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Evaluation of Pediatric Measles Cases in 2019: Single Center Experience

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ABSTRACT

Measles, though able to be prevented and eliminated by vaccination, is a highly contagious viral disease that can lead to serious complications, disability, and death. The aim of this study was to evaluate the characteristics of measles cases in single center. This retrospective study consecutively enrolled children who were considered to be suspicious measles cases based on their clinical features and attended the Pediatric Clinic at Esenler Gynecology and Pediatrics Hospital between January 1 and June 30, 2019. There were no fully vaccinated patients in measles cases. Conjunctivitis was significantly more common in the unvaccinated group than in the partially vaccinated group (p=0.027). Moreover, the duration of conjunctivitis was significantly longer in the unvaccinated group (p=0.019). Unvaccinated patients had a significantly lower median leukocyte count and significantly higher median CRP level (p=0.019, p=0.021). Vitamin A (VA) level and leukocyte count had a moderate positive correlation (r=0.698; p=0.008). In order to prevent measles, it is necessary to implement controlled migrant movement, to vaccinate and follow-up this population for measles as well as vaccine preventable diseases.

INTRODUCTION

Measles, though able to be prevented and eliminated by vaccination, is a highly contagious viral disease that can lead to serious complications, disability, and death (1). As a result of strategies developed by the World Health Organization (WHO) and the United Nations International Children's Emergency Fund, the annual global incidence of measles decreased by 75% and the estimated global mortality rate fell by 73% from 2000 to 2015 (1). Although the WHO 2012–2020 Global Measles and Rubella Strategic Plan aimed to eliminate the disease by 2020 or earlier in five WHO regions, measles outbreaks continue to spread rapidly around the

world (2). In the first 6 months of 2019, reported measles cases reached the highest number they have been in any year since 2006 (3).

In 2018, it was reported that more than 140,000 measles deaths worldwide occurred in individuals to whom the safe and cost-effective measles vaccine was unavailable (4). In 2019, the European and Eastern Mediterranean regions recorded more than twofold and 1.5-fold increases in reported measles cases, respectively (5).

Uncontrolled immigrant movement, increasing numbers of refugee camps, high birth rates, and low population immunity (the global immunization rate is 85% for the first dose and 67% for the second dose) have contributed to this increase in measles cases (4).

Measles is still an endemic disease in Turkiye. In 2018 and 2019 Turkiye reported 716 and 2904 measles cases respectively (no data after 2020) (3) and measles vaccination coverage for 1st dose 96.1% and 2nd dose 93.03% was reported in 2021 (6). Although the European Regional Verification Commission for Measles and Rubella Elimination commends Turkey on its immunization programme activities, and on the high quality of measles laboratory surveillance, they pointed the inconsistent or missing data related to mobile non-Turkish populations (3). In the latest report of the Presidency of Migration Management Turkiye, it was mentioned as the number of refugees under temporary protection was 3513776 people and 1671997 of them were under 18 years of age (7). It was crucial that the WHO strategies and recommendations for the elimination of Measles must cover all populations to achieve measles elimination, especially for these risky groups. The WHO recommends administering VA to all children, regardless of their country, during acute measles infection (4). No specific antiviral treatment exists for the measles virus; therefore, vaccination is still the most effective method of preventing the disease.

The aim of this study was to evaluate the characteristics of measles cases in districts of Istanbul/Turkey with large populations of refugees.

MATERIAL AND METHODS

This retrospective study consecutively enrolled children who were considered to be suspicious measles cases based on their clinical features and attended the Pediatric Clinic at Esenler Gynecology and Pediatrics Hospital between January 1 and June 30, 2019.

Data collection and setting

A Measles/Rubella Case Notification and Laboratory Request and Result form and a Measles/Rubella Case Study form were completed for each suspicious case of measles and sent to the Provincial Health Department with blood, nasopharyngeal swab and urine specimens.

The measles definition was made according to "Surveillance Guidelines for Measles, Rubella and Congenital Rubella Syndrome" of the Turkiye Ministry of Health. The diagnosis of Measles was made on the basis of clinical features consistent with the illness (fever, maculopapular rash, and at least one cough, coryza or conjunctivitis), epidemiological features and identification/detection of specific Ig M antibodies or positive measles virus RNA detection with reverse transcription polymerase chain reaction (RT-PCR) or 4 times increased in measles specific Ig G antibodies the 2-4 weeks in blood, nasopharyngeal swab and urine specimens (8).

