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Disease spectrum and management of children admitted with acute respiratory infection in Viet Nam

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Abstract

OBJECTIVE To assess the acute respiratory infection (ARI) disease spectrum, duration of hospitalisation and outcome in children hospitalised with an ARI in Viet Nam.

METHODS We conducted a retrospective descriptive study of ARI admissions to primary (Hoa Vang District Hospital), secondary (Da Nang Hospital for Women and Children) and tertiary (National Hospital of Paediatrics in Ha Noi) level hospitals in Viet Nam over 12 months (01/09/2015 to 31/08/2016).

RESULTS Acute respiratory infections accounted for 27.9% (37 436/134 061) of all paediatric admissions; nearly half (47.6%) of all children admitted to Hoa Vang District Hospital. Most (64.6%) of children hospitalised with an ARI were <2 years of age. Influenza/pneumonia accounted for 69.4% of admissions; tuberculosis for only 0.3%. Overall 284 (0.8%) children died; most deaths (269/284; 94.7%) occurred at the tertiary referral hospital. The average duration of hospitalisation was 7.6 days (median 7 days). The average direct hospitalisation cost per ARI admission was 157.5 USD in Da Nang Provincial Hospital. In total, 62.6% of admissions were covered by health insurance.

CONCLUSION Acute respiratory infection is a major cause of paediatric hospitalisation in Viet Nam, characterised by prolonged hospitalisation for relatively mild disease. There is huge potential to reduce unnecessary hospital admission and cost.

keywords child, pneumonia, acute respiratory infection, Viet Nam

Introduction

Globally, pneumonia is the leading cause of disease and death in young children [1,2]. An estimated 900 000 children <5 years of age died from pneumonia in 2015 [3]. In the Western Pacific region, 14% of under-five mortality have been attributed to pneumonia with the majority (>75%) of deaths occurring in six countries: Cambodia, China, Laos, Papua New Guinea, the Philippines and Viet Nam [4]. Despite recent progress, the pneumonia disease burden in Viet Nam remains nearly 10 times higher than in high-income countries in the region such as Australia and Japan [5]. In 2015, pneumonia accounted for 11% of under-five mortality in Viet Nam and was the leading cause of death beyond the neonatal period [5,6].

Moreover, acute respiratory infections (ARIs) place a huge cost burden on families and health services [7,8]. Health care costs and adverse impacts are amplified if children are inappropriately managed, including unnecessary hospitalisation and excessive antibiotic use those with mild disease. WHO recently revised their pneumonia case management guidelines, emphasising that only the most severe acute respiratory infection (ARI) cases require hospitalisation and encouraging more considered antibiotic use [9]. These new recommendations have not been adopted in Viet Nam, where frequent hospitalisation for the administration of intravenous antibiotics remains standard practice [10], even though studies have demonstrated that non-severe pneumonia cases do not require hospitalisation and even severe cases can mostly be managed as outpatients [11]. Asia is an epicentre for antimicrobial resistance amplification, given the ease of access and frequency of antibiotic use in many Asian countries, including Viet Nam [12]. Hence, critical

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evaluation of how to reduce unnecessary hospitalisation for intravenous antibiotics is important to reduce the morbidity and health care cost associated with ARIs.

Acute respiratory infection is the most common reason for admission to paediatric wards in Viet Nam [8,9], being responsible for 39.9% of hospital admissions and 7.9% of hospital deaths in southern Viet Nam [13]. However, few studies have explored the ARI disease spectrum observed in central Viet Nam or differences between primary (district), secondary (provincial) and tertiary (national) level hospitals. We aimed to assess the caseload, duration and cost of hospitalisation, and outcome of children hospitalised with an ARI; focussing on central Viet Nam where less research has been carried out than in the major academic centres in Ha Noi and Ho Chi Minh City.

Methods

We conducted a retrospective descriptive study of all children (<15 years old) admitted to hospital with an ARI over a 12-months period (01/09/2015 to 31/08/2016).

Study setting

Three study sites were selected to represent primary, secondary and tertiary hospital settings in Viet Nam. Hoa Vang District Hospital represents a typical primary hospital in Da Nang province, central Viet Nam, with 100 inpatient beds that accommodate adults and children. Hoa Vang District Hospital refers children with severe illness or poor treatment response to the provincial referral hospital, the Da Nang Hospital for Women and Children. The Da Nang Hospital for Women and Children receives children from seven district hospitals in Da Nang province and provincial hospitals at Quang Nam and Quang Ngai, serving as the referral hospital for central Viet Nam. Complicated cases are referred to tertiary centres in Ho Chi Minh City or Ha Noi, including the leading paediatric referral centre in the North of Viet Nam – the National Hospital of Paediatrics in Ha Noi. The locations of the three participating hospitals are displayed in Figure 1. Each of the referral hospitals also serves a primary hospital function to surrounding neighbourhoods. Patients can be referred by community clinics or private practitioners to outpatients or present directly to emergency services. The recent roll out of electronic hospital records in Da Nang Province, and the replacement of antiquated data systems at the National Hospital of Paediatrics in Ha Noi, facilitated data collection and analysis.

