

## ORIGINAL ARTICLE

# A Two Years Retrospective Study on Epidemiology Characteristics of Sexually Transmitted Infections From Malaysian Private Healthcare Perspective

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## ABSTRACT

**Introduction:** Sexually transmitted Infections (STIs) are major public health concerns reaching an all-time high, globally. In Malaysia data on the prevalence of STIs remains scarce which limits the understanding of STI transmission dynamics and the role of interventions in the control of STIs. The aim of this study is to determine the epidemiology characteristics of STIs mainly from Malaysian private healthcare institutions. **Method:** A two years (2016 and 2017) retrospective review was conducted on 160 multiplex RT-PCR STI reports from KPJ hospitals, Malaysia. **Results:** There were 65 (40.6 %) patients positive STIs [male: 21/65 (32.3 %); female: 44/65 (67.7 %)]. The STIs was prevalent among young adults (56/65; 86.2 %) from the central region (46/65; 70.8 %). Females had 1.7 times greater risk to develop STI (20 per 100) and two times higher chance to have multiple STIs (10 per 100) in comparison to male. The single STIs was caused mainly by *U. parvum* (N=17). In males, *U. urealyticum* (N=3) and *C. trachomatis* (N=3) were prevalent, while *U. parvum* (N=15) was prevalent in females. There were 19 dual infections of STIs which were commonly caused by *U. parvum* and *M. hominis* (N=5). There were seven STIs cases caused by three pathogens concurrently including *U. urealyticum*, *U. parvum* and *C. trachomatis* (N=2) and *U. urealyticum*, *M. genitalium* and *C. trachomatis* (N=2). Females from urban communities have higher risk in comparison to males for developing multiple STIs. **Conclusion:** This study provides an imperative platform for temporal trends of STIs in Malaysia which reflects the health status of certain populations that warrant immediate public health interventions.

**Keywords:** Sexually Transmitted Infections, Sociodemographic, Prevalence ratio, KPJ Hospitals

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## INTRODUCTION

Sexually transmitted infection (STIs) consists of bacterial, viral and parasitic infections which can be transmitted through sexual activity, oral-genital contact, sharing needles as in intravenous drug users and from mother to baby at birth. To date, there are seven predominant STI pathogens identified including Chlamydia trachomatis (CT), Neisseria gonorrhoea (NG), Trichomonas vaginalis (TV), Mycoplasma hominis (MH), Mycoplasma genitalium (MG), Ureaplasma urealyticum (UU) and Ureaplasma parvum (UP). The protozoan, Trichomonas

vaginalis is responsible for trichomoniasis and is associated with a high risk of HIV infection and adverse pregnancy (1). The mollicutes such as *M. hominis*, *M. genitalium*, *U. urealyticum* and *U. parvum* are difficult to cultivate for diagnosis and have been associated with stillbirth, preterm birth, neonatal morbidity, pelvic inflammatory disease and male infertility as described by various studies (1-9).

Interestingly, Ureaplasma and Mycoplasma species are one of the common vaginal flora of healthy women (10). Amongst these, syphilis, gonorrhoea, chlamydia and trichomoniasis are the only known curable STIs. Whereas viral STI such as hepatitis B, herpes simplex virus (HSV), HIV, and human papillomavirus (HPV) are incurable but the symptoms could be reduced by treatment (11).

STIs have been acquired by more than one million people every day globally with the burden reportedly to increase the risk of HIV acquisition three-fold or more in people positive with herpes and syphilis (11). The global estimates of new cases of curable STIs in 2016 revealed that chlamydial infection is the highest STIs with 127 million cases as compared to gonorrhoea (87 million cases), syphilis (6 million cases) and trichomoniasis (156,000 cases) (12). In 2018, the Centers for Disease Control and Prevention (CDC) reported an increment of chlamydial infection (1.8 million cases; 19% increase), gonorrhoea (583,405 cases; 63% increase) as well as primary and secondary syphilis (35,063 cases; 71% increase) over the four years in the United States of America (USA) (13).

The same surveillance report revealed a drastic increase (185%) in congenital syphilis with a total of 1,306 new cases over the same period in the USA. The same STIs surveillance report revealed an alarming public health issue which is an increase of death in newborn from syphilis by 22% from 2017 to 2018 in the USA. The increment of congenital STD indicates the vulnerability of women to get infected with STI pathogens as compared to men (13). This is worrisome as the majority of STIs have shown no symptoms or only mild symptoms which may not be diagnosed as STIs initially (11).

