

Current Status And Genetic Analysis of Artemisinin Resistance in Malaria

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Abstract

Malaria is still an important public health issue to date. Artemisinin-based combination therapies (ACTs) are highly effective and have been recommended by the World Health Organization as the first-line treatment for *Plasmodium falciparum* infection.

Since 2008, ACT resistance has been reported in the Greater Mekong Subregion. The efficacy of ACTs has gradually decreased with its widespread use. Now the world is deeply concerned with the spreading of artemisinin resistance and ACT multidrug resistance. Mutations in the propeller domain of the *P. falciparum kelch13 (pfK13)* gene are associated with artemisinin resistance. In order to assess the artemisinin resistance of imported malaria in Taiwan, we sequenced *pfK13* gene of four falciparum malaria cases imported from Kenya, Solomon Islands and Uganda in 2018 and no mutations were found in *pfK13* gene.

To better cope with imported malaria cases, measures such as clinical observations, travel history inquiry, laboratory diagnosis and follow-up should be reinforced. In addition, for patients from Greater Mekong Subregion with parasitemia after therapy

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regimen, the possibility of resistance should be evaluated, and malaria drug resistance genes, such as *pfKelch-13* gene, should be sequenced to assess the resistance of artemisinin for timely adjustment of treatment strategies. These efforts assist in more rational use of antimalarial drugs, delay the development of drug resistance and maintain the effectiveness of artemisinin.

Keywords: Malaria, *Plasmodium falciparum*, artemisinin, resistance

week 49–50(Nov.29–Dec.12, 2020)

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Weekly Data of Notifiable Infectious Diseases (by week of diagnosis)

Case diagnosis year		Week 49★		Week 1-49			
Classification	Disease Diagnosed	2020	2019	2020		2019	
				Total cases★	Imported cases	Total cases★	Imported cases
Category I	Plague	0	0	0	0	0	0
	Rabies	0	0	0	0	0	0
	SARS	0	0	0	0	0	0
	Smallpox	0	0	0	0	0	0
Category II	Acute Flaccid Paralysis	2	0	30	0	59	1
	Acute Viral Hepatitis type A	1	0	73	8	95	25
	Amoebiasis	8	8	235	121	327	182
	Anthrax	0	0	0	0	0	0
	Chikungunya Fever	0	1	3	3	114	93
	Cholera	0	0	1	0	0	0
	Dengue Fever	2	10	140	68	622	522
	Diphtheria	0	0	0	0	0	0
	Enterohemorrhagic E. coli Infection	0	0	0	0	1	0
	Epidemic Typhus Fever	0	0	0	0	0	0
	Hantavirus Pulmonary Syndrome	0	0	0	0	0	0
	Hemorrhagic Fever with Renal Syndrome	0	0	11	0	2	1
	Malaria	0	0	2	2	7	7
	Measles	0	0	2	2	135	55
	Meningococcal Meningitis	0	0	7	0	7	0
	Paratyphoid Fever	0	0	0	0	7	6
	Poliomyelitis	0	0	0	0	0	0
	Rubella	0	1	0	0	24	17
Shigellosis	2	3	147	24	135	43	
Typhoid fever	0	0	9	3	24	20	
West Nile Fever	0	0	0	0	0	0	
Zika virus infection	0	0	2	2	4	4	
Category III	Acute Viral Hepatitis type B	1	1	106	2	106	4
	Acute Viral Hepatitis type C	11	12	558	4	579	3
	Acute Viral Hepatitis type D	0	0	0	0	0	0
	Acute Viral Hepatitis type E	0	0	8	0	9	4
	Congenital Syphilis	0	0	0	0	0	0
	Congenital Rubella Syndrome	0	0	0	0	0	0
	Enteroviruses Infection with Severe Complications	0	0	7	0	64	1
	Haemophilus Influenza type b Infection	0	1	3	0	2	0
	Japanese Encephalitis	0	0	21	0	21	2
	Legionnaires' Disease	9	4	273	8	250	16
	Mumps	6	8	463	6	557	9
	Neonatal Tetanus	0	0	0	0	0	0
Pertussis	0	1	8	0	26	0	
Tetanus	0	0	7	0	4	1	
Category IV	Botulism	0	0	1	0	0	0
	Brucellosis	0	0	0	0	0	0
	Complicated Varicella	0	0	48	0	57	1
	Endemic Typhus Fever	1	0	21	0	28	3
	Herpesvirus B Infection	0	0	0	0	0	0
	Influenza Case with Severe Complications	0	38	548	6	2089	8
	Invasive Pneumococcal Disease	1	6	223	0	409	2
	Leptospirosis	2	1	84	0	114	1
	Listeriosis	5	3	130	0	164	1
	Lyme Disease	0	0	0	0	1	1
	Melioidosis	0	1	17	1	46	1
	Q Fever	0	0	13	0	23	5
	Scrub Typhus	7	4	394	1	443	6
Toxoplasmosis	0	1	16	0	17	4	
Tularemia	0	0	0	0	0	0	
Category V	Ebola Virus Disease	0	0	0	0	0	0
	Lassa Fever	0	0	0	0	0	0
	Marburg Hemorrhagic Fever	0	0	0	0	0	0
	Middle East Respiratory Syndrome	0	0	0	0	0	0
	Coronavirus Infections	0	0	0	0	0	0
	Novel Influenza A Virus Infections	0	0	0	0	0	0
	Rift Valley Fever	0	0	0	0	0	0
Severe Pneumonia with Novel Pathogens	46	-	694	639	-	-	
Yellow Fever	0	0	0	0	0	0	

