

Research Article**Infections and colonisation of central venous catheters in patients admitted to intensive care units at two tertiary care hospitals**S Medis<sup>1</sup>, T Dissanayake<sup>2</sup>, D Namali<sup>3</sup>, S Gunasekara<sup>4</sup>, J Kottahachchi<sup>2</sup>*Sri Lankan Journal of Infectious Diseases 2022 Vol.12(1):E10 1-11*DOI: <http://dx.doi.org/10.4038/sljid.v12i1.8425>**Abstract**

**Introduction:** Central venous catheters (CVC) are frequently used in modern health care systems. However, CVCs are likely to get colonised with microorganisms, resulting in catheter-related blood stream infections (CRBSI). This study investigated microorganisms causing CRBSI and CVC colonisation, their antibiotic resistance, and factors associated with CRBSI in patients in the intensive care units (ICU) at the Colombo North Teaching Hospital (CNTH) and Apeksha hospital, Sri Lanka.

**Methods:** The study included 300 adult patients in ICUs with a CVC in-situ for >48 hours. Blood taken through the CVC, peripheral blood and CVC tips were cultured. Microorganisms were identified and tested for antibiotic susceptibility. Demographic factors were recorded.

**Results:** Seventeen patients (13.1%) developed CRBSI. The CRBSI rate was 13.3 per 1,000 catheter days in CNTH while it was 10 (5.9%) cases and 5.2 per 1,000 catheter days in Apeksha hospital. In CNTH, CVC colonisation was detected in 35 (26.9%). Coagulase negative staphylococci (CoNS) were the leading cause of both CRBSI (41%) and colonisation (58%). In Apeksha hospital, *Klebsiella* sp. (5/10) were the predominant pathogens that caused CRBSI. Eighty-nine CVCs (52.3%) were colonised by CoNS (58%). In CNTH, CRBSI was detected more in males (14/17) ( $p < 0.05$ ). The majority of microorganisms that caused CRBSI and CVC colonisation in both hospitals showed resistance to commonly used antibiotics.

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<sup>1</sup> Department of Medical Laboratory Sciences, Faculty of Allied Health Sciences, General Sir John Kotelawala Defence University, Werehera, Sri Lanka

<sup>2</sup> Department of Microbiology, Faculty of Medical Sciences, University of Sri Jayewardenepura, Sri Lanka

<sup>3</sup> Colombo North Teaching Hospital, Ragama, Sri Lanka

<sup>4</sup> Apeksha Hospital, Maharagama, Sri Lanka

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Address for correspondence: S. Medis, Department of Medical Laboratory Sciences, Faculty of Allied Health Sciences, General Sir John Kotelawala Defence University, Werehera, Sri Lanka Telephone: +9471 1042277, +9476 2067734 email: [sohanimm@gmail.com](mailto:sohanimm@gmail.com)

 <https://orcid.org/0000-0002-2984-6996>

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**Conclusion:** The CRBSI rates and the incidences were higher in CNTH. CoNS was the most common cause of CRBSI in CNTH and Gram negative bacteria in Apeksha hospital. CVC colonisation with CoNS was common in both hospitals. Antibiotic resistance was high among bacteria causing CRBSI and colonisation.

**Keywords:** *Catheter related bloodstream infections, CVC colonisation*

## **Introduction**

In the past few decades, the use of intravascular catheters, including central venous catheters (CVC) have become common practices in health care settings. These CVCs are used to administer chemotherapeutic drugs, blood products, nutrients, and antibiotics as well as for hemodialysis procedures.<sup>1</sup> CVCs can be a predisposing factor of catheter-related bloodstream infections (CRBSI) which lead to hospital acquired bacteremia and sepsis. CRBSIs are associated with high morbidity and mortality rates as well as increased healthcare costs.<sup>2</sup>

Microorganisms which are normal flora of the skin such as *Staphylococcus aureus* and *Staphylococcus epidermidis* are common aetiological agents of CRBSI.<sup>1,3</sup> However, some Gram-negative bacteria, such as *Escherichia coli* and *Klebsiella* species have also been reported, especially in patients with malignancies.<sup>3,4</sup>

Studies have found some risk factors associated with CRBSI such as old age, prolonged catheterisation, co-existing diseases such as head and neck cancer, immunosuppression, neutropaenia, diabetes, malnutrition, and chronic use of steroids.<sup>4</sup>

Early diagnosis and proper treatment plans are the key to successful management of CRBSI. Information regarding the causative organisms and their antimicrobial susceptibility patterns in the local health care settings are important for timely initiation of appropriate empirical therapy. Identification of risk factors help not only to determine the most effective patient management plan in the case of development of CRBSI, but also to recognise better prevention methods. There is a lack of available information regarding CRBSI, its etiological agents and their susceptibility patterns in south asian healthcare facilities. Studies conducted on CRBSI will be most useful for developing and updating treatment and infection prevention guidelines in this context, especially in the ICU setting.