To the best of our knowledge, there is a limited population-based study that has been published in Malaysia. There was only one recent cross-sectional study carried out by Yeoh and colleagues (14) was reported which focused on two government hospitals located in the northern region of Malaysia. Yeoh et al. (14) reported that five common STIs were detected in 83 sexually active patients, especially in the younger age groups (median age 28 years) attending STD clinics at Penang and Kedah, Malaysia in 2014. The prevalence of detected STIs by multiplex real-time PCR are UP (28.9%), CT (21.7%), NG (18.1%), UU (18.1%), MH (16.9%), and MG (4.8%) (14). Furthermore, the majority of infected patients in the said study were asymptomatic.

Nevertheless, the global estimates of the prevalence of these four curable STIs remain high. Thus, there is a need to update a regional spectrum-STIs database to provide an initial baseline for surveillance programmes in countries with alarming sexual behaviour statistics such as Malaysia. Based on the National Health and Morbidity Survey (NHMS) in 2017 on 27,202 secondary school students aged between 13 to 17 years old, there were notable high-risk sexual activity traits (15). The report highlights the risky sexual behaviour which may contribute to the increment of STI cases in Malaysia, particularly among young adolescents. Other recent published data on STIs in Malaysia was only focusing on the socio-demographic and behavioural pattern of the selected cohorts as reported by Yuen (16), Kawi (17), Panting and Mien (18), Abdullah et al. (19). However,

data on the recent clinico-laboratory spectrum of STIs in Malaysia is still limited and continuous data sharing from the private and public healthcare sectors are warranted. Furthermore, advances in molecular technology allow us to detect multiple common STI pathogens simultaneously using a multiplex real-time PCR (RT-PCR) assay.

Therefore, the present study aims to describe recent spatial and temporal trends in STIs incidence with epidemiological and some clinical characteristics from one of the largest homegrown healthcare groups in Malaysia which is KPJ healthcare group of hospitals. In 2017, there are 25 KPJ hospitals nationwide with 3052 operating beds and recording 286,465 inpatients and 2,473,851 outpatients (20). The present study emphasises analysis on the diversity of circulating agents causing STIs detected by multiplex RT-PCR Allplex™ STI Essential Assay (Seegene®, Seoul, Korea) for the year of 2016 and 2017.

## MATERIALS AND METHODS

A retrospective review was conducted on 160 laboratory requests of suspected STIs from KPJ hospitals nationwide. All specimens were subjected to PCR Allplex™ STI Essential Assay (Seegene®, Seoul, Korea) between January 2016 to December 2017. The laboratory requests originated from all the 25 KPJ hospitals and categorised into five regions as summarized in Table I. The PCR Allplex™ STI Essential Assay (Seegene®, Seoul, Korea) is a multiplex real-time PCR (RT-PCR) assay which has the capability to simultaneously detect seven common STIs pathogens including *Ureaplasma urealyticum*, *Ureaplasma parvum*, *Mycoplasma genitalium*, *Mycoplasma hominis*, *Neisseria gonorrhoeae*, *Chlamydia trachomatis* and *Trichomonas vaginalis*. The present study was approved by the Universiti Teknologi MARA (UiTM) Research Ethics Committee (REC/654/19) and KPJ Clinical and Research Ethics Review Committee (CRERC).

Information regarding hospital origin, gender, age, physical findings, types of infections and PCR laboratory results for STIs were documented. The age of the patient was categorised into infant (<2-year-old), childhood (2 to 10-year-old), adolescent (11 to 17-year-old), young adult (18 to 40-year-old), adult (41 to 65-year-old), and elderly (>66-year-old) (21). The STIs screening outcomes were also stratified according to a single infection, dual and multiple infections (co-infection), and negative infection. Single infection is defined as infection by either CT or MG/MH/NG/TV/UP/UU. Whereas multiple infections are defined as infection by two or more different STIs pathogens (e.g. UU + NG or UU + UP + MH). The causal relationship between gender and positive rate of multiple STI was explained by prevalence proportion (Equation 1), prevalence ratio (PR) (Equation 2) and prevalence difference (PD) (Equation 3) as

described by Spronk et al. (22) and Tamhane et. al. (23).