Data collection and analysis

Anonymous data for each participating hospital were collected from routine discharge information, including International Statistical Classification of Diseases and Related Health Problems (ICD)-10 coding data. The study focused on ARI-related ICD-10 codes; J00–J06 [upper respiratory tract infections (URTI)], J09–J18 (influenza/pneumonia); J20-J22 (other lower respiratory tract infections) and A15–19 (tuberculosis). Information extracted for children admitted with an ARI included age, gender, date of admission and discharge, outcome (discharged, referred, died), direct hospitalisation cost and health insurance. Total ARl admissions included all specified ICD-10 codes (see above), with the ARI fraction calculated using all admissions as the denominator. We categorised children into three age groups: <2 years; 2–4 years; and 5–14 years. Direct hospitalisation costs considered expenditure related to hospital admission, tests and investigations, medication, transportation and clinical consultation. We examined seasonality by comparing the frequency of ICD-10 codes by calendar quarter and differentiating 'dry and rainy seasons' in central Viet Nam. The study was approved by the Ethics Review Committees of each participating hospitals and the Human Research Ethics Committee at the University of Sydney, Australia.

Results

We recorded 37 436 ARI admissions, accounting for 27.9% of all paediatric admissions during the study period. The profiles of children admitted to each of the participating hospitals are summarised in Table 1. In Hoa Vang District Hospital ARIs accounted for nearly half (639/1342; 47.6%) of all paediatric admissions, although they admitted a lower proportion of children <2 years of age than the two referral hospitals (28.4% *vs.* 52.7% at Da Nang Hospital for Women and Children and 69.8% at Ha Noi National Hospital for Paediatrics). More boys than girls were admitted with an ARI (23 884; 63.8%). The gender difference was apparent in all three hospitals and most pronounced in children <2 years of age (males 16 201; 67.0%). The majority of families (62.6%) had health insurance cover, with universal coverage of children admitted to Hoa Vang District Hospital.

Table 2 summarises the ARI disease spectrum observed and outcomes achieved at the three participating hospitals. Influenza/pneumonia was responsible for 69.4% of all ARI admissions; 87.0% at the Da Nang Hospital for Women and Children. There were a total of 5740 (15.0%) admissions with a diagnosis of URTI. Hoa Vang

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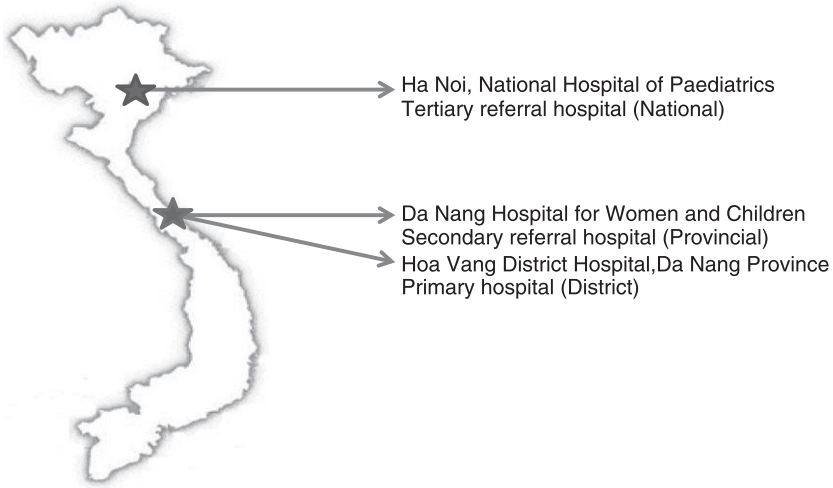

Figure 1 Location of three participant hospitals in Viet Nam.

Table 1 Profile of children admitted to hospital with an acute respiratory infection

	Hospital (District, Provincial, National)			
Demographics	Hoa Vang *n* (%)	Da Nang *n* (%)	Ha Noi *n* (%)	Combined *n* (%)
Total admissions	1342	49 456	83 263	134 061
ARI admissions	639 (47.6)	9920 (20.1)	26 877 (32.3)	37 436 (27.9)
ARI admissions only				
Age				
<2 years	181 (28.4)	5231 (52.7)	18 764 (69.8)	24 176 (64.6)
2–4 years	321 (50.2)	3960 (40.0)	5752 (21.4)	10 033 (26.8)
5–14 years	137 (21.4)	729 (7.3)	2361 (8.8)	3227 (8.6)
Gender: Male	359 (56.2)	6 130 (61.8)	17 395 (64.7)	23 884 (63.8)
Rural	639 (100)	2811 (28.3)	12 364 (46.0)	15 814 (42.2)
Health insurance	639 (100)	8955 (90.2)	13 854 (51.5)	23 448 (62.6)

ARI, acute respiratory infection (including ICD-10 codes A15-A19, J00-J06, J09-J18 and J20-J22) [14].