The current study was conducted to investigate the incidence of CRBSI and CVC colonisation with causative microorganisms and their antibiotic susceptibility, along with factors associated with the development of CRBSI in ICU patients at two tertiary care hospitals, CNTH, Ragama and Apeksha hospital, Maharagama, Sri Lanka.

## **Methods**

### ***Study population***

This descriptive cross-sectional study was conducted over a 10-month period from November 2018 to August 2019 at CNTH and Apeksha hospital, Maharagama, Sri Lanka. Both male and female adult (>18 years) patients admitted to the ICUs who had a central venous catheter (CVC) in-situ for more than 48 hours were included in this study.

### ***Definitions and calculations***

CRBSI was identified according to the following standard definitions.<sup>2</sup>

1. A shorter time to positive culture (>2 hours earlier) with the same organism in a central line blood sample than a peripheral blood sample drawn at the same time.
2. When both positive peripheral blood cultures (one or more) and catheter tip culture isolate the same microbial species

Catheter colonisation was determined by the presence of a significant growth of microorganisms using a semi-quantitative culture  $\geq 15$  colony forming units (CFU) using a 4cm segment from the tip of the catheter or a positive culture from blood drawn from the catheter and a negative peripheral blood culture.<sup>2</sup>

The occurrence of CRBSI was calculated as incidence per 1000 catheter-days.<sup>5</sup>

### ***Patients' demographics and clinical data***

Clinical data including duration of the catheterisation, type of catheter, catheter insertion site, underlying diseases, type of malignancy (haematological or nonhaematological), neutrophil status (in cancer patients), days of ICU stay and demographic data including gender and age were collected from each patient and analysed to identify the associated factors for developing CRBSI.

### ***Microbiological analysis***

Peripheral blood and line blood from CVC were processed according to standard microbiological methods<sup>6</sup> and CVC tips were cultured according to Maki's roll over plate method.<sup>7</sup> The isolated microorganisms were identified using biochemical tests and commercially available kits (API<sup>®</sup> Staph and API<sup>®</sup> 20E- Analytical Profile Index System; bioMérieux, Paris, France).

Antibiotic susceptibility testing was carried out by disk diffusion method according to the Clinical and Laboratory Standard Institute (CLSI – 2016) methodology.<sup>8</sup>

### ***Statistical analysis***

Data were analysed by a computer-based programme, statistical package for social sciences (SPSS V26). All p values were based on 2-tailed tests and a p value of less than 0.05 was considered significant ( $p < 0.05$ ).

## **Results**

Three hundred (300) patients, 130 from CNTH and 170 from Apeksha hospital were included in the study.

Seventeen (13.1%) patients with CRBSI were detected in CNTH. The CRBSI rate was 13.4 per 1,000 catheters days. Colonisation was detected in 35 (26.9%) CVCs.

In Apeksha hospital 10 patients (5.9%) developed CRBSI and CRBSI rate was 5.2 per 1,000 catheters days. Colonisation was detected in 89 (52.4%) CVCs.

### ***Demographic and clinical characteristics of patients with CRBSI***

In CNTH the mean age of patients was 48.3 ( $\pm 16.9$ ) years. Fourteen of 67 males and 3 of 63 females developed CRBSI which was statistically significant ( $P=0.006$ ). The most frequent co-morbid conditions included diabetes in 02 (11.7%) patients. The jugular vein ( $n=15$ ; 88.2%) was the most common site of CVC insertion. Local complications were seen in 2 (11.7%) patients. Mean duration to develop CRBSI was 6.5 days after catheterisation (Table 1).