$$\frac{\text{Number of multiple STI}}{\text{Total study population (suspected with STI)}} \quad (\text{Eq 1})$$

$$\frac{\text{Prevalence proportion of multiple STIs in females}}{\text{Prevalence proportion of multiple STIs in males}} \quad (\text{Eq 2})$$

$$\frac{(\text{Prevalence proportion of multiple STIs in females})}{(\text{Prevalence proportion of multiple STIs in males}) \times 100} \quad (\text{Eq 3})$$

**Table I: Data catchment area of KPJ hospitals around Malaysia**

Regions	KPJ hospital involved	No of hospital	No of laboratory request
Southern (Johor, Melaka and Negeri Sembilan)	<ul style="list-style-type: none"> <li>Seremban Specialist Hospital</li> <li>Bandar Maharani Specialist Hospital</li> <li>Kluang Utama Specialist Hospital</li> <li>Pasir Gudang Specialist Hospital</li> <li>KPJ Puteri Specialist Hospital</li> <li>KPJ Bandar Dato' Onn Specialist Hospital</li> </ul>	6	24
Central (Kuala Lumpur and Selangor)	<ul style="list-style-type: none"> <li>KPJ Ampang Puteri Specialist Hospital</li> <li>KPJ Klang Specialist Hospital</li> <li>KPJ Kajang Specialist Hospital</li> <li>KPJ Damansara Specialist Hospital</li> <li>KPJ Tawakkal Specialist Hospital</li> <li>KPJ Sentosa KL Specialist Hospital</li> <li>KPJ Rawang Specialist Hospital</li> <li>KPJ Selangor Specialist Hospital</li> </ul>	8	110
Northern (Perak, Kedah, Penang and Perlis)	<ul style="list-style-type: none"> <li>KPJ Penang Specialist Hospital</li> <li>KPJ Ipoh Specialist Hospital</li> <li>Taiping Medical Centre</li> <li>Sri Manjung Specialist Centre</li> </ul>	4	7
East (Pahang, Kelantan and Terengganu)	<ul style="list-style-type: none"> <li>KPJ Pahang Specialist Hospital</li> <li>KPJ Perdana Specialist Hospital</li> </ul>	2	11
West (Sabah and Sarawak)	<ul style="list-style-type: none"> <li>Sibu Specialist Medical Centre</li> <li>KPJ Sabah Specialist Hospital</li> <li>Damai Specialist Hospital</li> <li>Kuching Specialist Hospital</li> <li>KPJ Miri Specialist Hospital</li> </ul>	5	1

## RESULTS

### Demographic characteristics of the patients

A total of 160 patients had attended the KPJ hospitals for the diagnosis of STIs. Majority of studied population were female (N=92; 57.5 %) and men accounted for 42.5 % (N=68) with the sex ratio of male:female (1:1.35). The median age of the patients was 33 years (range eight to 63 years). The patients were mainly from the age group of young adults (N=120; 75.0 %). While no data gathered from both the infant and elderly group. Of 160 patients, 68% (109/160) were from the central region.

### Laboratory results of studied population

Table II showing the frequency of STIs as single and multiple infections confirmed by multiplex RT-PCR assay. Of 160 patients suspected with STIs, 39 (24.4 %) were confirmed to have a single infection and 26

**Table II: Distribution of single and multiple STIs confirmed by multiplex RT-PCR assay according to gender, age group of patients and catchment area**

Demographic	N (%)			
	Single	Multiple	Negative	Total
<b>Gender</b>				
Male	13 (19.1)	8 (11.8)	47 (69.1)	68 (42.5)
Female	26 (28.3)	18 (19.6)	48 (52.2)	92 (57.5)
Total	39 (24.4)	26 (16.3)	95 (59.4)	160 (100)
<b>Age Group</b>				
Childhood (2 to 10 y/o)	0	0	1 (100)	1 (0.6)
Adolescent (11 to 17 y/o)	0	0	1 (100)	1 (0.6)
Young Adult (18 to 40 y/o)	33 (27.5)	23 (19.2)	64 (53.3)	120 (75)
Adult (41 to 65 y/o)	6 (15.8)	3 (7.9)	29 (76.3)	38 (23.8)
<b>Region</b>				
Southern	4 (17.4)	2 (8.7)	17 (73.9)	23 (14.4)
Central	28 (25.7)	18 (16.5)	63 (57.8)	109 (68.1)
Northern	3 (42.9)	0	4 (57.1)	7 (4.4)
East	3 (27.3)	1 (9.1)	7 (63.6)	11 (6.9)
West	1 (10.0)	5 (50.0)	4 (40.0)	10 (6.2)

y/o: year-old. Southern Region: Johor, Melaka, Negeri Sembilan; Central Region: Selangor, Kuala Lumpur, Putrajaya; Northern: Perak, Kedah, Penang, Perlis; East: Pahang, Kelantan, Terengganu; West: Sabah and Sarawak.