- ★The weekly and cumulative total numbers include indigenous and imported cases of notifiable infectious diseases.
- MDR-TB, Tuberculosis, Syphilis, Gonorrhoea, HIV Infection, AIDS, Hansen's Disease and Creutzfeldt-Jakob Disease are excluded from the table.
- Numbers of mumps and tetanus cases are summed up by the week of report.
- Since 2020/1/15, "Severe Pneumonia with Novel Pathogens" was listed as a Notifiable Infectious Disease.

Suspected Clusters

- Fourteen clusters related to tuberculosis (7), diarrhea (5), and upper respiratory tract infection (2) were reported during week 49.

Imported Infectious Diseases

- There were 49 imported cases from 9 countries during week 49.

Diseases	Countries									Total
	Indonesia	USA	Philippines	UK	Belarus	Ireland	France	Germany	Vietnam	
Severe Pneumonia with Novel Pathogens	30	8	2	2	1	1	1	1		46
Amoebiasis			1						1	2
Dengue Fever	1									1
Total	31	8	3	2	1	1	1	1	1	49

- As of week 49, there were 894 imported cases from 57 countries. The top three countries are Indonesia (263), USA (115), and Philippines (107).
- The three notifiable diseases with the highest number of imported cases are Severe Pneumonia with Novel Pathogens (639), Amoebiasis (121), and Dengue Fever (68).

Summary of Epidemic

- **Severe Pneumonia with Novel Pathogens** : The COVID-19 pandemic is still critical and the number of returning Taiwanese citizens is increasing, therefore it is expected that the number of imported cases and the risk for local transmission will raise.
- **Dengue Fever** : The peak of dengue fever season has passed. The risk of infection in the community decrease gradually.
- **Influenza-like illness** : The influenza activity is expected to continue. The respiratory syncytial virus (RSV) dominant in the community.
- **Enterovirus** : The epidemic status increase gradually.

Weekly Data of Notifiable Infectious Diseases (by week of diagnosis)