Study design and group definitions

During the outbreak session, all patients who had a maculopapular rash which can not be explained by another clinical situation and/or contact with the index case was determined as suspected measles case.

A confirmed case of measles was determined based on clinical findings (fever, rash, lymphadenopathy, nasal congestion, cough, pneumonia, photophobia, diarrhea, intraoral sores) and/or pathognomonic findings (maculopapular rash, conjunctivitis, etc.) and the positive measles specific IgM antibodies test or positive measles RT-PCR or 4 times increased measles specific Ig G antibodies the 2-4 weeks serum result. All laboratory tests were made by WHO-

registered national public health laboratories and results were declared to the surveillance team via a secured login system.

Demographic features, medical records and laboratory results were obtained for the suspected cases from the completed forms and hospital records. Patient files and case notification forms were examined for patient age (in months), gender, nationality, malnutrition, general vaccine history, measles vaccine history, number of vaccination doses, complaint on admission, number of admissions, index case contact, complaints and physical examination findings, VA treatment, VA doses, VA level, duration of each complaint, total time until recovery, hospitalization duration, total treatment cost (Turkish lira) (TL), mortality, and referrals.

Per-patient costs (TL)

Invoice data in TL were calculated by our hospital as well as the other health centers to which patients were referred via healthcare information and management system (HIMS).

Measles vaccine schedule

As of June 2019, according to the National Immunization Schedule, the two-dose measles vaccination (including measles, mumps, and rubella) is recommended at 12 months of age and 6 years of age (first year of primary school) (6). Individuals are considered fully vaccinated if they have received two doses at the appropriate ages, partially vaccinated if they have received one dose, and unvaccinated if they have received no doses (6, 9).

In our country, all data about the vaccination history of the citizens were recorded in the national electronic personal health system of the Ministry of Health Turkiye “enabız.gov.tr” which all health professionals can access through the secured login system. The vaccination status of patients was confirmed in 3 ways: 1) Vaccination cards in which all the date and vaccine name was recorded by nurses in the primary settings and belongs to parents; 2) Parent's verbal declaration and; 3) national electronic personal health system (enabız.gov.tr).

Vitamin A deficiency (VAD)

A widely used method to assess VA status is to measure serum retinol concentrations, with values below a cutoff point of 0.70 μmol/L (196 ng/mL) representing VA deficiency, and values below 0.35 μmol/L (98 ng/mL) representing severe VA deficiency, independent of age (10). In this study, a serum retinol concentration cutoff of 1.05 μmol/L (294 ng/mL) was used to determine immune deficiency risk (11).

Malnutrition

To determine malnutrition status, a weight-for-height z-score of < –2 standard deviations (SD) was used for children under 5 years of age, and a body mass index z-score of < –2 SD (weight [kg]/height $[m]^2$) was used for children over 5 years of age (12).

The study protocol was approved by the local institutional ethics committee (protocol decision number: 2019.10.2.02.075) and registered with Clinical Trials (NCT05614791).

Statistical analysis

Statistical analysis was performed using Statistical Package for the Social Sciences (SPSS) 22.0 software (IBM Corp, Armonk, NY, USA). The variables were investigated using histograms, probability plots, and analytical methods (the Kolmogorov–Smirnov/Shapiro–Wilk's tests) to determine if they were normally distributed. Categorical variables were expressed as numbers and percentages, and numerical variables were expressed as mean ± SD or median with interquartile range (IQR). Continuous variables were expressed according to the parametric or nonparametric distribution.

Spearman's and Pearson's correlation tests were used to reveal relationships between parameters. Based on the determination of normality in the quantitative data, the t test, Mann–Whitney U test, or Wilcoxon signed-rank test was used to analyze differences in independent variables. The chi-square test was used to compare qualitative data. Differences were considered significant when $p < 0.05$.

RESULTS

A total of 143 children who were considered suspicious measles cases according to the Surveillance Guidelines for Measles, Rubella and Congenital Rubella Syndrome were enrolled in the study. The frequency of confirmed measles was 27.9% (40/143). All confirmed cases were diagnosed with measles-specific IgM antibody positivity and verified with RT-PCR test (40/40). Due to the national surveillance program, except for confirmed cases, all other suspicious cases were controlled for measles-specific IgG antibodies after 2-4 weeks and all were negative. There were no significant differences in age distribution or sex between the groups.