(16.3%) cases were positive for multiple infections [Total: 65/160 (40.7 %)]. Female patients had more single STI (N=26) and multiple STIs (N=18) [Total: 44/65 (67.7 %)] as compared to male patients with only 13 for single STI and eight multiple STIs respectively [Total: 21/65 (32.3 %)]. The young adult group had the highest number of single STI (N=33) and multiple STIs (N=23) [Total: 56/65 (86.2 %)]. There were no STIs cases recorded from infant and elderly age groups. Single STI and multiple STIs were recorded highest in the central region [Total: 46/65 (70.8 %) with 28 and 18 cases, respectively (Table II)].

### Prevalence Ratio (PR) & Prevalence Difference (PD) of STIs between gender

Based on the PR values in Table III, the prevalence of overall (single and multiple STIs) cases in females was one point seven times greater and two times greater, respectively than males. The PD for overall STIs cases explains that among the female patients there were 20 % prevalence of positive STI and 10 % prevalence of multiple STIs per 100 females as compared to male patients in the present study.

### Prevalence proportion of single STI pathogen according to gender and age groups of patients

Based on the descriptive analysis of the single STI cases, the *U. parvum* was the most frequent pathogen identified (N=17; 43.6 %), followed by *U. urealyticum* (N=8; 20.5 %) and *C. trachomatis* (N=6; 15.4 %). In male patients that had single STI, the prevalent pathogens detected were *U. urealyticum* (N=3; 23.1 %) and *C. trachomatis* (N=3; 23.1 %). Whereas in female patients, the predominant pathogen was *U. parvum* (N=15; 57.8 %). Single STI cases were detected mainly in the young adult patients (N=33) with *U. parvum* was the most common pathogen detected.

**Table III: Prevalence Ratio (PR) & Prevalence Difference (PD) of positive single and multiple STI between female and males in KPJ hospitals between 2016 and 2017**

Type of STI	Gender	Positive STI	Negative STI	Total Study Population	Prevalence Proportion of STI <sup>a</sup>	Prevalence Ratio (PR) <sup>b</sup>	Prevalence Difference (PD) <sup>c</sup>
Overall*	Female	44	48	92	0.5	1.7	20
	Males	21	47	68	0.3		
Type of STI	Gender	Positive STI	Negative STI	Total Study Population	Prevalence Proportion of STI <sup>d</sup>	Prevalence Ratio (PR) <sup>e</sup>	Prevalence Difference (PD) <sup>f</sup>
Multiple#	Female	18	74	92	0.2	2	10
	Males	8	60	68	0.1		

\*Sum of single, dual and triple positive STI cases

# Sum of dual and triple positive STI cases

a. Number of positive STI cases / Total study population (suspected with STI)

b. Prevalence proportion of positive STI in female / Prevalence proportion of overall positive STI in male

c. (Prevalence proportion of positive STI in female - Prevalence proportion of multiple STI in male) x 100

d. Number of multiple STI / Total study population (suspected with STI)

e. Prevalence proportion of multiple STI in female/Prevalence proportion of multiple STI in male

f. (Prevalence proportion of multiple STI in female - Prevalence proportion of multiple STI in male) x 100

### Prevalence proportion of multiple STI pathogens according to gender and age groups of patients

There were 26 patients who had more than one pathogen causing STI. Of 26, a total of 19 cases of dual pathogens causing STIs recorded particularly among female and young adult patients. Co-infection between *U. parvum* and *M. hominis* were the most prevalent (N=5) across the groups particularly in the female and young adult patients. There were seven young adult patients who had three concurrent pathogens causing STIs. The prevalent pathogens causing multiple STIs include a combination of these organisms namely *U. urealyticum*, *U. parvum*, *C. trachomatis*, and *M. genitalium*.