Case diagnosis year		Week 50★		Week 1-50			
Classification	Disease Diagnosed	2020	2019	2020		2019	
				Total cases★	Imported cases	Total cases★	Imported cases
Category I	Plague	0	0	0	0	0	0
	Rabies	0	0	0	0	0	0
	SARS	0	0	0	0	0	0
	Smallpox	0	0	0	0	0	0
Category II	Acute Flaccid Paralysis	1	0	31	0	59	1
	Acute Viral Hepatitis type A	0	4	73	8	99	25
	Amoebiasis	1	5	236	121	332	186
	Anthrax	0	0	0	0	0	0
	Chikungunya Fever	0	0	3	3	114	93
	Cholera	0	0	1	0	0	0
	Dengue Fever	1	4	141	68	626	526
	Diphtheria	0	0	0	0	0	0
	Enterohemorrhagic E. coli Infection	0	0	0	0	1	0
	Epidemic Typhus Fever	0	0	0	0	0	0
	Hantavirus Pulmonary Syndrome	0	0	0	0	0	0
	Hemorrhagic Fever with Renal Syndrome	0	0	11	0	2	1
	Malaria	0	1	2	2	8	8
	Measles	0	2	2	2	137	55
	Meningococcal Meningitis	0	0	7	0	7	0
	Paratyphoid Fever	0	0	0	0	7	6
	Poliomyelitis	0	0	0	0	0	0
Rubella	0	0	0	0	24	17	
Shigellosis	2	2	149	24	137	43	
Typhoid fever	0	0	9	3	24	20	
West Nile Fever	0	0	0	0	0	0	
Zika virus infection	0	0	2	2	4	4	
Category III	Acute Viral Hepatitis type B	0	3	106	2	109	4
	Acute Viral Hepatitis type C	18	21	575	4	600	4
	Acute Viral Hepatitis type D	0	0	0	0	0	0
	Acute Viral Hepatitis type E	0	0	8	0	9	4
	Congenital Syphilis	0	0	0	0	0	0
	Congenital Rubella Syndrome	0	0	0	0	0	0
	Enteroviruses Infection with Severe Complications	0	1	7	0	65	1
	Haemophilus Influenza type b Infection	0	1	3	0	3	0
	Japanese Encephalitis	0	0	21	0	21	2
	Legionnaires' Disease	4	7	277	8	257	16
	Mumps	4	9	467	6	566	9
	Neonatal Tetanus	0	0	0	0	0	0
	Pertussis	1	2	9	0	28	0
Tetanus	0	1	7	0	5	1	
Category IV	Botulism	0	0	1	0	0	0
	Brucellosis	0	0	0	0	0	0
	Complicated Varicella	0	0	48	0	57	1
	Endemic Typhus Fever	0	1	21	0	29	3
	Herpesvirus B Infection	0	0	0	0	0	0
	Influenza Case with Severe Complications	0	44	548	6	2133	8
	Invasive Pneumococcal Disease	7	13	230	0	422	2
	Leptospirosis	0	1	84	0	115	1
	Listeriosis	0	1	130	0	165	1
	Lyme Disease	0	0	0	0	1	1
	Melioidosis	0	0	17	1	46	1
	Q Fever	1	0	14	0	23	5
	Scrub Typhus	12	7	406	1	450	6
Toxoplasmosis	0	0	16	0	17	4	
Tularemia	0	0	0	0	0	0	
Category V	Ebola Virus Disease	0	0	0	0	0	0
	Lassa Fever	0	0	0	0	0	0
	Marburg Hemorrhagic Fever	0	0	0	0	0	0
	Middle East Respiratory Syndrome	0	0	0	0	0	0
	Coronavirus Infections	0	0	0	0	0	0
	Novel Influenza A Virus Infections	0	0	0	0	0	0
	Rift Valley Fever	0	0	0	0	0	0
Severe Pneumonia with Novel Pathogens	39	-	733	678	-	-	
Yellow Fever	0	0	0	0	0	0	

1. ★The weekly and cumulative total numbers include indigenous and imported cases of notifiable infectious diseases.
2. MDR-TB, Tuberculosis, Syphilis, Gonorrhoea, HIV Infection, AIDS, Hansen's Disease and Creutzfeldt-Jakob Disease are excluded from the table.
3. Numbers of mumps and tetanus cases are summed up by the week of report.
4. Since 2020/1/15, "Severe Pneumonia with Novel Pathogens" was listed as a Notifiable Infectious Disease.

Suspected Clusters

- Twenty-seven clusters related to diarrhea (16), tuberculosis (6), enterovirus (2), varicella (2), and upper respiratory tract infection (1) were reported during week 50.

Imported Infectious Diseases

- There were 39 imported cases from 6 countries during week 50.

Diseases \ Countries	Countries						Total
	Indonesia	Philippines	USA	UK	China	Myanmar	
Severe Pneumonia with Novel Pathogens	27	5	4	1	1	1	39
Total	27	5	4	1	1	1	39

- As of week 50, there were 933 imported cases from 57 countries. The top three countries are Indonesia (290), USA (119), and Philippines (112).
- The three notifiable diseases with the highest number of imported cases are Severe Pneumonia with Novel Pathogens (678), Amoebiasis (121), and Dengue Fever (68).

Summary of Epidemic

- **Severe Pneumonia with Novel Pathogens** : The COVID-19 pandemic is still critical and the number of returning Taiwanese citizens is increasing, therefore it is expected that the number of imported cases and the risk for local transmission will raise.
- **Dengue Fever** : The peak of dengue fever season has passed. The risk of infection in the community decrease gradually.
- **Influenza-like illness** : The influenza activity is expected to continue. The number of respiratory syncytial virus (RSV) positive specimens decrease.
- **Enterovirus** : The epidemic status is similar to last week.

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