**Table 1. Factors associated with CRBSI in the study population of CNTH and Apeksha hospital**

Demographic and clinical characteristics	Patients with CRBSI (n=17)		Patients without CRBSI (n=113)		p value
<b>CNTH</b>					
Mean age (years)	48.3		54.1		0.14
	n	%	n	%	
Male gender	14	82.4	53	46.9	0.006 *
Diabetes mellitus	2	11.8	24	21.2	0.36
Local complications at the catheter site	2	11.8	4	3.5	0.13
CVC location in jugular vein	15	88.2	108	95.6	0.21
<b>Apeksha hospital</b>	<b>Patients with CRBSI (n=10)</b>		<b>Patients without CRBSI (n=160)</b>		<b>p value</b>
Mean age (years)	47.5		49.8		0.69
Male gender	6	60.0	64	40.0	0.21
Diabetes mellitus	3	30.0	45	28.1	1.00
Presence of local complications	1	10.0	0	0	-
Neutropenia	4	40.0	39	24.4	0.27
Haematological malignancy	2	20.0	48	30.0	0.72
CVC location in Jugular vein	7	70.0	111	69.4	0.96

\* $P < 0.05$  significant

Patients in Apeksha hospital developed CRBSI after a mean duration of 18.9 days following CVC insertion. The patient's age, gender, presence of diabetes mellitus, type of malignancy, neutropenia, location, or the type of catheter did not have a statistically significant association with development of CRBSI (Table 1).

### ***Causative organisms and antibiotic susceptibility***

In CNTH, coagulase negative *Staphylococcus* spp (CoNS) was the leading cause of both CRBSI ( $n=7$ ; 41%) and CVC colonisation ( $n=20$ ; 58%). *Pseudomonas* spp. ( $n=2$ ; 12%), *Acinetobacter* spp. ( $n=2$ ; 12%), diphtheroids ( $n=2$ ; 12%) were isolated from patients with CRBSI followed by other Gram-negative organisms and *Candida* spp. The second leading cause of CVC colonisation was *Pseudomonas* spp. ( $n=6$ ; 17%) followed by other organisms as shown in Table 2. Two specimens revealed polymicrobial colonisation, *Staphylococcus aureus* with *Pseudomonas* spp. and *Acinetobacter* spp. with CoNS.

**Table 2. Organisms causing CRBSI and catheter colonization**

Organisms	CNTH				Apeksha hospital			
	CRBSI		colonisation		CRBSI		colonisation	
	no	%	no	%	no	%	no	%
CoNS	7	41	20	58	1	10	52	58
<i>Pseudomonas</i> species	2	12	6	17	3	30	6	7
<i>Acinetobacter</i> species	2	12	2	6	0	0	6	7
Diphtheroids	2	12	00	0	0	0	0	00
<i>Klebsiella</i> species	0	0	00	0	5	50	5	6
<i>Serratia marcescens</i>	1	6	1	3	0	0	1	1
<i>Stenotrophomonas maltophilia</i>	1	6	00	0	0	0	2	2
<i>Morganella morganii</i>	0	0	00	0	0	0	1	1
<i>Burkholderia cepacia</i>	1	6	00	0	0	0	0	0
<i>Candida</i> (non albicans)	1	6	00	0	0	0	7	8
<i>Staphylococcus aureus</i>	0	0	2	6	0	0	2	2
<i>Escherichia coli</i>	0	0	1	3	0	0	0	0
<i>Enterococcus</i> species	0	0	00	0	0	0	3	3
Gram positive bacilli	0	0	1	3	0	0	2	2
Mixed growth	0	0	2	6	1	10	2	2
<b>Total (n=82)</b>	<b>17</b>		<b>35</b>		<b>10</b>		<b>89</b>	

The CoNS isolates were identified as *S. haemolyticus* (n=7), *S. cohnii* (n=5), *S. hominis* (n=06), *S. epidermidis* (n=02), *S. chromogenes* (n=03), *S. capitis* (n= 01), *S. sciuri* (n=01) and *S. saprophyticus* (n=3). Among them, *S. haemolyticus* (n=3), *S. cohnii* (n=1), *S. hominis* (n=01), *S. chromogenes* (n=1) and *S. saprophyticus* (n=1) were associated with CRBSI.