Clinical and laboratory features of confirmed measles cases

The median age of the patients with confirmed measles was 30 (IQR: 10.3-62.3) months, and 21 (52.5%) patients were male. Among these cases, 33 (82.5%) were refugees.

There were no fully vaccinated patients in the sample. Based on the National Immunization Schedule definitions, 50% (n=20) of confirmed cases were partially vaccinated and 50% (n=20) were unvaccinated. During the epidemic period, more than half of confirmed measles cases were admitted in the spring, followed by winter.

The demographic and clinical features (symptoms, symptom duration, admission, and hospitalization data) of the confirmed measles cases are summarized in Table 1. Rash (100%) and fever (97.5%) were the most common physical examination findings.

Twenty-nine patients were readmitted during their disease course. Among the non-hospitalized patients with confirmed measles, 17 (62.9%) were treated as outpatients and 10 (37.1%) required less than 24 hours of care in an isolated emergency department. Four patients (10%) required intensive care unit monitoring, three of whom (75%) were under 1 year of age.

The hospitalization rate was significantly higher in males than in females (47.6% vs. 15.8%, p=0.046).

Conjunctivitis was significantly more common in the unvaccinated group than in the partially vaccinated group (p=0.027). Moreover, the duration of conjunctivitis was significantly longer in the unvaccinated group than in the partially vaccinated group (p=0.019). Complications were observed in 15 (37.5) measles cases and although more frequent in the unvaccinated group, there were no significant differences in groups (9 vs 6 patients, p=0.333) (Table 1).

Laboratory data were obtained for 33 (82.5%) patients with confirmed measles and are summarized in Table 2. Unvaccinated patients had a significantly lower median leukocyte count and significantly higher median C-reactive protein (CRP) level compared to partially vaccinated patients (5770/uL vs. 8295/uL, p=0.019; 9.4 mg/L vs. 2.1 mg/L, p=0.021). On the other hand, median lymphocyte and platelet counts were lower in unvaccinated patients than in partially vaccinated patients, though the differences were not statistically significant (2300/uL vs. 3800/uL, p=0.060; 267066/uL vs. 340611/uL, p=0.072). Leukopenia, lymphopenia, and high CRP levels were significantly more frequent in unvaccinated patients than in partially vaccinated patients (Leukopenia: 26.7% vs. 0%, p=0.033; lymphopenia: 53.3% vs. 11.1%, p=0.020).

Vitamin A level and treatment

Vitamin A level values were obtained for 40% (n=16) of confirmed measles patients. The median VA level was 233 ng/mL (IQR: 155.8-321.5). Among the patients with VA data, in 11 (68.75%) patients, VA levels were lower than 294 ng/mL. No significant associations were found between VAD and symptoms and symptom duration, complications, hospitalization and hospitalization duration, time to full clinical recovery, readmission, or laboratory findings. Median leukocyte count was lower in patients with VAD than in patients with normal VA levels,

though the difference was not significant (p=0.107). In addition, VA level and leukocyte count had a moderate positive correlation (n=0.698; p=0.008; Figure 1).

Eighteen patients (45%) received VA treatment. The duration of conjunctivitis was significantly shorter in patients who received VA treatment compared to those who did not (1 day vs. 5 days, p=0.024).

Cost analysis

The total treatment costs for the confirmed measles patients were 19745.05 TL, and the median per-patient cost was 221.02 (IQR: 240.80) TL. The total cost was 14436.71 TL for the 13 confirmed measles cases requiring hospitalization, and the total outpatient cost was 5358.34 TL for the 27 confirmed measles cases only requiring outpatient treatment. There was a moderate and significant positive correlation between fever duration and cost (r=0.428, p=0.021), while age and cost had a weak negative correlation (r=0.241 p=0.134). Although there was not a significant difference between complication occurrence and cost, the median cost was significantly higher in patients who contracted pneumonia compared to those who did not (381.36 vs. 181.86, p=0.007). There were no statistically significant correlations between cost and vaccination status, VA treatment, gender, or nationality.

