MEASLES ORAL SWAB AS FIELD BASED SCREENING TEST IN CHILDREN

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Background

- Indonesia suffered from measles outbreak for many times, especially in the last five years
- The coverage of measles vaccination was constantly low
- Most measles patients were children
- WHO use antimeasles specific IgM from the serum as the gold standard to diagnose measles, however this test is invasive.
- Antimeasles IgM oral swab has been used as an alternative, however there has not been any study about this method in Indonesia

Aim

To validate antimeasles IgM oral swab for the diagnosis of measles in children

Methods

- Cross sectional study with diagnpstic test approach
- At Dr. Soetomo Hospital, Surabaya, Indonesia
- Three months period of collecting samples
- Inclusion criteria :
  - Age 6 month – 15 year-old
  - Maculopapular rash
  - Fever for at least three days
  - At least one of coryza, cough, and conjunctivitis
- Exclusion criteria :
  - *Immunocompromized*
  - History of fever and rash
  - Measles vaccination in the last 12 weeks
- For every participant :
  - History taking
  - Physical examination
  - Blood drawing
  - Oral swab
- Oral swab was taken from transudate at gingivo-cervicular sulcus
- Method for oral specimen was microimmune (EIA) captured antibody assay for antimeasles IgM
- Antimeasles specific IgM from serum was measured by Enzygnost® (Siemens) antimeasles test. With the cutoff of 1.00, both the sensitivity and specificity were 100%.
- The specimens were taken at least 3 days after the rash appearance
- McNemar and Kappa tests were used to analyze the result, with $p<0.05$ considered as significant
- Ethical approval from Ethical Committee of Dr. Soetomo Hospital Surabaya

Results

- Fifty six children were enrolled in the study, with the age range of 6-72 months
- Boys:girls = 1.6:1
- Mean of age : 27.5 months (SD 18.1); range 6-72 months
- Most patients came in the 3rd-6th day of illness
- Uniimunized children : 75.7%
- Antimeasles IgM of serum and oral swab were both positive in 50 participants
- *Antimeasles IgM of serum were positive in 52 participants*
- Antimeasles IgM of oral swab were positive in 51 participants
- Three children were negative for both methods
- Mean of antimeasles IgM of serum was 0.57 OD (SD 0.26) → range of 0.01-1.14 OD.
- Mean of antimeasles IgM of oral swab was 1.88 OD (SD 1.05) → range of 0.01-1.14 OD.
- Detection of antimeasles IgM were similar by both method (McNemar, p=1.00)
- Kappa coefficient 0.638 (moderate); McNemar p=1.00
- Best AUC of ROC Curve by oral swab was shown at the value of 0.2

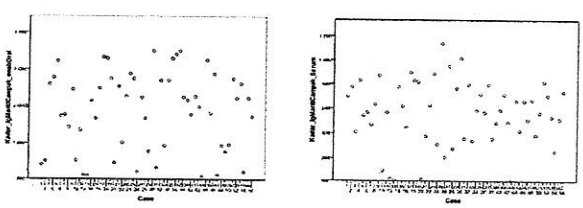

Figure 1. Scatter plot of antimeasles IgM of serum and oral swab

***Keywords** : antimeasles IgM, oral swab, field-based screening test, children*

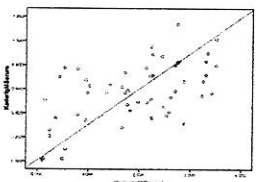

Figure 2. The correlation of serum and oral swab antimeasles IgM
(P<0.001 ; r=0.60)

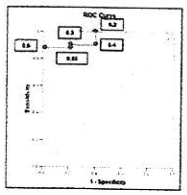

Figure 3. Several ROC curves of oral swab antimeasles IgM

Table 1. The characteristics of the participants

CHARACTERISTICS	NUMBER (n=56)	%
Sex :		
Boys	34	60.7
Girls	22	39.3
Age :		
6–9 months	9	16.1
9-72 months	47	83.9
Serum examination :		
Antimeasles IgM (+)	51	91.1
Antimeasles IgM (-)	5	8.9
Oral swab :		
Antimeasles IgM (+)	52	92.9
Antimeasles IgM (-)	4	7.1
Day of specimen taking		
3 days after the rash appeared	11	19.6
4	18	32.1
5	11	19.6
6	12	21.4
7	4	7.1
Coryza	47	83.9
Cough	51	91.1
Conjunctivitis	48	85.7

Table 2. Performance of several cutoff values of oral swab antimeasles IgM

PARAMETER (95% CI)	CUTOFF VALUES				
	0.6	0.55	0.5	0.4	0.2
Sn (%)	88 (79-97)	88 (79-97)	90 (82-98)	92 (85-100)	98 (94-100)
Sp (%)	100 (100)	80 (45-100)	80 (45-100)	60 (17-100)	60 (17-100)
PPV (%)	100 (100)	98 (94-100)	98 (94-100)	96 (91-100)	96 (91-100)
NPV (%)	45 (16-75)	40 (10-70)	44 (12-77)	43 (6-80)	75 (33-100)
LR+		4.41 (0.76-25.54)	4.51 (0.78-26.09)	2.30 (0.79-6.76)	2.45 (0.84-7.18)
LR–	0.12 (0.06-0.25)	0.15 (0.06-0.35)	0.12 (0.05-0.31)	0.13 (0.04-0.43)	0.03 (0.00-0.62)
Prevalence (%)	91	91	91	91	91
Kappa test	0.573	0.47	0.516	0.442	0.638
(p)	< 0.001	<0.001	<0.001	<0.001	<0.001
McNemar test (p)	0.031	0.125	0.219	0.687	1.00

Sn=sensitivity; Sp=specificity; PPV=positive predictive value; NPV=negative predictive value; LR+=positive likelihood ratio; LR-=negative likelihood ratio; CI=confidence interval; 0.2 is the cutoff from the comercial kit.

Discussion

- Saliva has been used as a specimen to check immunoglobulin level in several infectious diseases such as mumps, rubella, HIV, hepatitis, and Epstein-Barr virus
- Total immunoglobulin level of boys were commonly lower than those of girls.
- Most of measles patients were children age 1-6 year old.
- Different samples and procedures could give different results.
- In this study, serum antimeasles IgM showed good correlation with oral swab antimeasles IgM.
- The mean of IgG concentrations were higher than IgM in serum, crevicular fluid, and whole saliva.
- Highest sensitivity : cutoff 0.2; highest specificity : cutoff 0.5, since the 0.6 was not valid.
- Induced saliva was not recommended because it can lowering the IgM level.
- Cross reaction of IgM were shown at parvovirus and rubella patients.
- The cutoff value of 0.2 and 0.5 showed good Kappa and McNemar tests.
- The benefit of oral swab were : non invasive, easy, cheaper, simpler collecting and transport procedures, and more acceptable psychologically by the parents.
- Limitations of the study : single center, the gold standar was serum antimeasles IgM and not the PCR or viral culture/isolation.

Conclusions

Antimeasles IgM oral swab is highly sensitive and can be used as field-based alternative screening method to diagnose measles infection