Gram negative organisms were the most dominant in CRBSI in patients in Apeksha hospital. *Klebsiella* spp. (5/10) and *Pseudomonas* spp. (3/10) were the most common among them. Mixed infection with *Citrobacter freundii* and *Streptococcus* spp. was found in one patient. Eighty-nine (52.4%) patients had colonised CVCs. Colonisation was observed with both bacterial and fungal pathogens. The leading cause of CVC colonisation was CoNS (58%), followed by *Candida* spp. (8%), *Pseudomonas* spp. (7%), *Acinetobacter* spp. (7%), *Klebsiella* spp. (6%) and other organisms as shown in the table 2. Polymicrobial colonisation was also observed, including CoNS with non-albicans *Candida* spp. and *Acinetobacter* spp. with *Pseudomonas* spp.

The CoNS were identified as *S. haemolyticus* (n=27), *S. cohnii* (n=04), *S. hominis* (n=05), *S. epidermidis* (n=07), *S. chromogenes* (n=03), *S. capitis* (n= 03), *S. lugdunensis* (n=02), *S. sciuri* (n=01), *S. xylosus* (n=01) and *S. kloosi* (n=01).

The majority of isolates from patients with CRBSI showed resistance to several antibiotics.

Cloxacillin and clindamycin resistance rates in CoNS isolated from the CRBSI patients in CNTH were 71% and 57% respectively (Table 3). Among the CoNS that caused CVC colonisation in Apeksha hospital, 83% showed resistance to erythromycin and 66% to clindamycin. All *Acinetobacter* strains (n=5) isolated in CNTH were resistant to cefoperazone-sulbactam (Table 4). In addition, *Pseudomonas* spp. isolated from the patients in CNTH showed higher resistance to the antimicrobial agents than isolates from the patients in Apeksha hospital.

**Table 3. Percentage resistance of CoNS**

Antibiotics	CNTH		Apeksha hospital	
	CRBSI	CVC colonisation	CRBSI	CVC colonisation
<b>Number tested</b>	7	21	1	53
Erythromycin	86	86	100	83
Cloxacillin	71	86	00	75
Clindamycin	57	76	100	66
Ciprofloxacin	14	67	00	60
Linezolid	00	00	00	00
Vancomycin	00	00	00	00

**Table 4. Percentage resistance of commonly isolated Gram-negative bacilli**

Antibiotic	CNTH				Apeksha hospital	
	<i>Acinetobacter</i> spp.		<i>Pseudomonas</i> spp.		<i>Pseudomonas</i> spp.	
	CRBSI	CVC colonisation	CRBSI	CVC colonisation	CRBSI	CVC colonisation
<b>Number tested</b>	2	3	2	7	3	6
Amikacin	100	100	00	71	33	33
Cefoperazone +Sulbactam	100	100	50	100	67	33
Ceftazidime	100	100	00	86	33	17
Ciprofloxacin	100	100	00	71	33	33
Gentamicin	100	100	50	57	33	17
Imipenem	100	100	50	86	33	33
Meropenem	100	100	50	100	67	50
Netilmicin	100	100	00	71	33	17
Piperacillin+ Tazobactam	100	100	50	86	00	17*

\*P<0.05 significant

In CNTH, 66% of *S. haemolyticus* causing CRBSI were resistant to erythromycin, cloxacillin and clindamycin. No resistance was detected to linezolid and vancomycin. The single isolate from Apeksha hospital was resistant to erythromycin and clindamycin and sensitive to cloxacillin, linezolid and vancomycin. Resistance of CVC colonising CoNS is shown in Table 6.

**Table 5. Percentage resistance of *Klebsiella* species isolated from Apeksha hospital**

Antibiotic	CRBSI	CVC colonisation
<b>Number tested</b>	<b>5</b>	<b>5</b>
Amikacin	40	40
Amoxicillin/Clavulanate	80	80
Ampicillin	60	60
Cefoperazone +Sulbactam	80	60
Cefotaxime	60	60
Ceftazidime	60	60
Cefuroxime	60	60
Ciprofloxacin	60	60
Colistin	00	00
Gentamicin	60	60
Imipenem	80	60
Meropenem	40	40
Netilmicin	40	40
Piperacillin+ Tazobactam	80	60