Comparison of confirmed and suspected measles cases

A comparison of the demographic, symptoms, and laboratory findings of confirmed measles cases and suspected measles cases were presented in Table 3. There was a significant difference between the two groups according to the measles vaccination status and the fully vaccinated cases were significantly lower in confirmed measles cases (0% vs. 53.3%, p <0.001). As expected, measles-specific symptoms were more common (p values of all symptom variables except rash were <0.001) and leukocyte count was significantly lower and leukopenia and lymphopenia was significantly higher in confirmed cases (respectively p=0.001, p<0.001 and p:0.024).

DISCUSSION

During the measles epidemic period studied in this research, 27.9% of suspicious measles cases received a confirmed diagnosis of measles; none of these patients were fully vaccinated. Although the study population appears small, this is expected due to the high vaccine coverage and low incidence of measles in the European region. This cohort allowed us to perform sociodemographic, clinical presentation, complication, laboratory, and cost-effectiveness analyses. There was no significant difference in the gender distribution of the patients with measles, which is in line with previous studies (13-16). The median age of the patients with confirmed measles was 30 months. This is consistent with the historic epidemiological trends of measles reported in the literature; after the implementation of measles vaccination, the ages with the highest incidence of measles decreased from adolescents to preschool-aged children (13, 17, 18).

Among the confirmed measles cases in our study, half were partially vaccinated, half were unvaccinated, and none were fully vaccinated. In contrast, previous epidemiological studies have reported that more than 80% of measles cases were unvaccinated (13, 19-21). Our observation of higher numbers of partially vaccinated cases compared to the literature might be due to factors such as inadequate antibody response and insufficient vaccination of close contacts, which may cause higher rates of measles in children with a single dose of the vaccine.

Refugees comprised 82.5% of the measles cases in our study. This differs from study findings in Greece, where the rate of measles was lower in refugees than in citizens due to the success of refugee vaccination programs (22, 23). Moreover, it was found that three-quarters of the children diagnosed with measles belonged to the Romani population, who likely refused vaccination; measles is common in this community, with case rates reaching 92%. Due to the consistency and success of the National Vaccination Program implemented in our country, the

number of measles cases in Turkish children remained very low, with cases most frequently seen in refugees, likely due to disruptions in the vaccination program as a result of the intense influx of refugees. This may indicate a need for refugee-specific vaccination programs.

Confirmed measles cases were diagnosed predominantly in the spring and winter seasons, in contrast to previous studies that found that the incidence of measles peaked in winter before declining through autumn (20, 22). However, increased measles cases were also reported in the winter and spring seasons in South Korea (24). Although seasonality was observed in our study, a generalization regarding the seasonal distribution of measles cannot be reached due to the short epidemic period studied.

VAD was observed in 27.5% of the patients. Previous research has shown a relationship between low VA levels and higher measles disease severity (25). VAD was significantly higher in unvaccinated than in partially vaccinated patients. We hypothesize that parents who were not attentive to vaccinating their children might also have insufficient knowledge regarding nutrition and other childcare issues.

Rash and fever were present in almost all cases, followed by cough, nasal congestion, conjunctivitis, and mouth sores, consistent with the literature (18, 21, 26). The rate of conjunctivitis was significantly higher in the unvaccinated group than in the partially vaccinated group. Previous research has similarly shown that vaccinated children with measles present with mild clinical symptoms, such as minimal rash and no cough, cold, or conjunctivitis (24). The differing rates of conjunctivitis may have also been due to the higher incidence of VAD in the unvaccinated group (27).

Complications were present in one-third of the patients in this study, which is consistent with the average complication rate of 40% reported in previous studies of patients with measles. In these studies, diarrhea was observed in 30–60%, pneumonia in 20–80%, acute otitis media

in 4.6–21%, and encephalitis in 1–2.4% of patients, similar to our results (13, 14, 20, 22). In addition, arthritis and encephalitis were exclusively observed and pneumonia and acute otitis media were more frequently observed in unvaccinated children.

Previous studies have reported hospitalization rates of 20–60% and average hospital stays of 4–8 days in measles cases, in line with our results (13-15, 20, 28-30). The reported rates of intensive care unit admission have varied widely, from 1.2% to 18% (13-15, 18). Although we did not observe mortality in our study group, it has been estimated that measles-related death rates are 3–5% in developing countries, and this rate increases to 10% in undernourished regions (31). Three of the patients transferred to the intensive care unit in our study were under 1 year of age, representing a population that is vulnerable to measles due to being ineligible for measles vaccination.