### Clinical presentation of the studied population

Within the detected cases, 80.8 % of single STI and 82.1 % of multiple STI patients were asymptomatic (Table IV). The remaining STIs cases have symptoms including vaginal discharge and urethral discharge.

## DISCUSSION

Understanding the sociodemographic data may give a hint on the host predisposing factors that may assist us in determining the risk of infection to the affected individual. The observed high prevalence of STIs among female patients particularly within the young adult age group as presented here corresponds to recent study by Yeoh and colleagues (14), that reported a high prevalence of STIs (62.5 %) in female patients from the same age group attending the STIs clinics at both Hospital Pulau Pinang and Hospital Sultanah Bahiyah Kedah, Malaysia.

The higher STI prevalence ratio among females than male patients reported by the aforementioned studies highlights the vulnerability of women to get infected due to biological factors such as thinner lining of the vagina that facilitate both bacterial and viral infections (13). However, correlation between the high-risk behaviour

**Table IV: Distribution of symptoms in STIs cases according to types of STIs and age group of the patients**

Demographic	N (%)				Total
	Vaginal Discharge	Urethral Discharge	Other Symptoms	Asymptomatic	
<b>Types of STI</b>					
Single Infection	5 (12.8)	2 (5.1)	0	32 (82.1)	39 (100)
Multiple Infection	4 (15.4)	1 (3.8)	0	21 (80.8)	26 (100)
Negative Infection	5 (5.3)	0	9 (9.5)	81 (85.3)	95 (100)
<b>Age Groups</b>					
Childhood (2 to 10 y/o)	1 (100)	0	0	0	1
Adolescent (11 to 17 y/o)	0	0	0	1	1
Young Adult (18 to 40 y/o)	12	3	7	98	120
Adult (41 to 65 y/o)	1	0	2	35	38

y/o: year-old; Southern Region: Johor, Melaka, Negeri Sembilan; Central Region: Selangor, Kuala Lumpur, Putrajaya; Northern: Perak, Kedah, Penang, Perlis; East: Pahang, Kelantan, Terengganu; West: Sabah and Sarawak.

and sexual activity with any age group of patients confirmed with STIs could not be carried out, as detailed information on the sexual activity could not be obtained from the archived data. Thus, correlation of the sexual activity with the detected STI could not be inferred in the present study.

A substantial number of collected specimens belong to patients from the central region, KPJ hospitals were subjected to multiplex RT-PCR STI assay. This may indicate the clinician's preference to use molecular diagnostic technique within the central region to complement the other testing methods such as gram stain, culture, wet mount microscopy, rapid plasma reagin or particle agglutination assay to detect the presence of bacteria and protozoa associated with STIs. Furthermore, most pathogens causing STI cannot be cultivated on artificial laboratory media, hence the molecular, rapid diagnostic assay is preferred.

Other possible factors contributed to a higher number of samples from the central region are due to the fact that most KPJ hospitals are located in the central region of Malaysia. The other regions of KPJ hospitals could still depend solely on other aforementioned testing methods for STI diagnosis. The significant stratification of single, dual and multiple STI incidence rate by age group, gender and location reflects the influence of socio-demographic factors in STI prevalence ratio and prevalence difference values. Since the majority of the detected STIs were from Klang Valley, thus we could infer that the reported prevalence of STIs here could represent Malaysian urban community.

In this study, it was evident that young adult females are at a greater risk to develop STIs. The PR values and PD values for positive STI and multiple STI cases were used as an indicator of a population health status as suggested by Spronk et al. (22) and Tamhane et al. (23). Our analysis found that the female patients had one point seven times greater risk to have single STI and two times greater risk to be infected with multiple pathogens causing STIs than male patients. The PR and PD values indicate the widespread STIs among females, particularly the young adults from the central region of Malaysia.

The high STIs prevalence ratio among young adult females is in accordance with the recent CDC surveillance report highlighting the high STIs cases among females in the USA which led to an increment of congenital syphilis by 22 % (13). These epidemiological measures such as PR and PD values could be used as a baseline information in monitoring infectious diseases and to formulate better healthcare policy. The PD values in the present study revealed that there were 20 excess cases of positive STIs and 10 excess cases of multiple STIs per 100 females as compared to male patients. Thus, it indicates that females have higher risk in acquiring the STI. The high prevalence proportion of STIs among women and young adults were also found in other regions such as Brazil with a PR ratio of 1.4 (24) and Lebanon with the prevalence proportion of 62% (24). The predictors associated with STI reported in these two studies were being female, having multiple partners in the last year, and not using or irregularly using contraceptives (24,25).