**Table 3.2. Antibiotic susceptibility pattern of CoNS species causing CVC colonization**

Antibiotics	CNTH								Apeksha hospital									
	CVC colonization (n=21) (% resistance)								CVC colonization (n=53) (% resistance)									
	Organisms								Organisms									
	<i>S. haemolyticus</i> (n=4)	<i>S. colerae</i> (n=4)	<i>S. hominis</i> (n=5)	<i>S. epidermidis</i> (n=2)	<i>S. chromogenes</i> (n=2)	<i>S. capitis</i> (n=1)	<i>S. sciuri</i> (n=1)	<i>S. saprophyticus</i> (n=2)	<i>S. haemolyticus</i> (n=26)	<i>S. colerae</i> (n=4)	<i>S. hominis</i> (n=5)	<i>S. epidermidis</i> (n=7)	<i>S. chromogenes</i> (n=3)	<i>S. capitis</i> (n=3)	<i>S. sciuri</i> (n=1)	<i>S. lugdunensis</i>	<i>S. xylosum</i>	<i>S. klebsii</i>
Erythromycin	100	75	100	50	100	00	100	100	84	100	100	100	66	66	00	100	100	00
Cloxacillin	100	75	100	00	100	100	100	100	92	50	80	57	00	100	100	00	100	00
Clindamycin	75	100	60	50	100	00	100	50	73	50	100	57	33	100	100	100	00	100
Ciprofloxacin	75	100	60	00	100	100	100	00	69	25	60	57	66	33	00	00	100	100
Linezolid	00	00	00	00	00	00	00	00	00	00	00	00	00	00	00	00	00	00
Vancomycin	00	00	00	00	00	00	00	00	00	00	00	00	00	00	00	00	00	00

Among CoNS isolates, no resistance was detected to linezolid and vancomycin.

## Discussion

CVCs are significant in the care of critically ill patients. However, the use of CVCs is associated with severe complications, especially CRBSI. It is one of the most serious hospital acquired infections in the ICU setting, with increased rates of morbidity and mortality.<sup>16</sup> Colonisation of the CVC tip is considered to be a pre-requisite for CRBSI.<sup>2</sup>

In this study, CRBSI was confirmed in 17 (13.1%) of 130 patients in the study group at CNTH which is low when compared to several other studies.<sup>9,10</sup> However, it is higher compared to the studies done in ICUs by Kumari et al in 2009<sup>11</sup> and Jia et al in 2015<sup>12</sup> which showed 11% (11/100) and 5.3% (94/1773) CRBSI cases respectively. The rate of CRBSI was 13.4 per 1000 catheter days in the study population at CNTH. Rates of CRBSI vary considerably in different parts of the world. Kaur et al.<sup>9</sup> reported the incidence of CRBSI to be 14.59/1000 catheter days, which was higher than that of this study. Meanwhile, almost a similar CRBSI rate (13.64/1000 catheter days) was reported by Rao in 2018.<sup>10</sup>

The mean age of patients with CRBSI in CNTH and Apeksha hospitals were 48.3 and 47.5 years respectively, which is lower than in the study done by Rao<sup>10</sup> where the mean age was 51.25 years. The study group in CNTH showed CRBSI is more common in males (14/17) than in females (3/17). However, there was no significant gender difference in other studies.<sup>9,10</sup>

Hospital acquired infections are a significant problem, particularly in patients with malignancies. In the study group at Apeksha hospital, the CRBSI rate was 5.9 with an incidence of 5.2 per 1000 catheter days. Agrawal et al.<sup>13</sup> reported a rate of 2.1 per 1000 CVC days which was less than the present study in patients at medical and surgical oncology departments.

When comparing the two hospitals, the percentage of CRBSI cases at CNTH was higher than at Apeksha hospital (P=0.020). This may be due to several reasons. Cancer patients, who are immunocompromised are treated more often with antibiotics to prevent infections than other patients. It is also possible that infection control procedures at Apeksha Hospital contributed to the lower CRBSI rate. Oberoi et al.<sup>15</sup> suggested this irregularity of the incidence of CRBSI in various studies could be due to factors such as site of catheterisation, insertion techniques used, type(s) of catheter used, catheter care techniques and diagnostic criteria used to diagnose CRBSI.