Leukopenia and lymphopenia was notably more frequent in confirmed cases than in suspected cases and in unvaccinated cases than in partially vaccinated cases. These results may be related to the transient immunosuppression and loss of lymphocytes caused by the measles virus (32). Our observed rates of leukopenia, neutropenia, lymphopenia, and thrombocytopenia in measles patients were consistent with the literature (13, 14, 20, 22). In addition, CRP levels were significantly higher in unvaccinated cases than in partially vaccinated cases. Studies have shown that as the CRP value increases in patients with measles, the probability of complications increases (13, 22).

There were no significant relationships between VAD and symptoms and symptom duration, complications, hospitalization and length of stay, time to complete clinical recovery, hospital readmission, or laboratory results. This differs from previous findings that measles patients with VAD have higher disease severity and that mortality and low VA levels are significantly related (33). However, a correlation between VA level and leukocyte count was found in our study.

Eighteen patients received VA treatment, and the duration of conjunctivitis was significantly shorter in those who received VA treatment than in those who did not. The American Academy of Pediatrics recommends that all children with severe measles (i.e., requiring hospitalization) be administered age-specific doses of VA, while the WHO recommends VA therapy for "all acute cases" (5, 34). It has been shown that VA administration reduces the risk of death by 64% (35). However, variable use of VA in measles has been reported in the literature, despite official recommendations (36-38).

There was a moderate and significant positive correlation between fever duration and cost and a negative correlation between age and cost. Median treatment cost was significantly higher in patients with pneumonia. High rates of hospitalization and complications during measles outbreaks lead to high financial costs (39). In studies conducted in Austria and the Netherlands, the cost of one measles case was approximately US$1700, with staffing representing the primary cost component of the public health intervention (39, 40). The total cost of efforts to contain the measles epidemic in Iowa was US$142,452 (41).

The results of our study indicate that measles cases are frequently seen in immigrant and refugee children, and the overall frequency of measles cases may have risen as a result of the current refugee situation. This is seen as not only a problem related to our study population but also a global problem. Furthermore, studies in other countries have reported difficulties in containing measles outbreaks due to young pediatricians being unfamiliar with the disease and not recognizing it at an early stage (14, 25).

The strengths of our study include it being the first study to our knowledge to compare unvaccinated patients with partially vaccinated patients. In addition, no other studies have examined the relationship between VA and leukocyte levels. There is thus a need for more comprehensive studies on these issues. Unlike previous studies, all patients recovered and no

mortality was observed in our study, which could be due to early diagnosis and treatment by the physicians treating our study population.

Our cost analysis was limited in that personnel expenses, additional working hours, ambulance expenses, sample transfer costs, hospital meals, and hospital heating and lighting needs were not included in the cost calculation; our cost calculation per patient may thus have been lower than those reported in other studies. As our study was retrospective, the inability to measure all patients' VA levels is a limitation.

CONCLUSIONS

Although strict strategies for controlling measles, the frequency of measles increased 3 to 15 times between 2016 and 2018 in the United States, Europe, and other countries (42). The results of our study indicate that measles cases are frequently seen in immigrant and unvaccinated or partially vaccinated children. In order to prevent measles, it is necessary to vaccinate and follow up all risky populations for measles in line with the WHO strategies and recommendations for the elimination of Measles. From the perspectives of both public health and cost, measles vaccine programs should target and cover all the risky populations, including refugees, to return vaccination rates to high levels.

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Figure Legends:

Figure 1. Correlation between Vitamin A levels and leukocyte count

The dot plot was Vitamin A levels (ng/mL) (horizontal axis) versus leukocyte count (/uL) (vertical axis) for each patient confirmed measles (n=16). A moderate positive correlation was detected between vitamin A levels and leukocyte counts (R2=0.387).

