18] In addition, mostly the vaccination status was recorded from case history, so it is difficult to be confident about robustness of evidence for vaccination (recall bias). Secondary vaccine failure might contribute to the occurrence of measles in an epidemic. Lack of complete diagnostic testing limits the ability to confirm this.

The occurrence of the majority of complicated cases in age group ≥ 15 months might be due to the facts that the majority of measles cases admitted in this study were in this age group and the majority of them were malnourished as 59.09% of malnourished cases were in the ≥15 months age group. This might be attributed to the fact that malnourished children experience more severe measles infection at a greater frequency due to their altered immune response. [19]Out of 137 children admitted for measles, 6(4.38%) patients died which was approximate to that reported in Hirfanoglu et al [9] (3.8%).The case fatality (CF) of admitted children with measles was (1.2%) by Mishra et al. [20] Half of those who died were ≥15 months age group, and one was younger than 9 months while in Hirfanoglu et al [9] 66.67% occurred at age of 6 months. One third

of patients who died were malnourished and the same finding was noted by Hirfanoglu et al. [9] Two thirds of those patients who died were not vaccinated and the non-vaccination related case fatality was (5.88%) while it was (1.35%) in Mishra et al [20]. One case (16.67%) was under the age of vaccination. One of those patients who died received only one dose of measles vaccine and vaccination related case fatality was (2.32%), meanwhile it was (0.45%) in Mishra et al [20] and one patient with unknown status of vaccination regarding measles vaccine. Maternal history for 4 (66.67%) of patients who died was negative for measles vaccination and two (33.34%) was unknown. The majority of death was due to respiratory failure as a complication of pneumonia which occurred in 5 (83.33%) patients who died. This was also noted by Hirfanoglu et al [9] where (100%) of the death cases had pneumonia with respiratory failure.

One of them had also bloody diarrhea in addition to pneumonia. One patient (16.67%) died due to encephalitis. One death in this study had history of ALL with bone marrow relapse. The cause of death was due to complicated pneumonia after 28 days from admission. In Hirfanoglu et al [9] also the same was recorded one of the death had ALL complicated by giant cell pneumonia.

CONCLUSION:

The most common age group affected during outbreak was ≥15 months. One third of infection occurred before the age of 9 months. Large proportion of measles cases occurred among unvaccinated population in urban area. Measles is still attacking vaccinated children in our locality. The majority of the complicated cases had occurred in the unvaccinated children and in the age ≥15 months; the majority of them were malnourished. Pneumonia was found to be the most frequent complication of measles that necessitated admission and it is the most feared complication. Higher mortality is associated with 9-14 months age group followed by ≥15 months and then < 9 months, malnutrition, non-vaccination and pneumonia. Respiratory failure as a complication of pneumonia is the leading cause of mortality.

RECOMMENDATIONS:

Measles catch-up mass immunization campaign should be conducted to interrupt chains of transmission and prevent outbreak and use of strong routine two-dose schedule to prevent school age and post school age outbreak, in addition to studying the mothers to find out the level of maternal antibodies which is protective in early months of child life to decide if there is a need to change the age of first dose of measles vaccine.

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