CoNS were the most common organisms causing CRBSI in CNTH (41.17%). This was consistent with the findings of Patil et al.<sup>16</sup> in a study conducted on patients admitted to the medical intensive care unit, where CoNS accounted for 65% of CRBSI. In contrast to the above findings, Kumari et al. and Malek et al. found that the majority of organisms responsible for CRBSIs in medical/surgical ICUs at a tertiary care hospital and medical/coronary and surgical ICUs at a private hospital respectively were Gram-negative bacteria.<sup>11,17</sup> In addition to the bacterial pathogens, *Candida* spp also contributed to 6% (n= 1) of the CRBSI cases in the CNTH study population. This is consistent with the findings of Rao.<sup>10</sup>

Gram negative bacilli were the predominant microorganisms that cause CRBSI in the study population at Apeksha hospital. However, CVC colonisation was caused mainly by Gram positive cocci. This finding is consistent with the findings of Gupta et al.<sup>18</sup> which stated that the major cause of CRBSI was *Pseudomonas aeruginosa* while the most common coloniser was *Staphylococcus aureus*. As *Staphylococcus* spp. are skin commensals, they can cause a high proportion of catheter colonisation but in this susceptible group of patients, Gram negative bacilli seem to be the more important invasive pathogens.

During the last two decades, an epidemiological shift has taken place in CRBSI among cancer patients. Overall, CVCs became a less frequent source of blood stream infections (BSI) and

microorganisms that cause BSI and CRBSI have moved from Gram positive bacteria toward Gram-negative bacteria.<sup>3</sup>

Organisms responsible for CRBSI and colonisation in both hospitals showed high resistance rates to a number of commonly used antibiotics which is consistent with other similar studies.<sup>9,10</sup> In this study, all the isolated *Acinetobacter* strains from CNTH showed a very high rate of multi-drug resistance which is a major cause for worry as *Acinetobacter* species are very frequently isolated from patients in Sri Lankan ICUs.<sup>14</sup>

Antibiotic susceptibility patterns of bacteria show a significant variation in different geographical areas depending on many factors.<sup>18</sup> Data from this study show the gravity of the problem in Sri Lankan hospitals, especially due to the high resistance rates of Gram negative bacilli to available broad-spectrum life-saving antibiotics.

The presence of diabetes was found to be a significant factor in some studies<sup>9,12</sup> but in this study, there was no statistically significant association in both hospitals. Neutropenia is also reported as an important risk factor associated with CRBSI in cancer patients<sup>13</sup>, because when the absolute neutrophil count is  $<500/\mu\text{L}$ , immune control of the microbial flora, including pathogens, become insufficient.<sup>19</sup> The current study however did not find any statistically significant correlation between neutropenia and CRBSI in cancer patients. This result is consistent with those of Cairo et al. 2011<sup>20</sup> who reported that neutropenia was mainly seen in patients with non-CRBSI.

The majority of CRBSI are preventable. Implementation of educational programmes and the adherence to infection prevention practices as hand washing, cleaning the insertion site with chlorhexidine, using maximum barrier precautions when inserting CVC and avoiding the femoral insertion in adult patients if possible, can be used to minimise CRBSI.<sup>21</sup> The hospital infection control manual of the Sri Lanka College of Microbiologists<sup>22</sup>, states that CVC care should include use of 2%-4% chlorhexidine for hand washing and insertion site cleaning, adherence to strict aseptic precautions during the insertion, observation of insertion site for evidence of infection daily, and removal of CVC as soon as no longer required. However, in the present study, information on adherence to these guidelines was not obtained.

## Conclusion

CRBSI rate is higher in CNTH compared to Apeksha hospital. CoNS are the main cause of CRBSI in CNTH and Gram negative bacilli in Apeksha hospital. CVC colonisation with CoNS is common in both hospitals. Males are significantly associated with CRBSI in the CNTH study population. Antibiotic resistance is extremely high among bacteria causing colonisation and CRBSI, which necessitates urgent action to curtail the problem.

## Declarations

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- Conflict of Interest statement: There are no conflicts of interest.
- Ethics statement: Ethical approval was obtained from the Ethics Review Committees of the Faculty of Medical Sciences of University of Sri Jayewardenepura, Sri Lanka (Ref no27/18). Permission to carry out the study was taken from the Medical Directors of the two hospitals and from the Deputy Director General of Health Services, Ministry of Health.
- Author contributions:
- This study was designed, directed and supervised by T.D. and J.K. The sample collection was carried out by S.M. with the guidance of D.N. and S.G. The experiments were carried out by S.M. with many helpful suggestions from T.D. The manuscript was written by S.M. The manuscript was subsequently improved and edited by T.D and J.K. All authors discussed the results and commented on the manuscript.

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