The reported pathogens associated with STIs in KPJ were in accordance with the prevalence and epidemiological features of STI in northern Malaysia carried out by Yeoh et al. (14). The prevalence and the infectivity rates of the top three pathogens causing STIs in KPJ hospitals are *U. parvum* (43.6 %), *U. urealyticum* (20.5 %) and *C. trachomatis* with 15.4 % of positive rates. Yeoh and colleagues (14) also found a similar predominant STIs which are *U. parvum*, *U. urealyticum* and *C. trachomatis*, with different infectivity rates of 28.9 %, 18.1 % and 21.7 % respectively in the northern region of Malaysia.

Within the single STI cases, stratification by gender revealed that *U. parvum* was the prevalent pathogen causing STI in young adult female patients in KPJ hospital. For male positive single STI, *U. urealyticum* (N=3; 23.1 %) and *C. trachomatis* (N=3; 23.1 %) were the prevalent pathogens. Thus, the prevalent *U. parvum* infection among the young adult females in KPJ hospital and northern Malaysia indicate Malaysian women are at risk of acquiring the STIs from their partner.

The utilization of multiplex RT-PCR STI assay allows us to determine the health burden of patients diagnosed with more than one concurrent STIs. To date, this is the first study describing the multiple STIs in Malaysia. Other studies have reported data of multiple STI with the population in France (10) and within Asian region; one recent study from Korea has been published (26). The present study reported 19 cases of dual infection which involved co-infection of *U. parvum* and *M. hominis* that are prevalent particularly within the group of the young adult female patients. Furthermore, there are two concurrent STIs that were caused by three different pathogens. The first combination involved *U. urealyticum*, *U. parvum* and *C. trachomatis*, whereas the second multiple STI was caused by the combination of *U. urealyticum*, *M. genitalium* and *C. trachomatis*. The prevalent multiple STI from 748 Korean, reported to be caused by co-infection of *U. urealyticum*, *C. trachomatis* and *N. gonorrhoeae* (26). Whereas much earlier study in France reported the prevalent dual STI are caused by *C. trachomatis* and *U. parvum* among the 202 female subjects (10).

However, a routine testing and treatment of asymptomatic or symptomatic men and women for *U. parvum*, *M. hominis* and *U. urealyticum* are not common and subjected to the bacterial load detected within the sample (27). Although *U. urealyticum* has been common pathogens for urethritis in men, it is probably not causal unless a high bacterial load is present. Asymptomatic carriage of this bacteria is common and the majority of individuals do not develop disease (27). However, the infection could provide a greater risk for any female patients with the STI to have an adverse pregnancy such as stillbirth, neonatal morbidity, preterm birth and infertility due to pelvic inflammatory disease (1-9). Thus, the risk could be minimised particularly in females with multiple STIs. Thus, appropriate precaution could be advised and proposed to asymptomatic and not just for symptomatic patients with common STI symptoms such as vaginal discharge and urethral discharge.

Nevertheless, there were limitations in the current study as marital status, sexual orientation, number of sexual partners and other sexual behaviours were not able to be accessed due to incomplete and confidential information. Thus, limiting the correlation analysis on the risk factors of the studied population. A continuous surveillance study is warranted in Malaysia to avoid

any health consequences such as infertility, stillbirth or congenital STI as observed in the USA recently (13).

## CONCLUSION

Our present study achieved its objective evidenced by a two years prevalence of STIs and its pattern representing an urban community in Malaysia, which in turn contribute substantial data to the epidemiological surveillance of STIs. To the best of our knowledge, this is the first report on the STI pathogens from private hospitals in Malaysia, and this may serve as a yardstick for evaluation of future STI control and prevention programs.

## ACKNOWLEDGEMENTS

We thank KPJ Healthcare Berhad and Universiti Teknologi MARA (UiTM), Malaysia for their support in data sharing, facilities and financial supports. This study was supported in parts by the Ministry of Higher Education, Malaysia (RACER/1/2019/STG05/UITM//4).

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