Table 1. Sociodemographic, clinical and complication status of measles patients according to vaccination status

		Confirmed Measles Cases (n=40)	Unvaccinated (n=20)	Partially vaccinated (n=20)	p
Age, (month), Median (IQR)		30.0 (10.3-62.3)	39.0 (10.3-68.5)	20.5 (10.0-53.0)	0.369*
Gender, (n,%)	**Female**	19 (47.5)	11 (55)	8 (40)	0.342**
	Male	21 (52.5)	9 (45)	12 (60)	
Nationality (n,%)	**Turkish**	7 (17.5)	1 (5)	6 (30)	**0.037****
	Immigrant	33 (82.5)	19 (95)	14 (70)	
Vitamin A deficiency (n,%)		11 (27.5)	4 (20)	7 (35)	**0.001****
Average Vitamin A level (ng/ml), Median (IQR)*f*		233 (155.8-321.5)	128.5 (78-260)	259.5 (184.3-366.5)	0.129*
Index case contact¶ (Yes), (n,%)		14 (35.5)	9 (45)	5 (25)	0.190**
Malnutrition (Yes), (n,%)		2 (5)	1 (5)	1 (5)	1**
Symptom, (n,%)	**Rash**	40 (100)	20 (100)	20 (100)	1**
	Fever	39 (97,5)	20 (100)	19 (95)	0.317**
	Cough	30 (75)	16 (80)	14 (70)	0.470**
	Conjunctivitis	19 (47.5)	13 (65)	6 (30)	**0.027****
	Nasal congestion	18 (45)	9 (45)	9 (45)	1**
	Diarrhea	16 (40)	7 (35)	9 (45)	0.523**
	Stomatitis	6 (15)	4 (20)	2 (10)	0.381**
Symptom duration, median (IQR)	**Rash**	7 (3.0-12.0)	7 (3.0-16.5)	7 (3.5-12.0)	0.902*
	Fever	4 (2.0-5.0)	4.5 (2.8-5.0)	3 (2.0-5.0)	0.439*
	Cough	3 (2.0-7.0)	2 (2.0-6.0)	4 (2.0-7.0)	0.579*
	Conjunctivitis	3 (1.0-7.0)	5 (2.5-7.0)	1 (1.0-1.5)	**0.019***
Complication†, (n,%)	**Pneumonia**	13 (32.5)	7 (35)	6 (30)	0.739**
	Acute Otitis Media	4 (10)	3 (15)	1 (5)	0.298**
	Arthritis	1 (2,5)	1 (5)	0 (0)	0.317**
	Encephalitis	1 (2,5)	1 (5)	0 (0)	0.317**
Readmission, (n,%)		29 (72.5)	13 (65)	16 (80)	0.294**
Total recovery duration, (days), Median (IQR)		10 (7.0-14.0)	10 (7.0-14.0)	7 (1.0-14.0)	0.372*
Need of hospitalization, (n,%)		13 (32.5)	9 (45)	4 (20)	0.176**
Hospitalization duration days, Median (IQR)		2 (1.0-6.0)	2 (1.0-6.0)	1.5 (1.0-6.0)	0.685*

*Mann-whitney U [Median (IQR)], **Chi-square test, IQR: Interquartile range, Variable were given as n, % or median (IQR, ¶: Only 22 patient's contact information were available, †: Some patients have more than 1 complications, *f* Vitamin A values were obtained in 16 patients

Table 2. Laboratory data of Measles Cases

	Total (n=33)	Unvaccinated (n=15)	Partially vaccinated (n=18)	p
Leukocyte, Median (IQR), (/uL)	7910 (5415-12175)	5770 (3640-9810)	8295 (6887.5-13680)	**0.019**[*]
Leukopenia, (n,%)	4 (12.1)	4 (26.7)	0 (0)	**0.033**[**]
Neutrophile, Median (IQR), (/uL)	3050 (1475-4375)	2900 (1625-4525)	3300 (1400-4575)	0.955[*]
Neutropenia, (n,%)	8 (24.2)	3 (20)	5 (27.8)	1[**]
Lymphocyte, Median (IQR), (/uL)	3000 (1850-6400)	2300 (1300-6300)	3800 (2575-6725)	0.060[*]
Lymphopenia, (n,%)	10 (30.3)	8 (53.3)	2 (11.1)	**0.020**[**]
Thrombocyte, Mean±SD, (/uL)	307182±11721	267066±114503	340611±111249	0.072[*]
Thrombopenia, (n,%)	2 (6.1)	2 (13.3)	0 (0)	0.199[**]
C- reactive protein, Median (IQR), (mg/L)	5.6 (0.3-11.3)	9.4 (5.6-31.9)	2.1 (0.1-5.9)	**0.021**[*]
ALT, Median (IQR), (U/L)	16.5 (13.0-23.9)	17.0 (13.0-30.0)	16.0 (13.0-21.3)	0.447[*]
AST, Median (IQR), (U/L)	46.5 (33.3-59.5)	49.0 (35.1-61.3)	40.0 (26.0-62.8)	0.404[*]
Vitamin A, Median (IQR), (ng/mL)[†]	233.0 (155.8-321.5)	128.5 (78-260)	259.5 (192.5-353.0)	0.129[*]

*Mann-whitney U [Median (IQR)], ** T-test (Mean±SDS), mean test Abb: ALT: Alanine aminotransferase, AST: Aspartate aminotransferase, Vitamin A: serum retinol concentration, Leukopenia: leucocyte count <4000/ul, Neutropenia: Neutrophile count <1500/ul, Lymphopenia: lymphocyte count <1500/ul, Thrombopenia: Thrombocyte count <150000/ul, SD: standard deviation, † Vitamin A values were obtained in 16 patients

Table 3. A comparison of the demographic, clinical and laboratory finding of confirmed Measles cases and suspected Measles cases

		Confirmed Measles Cases(n=40)	Suspected Measles cases (n=103)	p
Age, (month), Median (IQR)		30.0 (10.3-62.3)	19 (8.0-54.0)	0.286*
Gender, (n,%)	**Female**	19 (47.5)	52 (50.5)	0.749**
	Male	21 (52.5)	51 (49.5)	
Measles Vaccination Status, (n,%)	**Fully**	0 (0)	57 (55.3)	<0.001**
	Partially	20 (50)	33 (32.1)	
	Unvaccinated	20 (50)	13 (12.6)	
Symptom, (n,%)	**Rash**	40 (100)	96 (93.2)	0.191**
	Fever	39 (97,5)	40 (38.8)	<0.001**
	Cough	30 (70)	0 (0)	<0.001**
	Conjunctivitis	19 (47.5)	2 (1.9)	<0.001**
	Nasal congestion	18 (45)	0 (0)	<0.001**
	Diarrhea	16 (40)	2 (1.9)	<0.001**
	Stomatitis	6 (15)	0 (0)	<0.001**
		Confirmed Measles Cases(n=33)	**Suspected Measles cases (n=93)**	**p**
Leukocyte, Median (IQR), (/uL)		7910 (5415-12175)	10370 (8395-13760)	**0.001***
Leukopenia, (n,%)		4 (12.1)	0 (0)	**<0.001****
Neutrophile, Median (IQR), (/uL)		3050 (1475-4375)	3200 (1600-5200)	0.438*
Neutropenia, (n,%)		8 (24.2)	18 (19.4)	0.355**
Lymphocyte, Median (IQR), (/uL)		3000 (1850-6400)	4000 (2100-5600)	0.408*
Lymphopenia, (n,%)		10 (30.3)	12 (12.9)	**0.024****
Thrombocyte, Mean±SD, (/uL)		307182±11721	310264±98969	0.883***
Thrombopenia, (n,%)		2 (6.1)	3 (3.2)	0.601**
C- reactive protein, Median (IQR), (mg/L)		5.6 (0.3-11.3)	2.3 (0.6-7.6)	0.346*
ALT, Median (IQR), (U/L)		16.5 (13.0-23.9)	17.0 (13.0-22.0)	0.958*
AST, Median (IQR), (U/L)		46.5 (33.3-59.5)	34.0 (28.0-53.0)	**0.050***

*Mann-whitney U [Median (IQR)], **Chi-square test, *** T-test (Mean±SDS), mean test Abb: ALT: Alanine aminotransferase, AST: Aspartate aminotransferase, Vitamin A: serum retinol concentration, Leukopenia: leucocyte count <4000/ul, Neutropenia: Neutrophile count <1500/ul, Lymphopenia: lymphocyte count count <1500/ul, Thrombopenia: Thrombocyte count <150000/ul, SD: standard deviation

Figure 1. Correlation between Vitamin A levels and leukocyte count