District Hospital had the highest proportion (39.2%) of URTI admissions, but even at Ha Noi National Hospital for Paediatrics, 17.6% of all ARI admissions were for an URTI. The majority of URTI admissions were for sore throat and pharyngitis (J02; 3039/5740; 52.9%) and tonsillitis (J03; 1070/5740; 18.6%). Tuberculosis was diagnosed in only 111 (0.3%) children, and most cases were diagnosed (100/111; 90.1%) at the Ha Noi National Hospital for Paediatrics; no tuberculosis cases were diagnosed at Hoa Vang District Hospital. The average duration of hospitalisation was 7.6 days (median 7 days; range 1–323 days). The average direct hospitalisation cost per ARI admission was 157.5 USD in Da Nang Provincial Hospital and 30 USD in Hoa Vang District Hospital. Less than 1% of children admitted with an ARI died (284; 0.8%), and only 34 were referred to a higher level of care. Being a tertiary referral centre, Ha Noi National Hospital for Paediatrics did not refer any patients to a higher level of care. Following discharge, 7.3% of children were re-admitted within 2 weeks for an ARI; in 3.2% of cases, the ARI diagnosis on re-admission differed from the first admission. We did not collect data on re-admission for non-ARI causes.

Table 3 reflects the age groups affected and disease outcomes achieved in different diagnostic categories. Of all children admitted with a lower respiratory tract infection (influenza/pneumonia and 'other') almost 70% (69.4%) were <2 years of age. The average duration of hospitalisation for children with influenza/pneumonia was 8.8 days (median 7 days; range 1–373 days); the duration of hospitalisation was longest for those <2 years of age (average 9.2 days), and the diagnosis of URTI was associated with the shortest average duration. Most children diagnosed with tuberculosis (52.2%) were also <2 years of age. The mortality rate in children diagnosed with tuberculosis was 5.4%, higher than the 1.0%

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Table 2 Disease spectrum and outcome in children admitted with acute respiratory infection in Viet Nam

	Hospitals (District, Provincial, National)			
ARI disease spectrum*	Hoa Vang *n* (%)	Da Nang *n* (%)	Ha Noi *n* (%)	Combined *n* (%)
URTI	250 (39.2)	749 (7.6)	4741 (17.6)	5740 (15.3)
Influenza/pneumonia	284 (44.4)	8627 (87.0)	17 077 (63.5)	25 988 (69.4)
Other LRTI	105 (16.4)	533 (5.3)	4959 (18.5)	5597 (15.0)
Tuberculosis	0	11 (0.1)	100 (0.4)	111 (0.3)
Total (*N*)	639	9920	26 877	37 436
Outcome				
Admission duration median (mean)	7 (6.8) days range 1–19 days	7 (8.5) days range 1–373 days	6 (7.3) days range 1–187 days	7 (7.6) range 1–373 days
Average cost	30 USD	157.5 USD	No information	No information
Died	0	15 (0.2)	269 (1.1)	284 (0.8)
Discharged	609 (95.3)	9901 (99.7)	26 283 (97.7)	36 793 (98.2)
Referred	30 (4.7)	4 (<0.1)	NA	NA
Readmission within 2 weeks				
Any ARI	0	1025 (10.0)	1723 (6.5)	2 748 (7.3)
Same ICD-10 code	0	793 (7.0)	728 (2.7)	1521 (4.1)

URTI, upper respiratory tract infection; LRTI, lower respiratory tract infection; Dx diagnosis; NA, not applicable; being a tertiary referral centre Ha Noi National Hospital for Paediatrics did not refer any patients to a higher level of care.
*ICD-10 codes are classified as: A15–19 – Tuberculosis; J00–J06 – Acute upper respiratory tract infections; J09–J18 – Influenza and pneumonia; J20–J22 – Other acute lower respiratory tract infections [14].

mortality rate observed with influenza/pneumonia. Table S1 provides an overview of infants (<1 year of age) admitted to Da Nang hospital for Women and Children. Influenza/pneumonia was the most common diagnosis (4545; 86.7%) with the vast majority (3618/4545; 79.6%) diagnosed in the 6–12-months age range. Figure 2 illustrates the frequency of common ARI diagnoses by calendar quarter, without any evidence of seasonality. Figure S1 reflects data for the dry and wet seasons in Da Nang province, also without any evidence of seasonality.

Discussion

To our knowledge, this is the first study to describe the paediatric ARI disease burden at primary, secondary and tertiary hospital level in Viet Nam. We identified influenza/pneumonia as the most common reason for hospital admission at all levels of care, especially in children <2 years of age. This is similar to previous findings in Viet Nam and other countries within the Western Pacific Region [13,15,16]. Given the high burden of disease in very young children, efforts to reduce the ARI disease burden should consider early interventions that focus on general risk-reduction strategies [17]. At present Viet Nam does not provide universal pneumococcal vaccination, and uptake of self-funded vaccine is low. Conjugated pneumococcal vaccines drastically reduce the risk of pneumococcal pneumonia and invasive disease [18], but its contribution to the ARI disease burden in Viet Nam remains poorly quantified. The mild disease phenotype suggested by the low mortality observed in our study indicates that most children admitted with an ARI likely had a viral infection. A microbiological diagnosis is rarely pursued in Viet Nam, and we were unable to confirm pathogen-specific disease aetiologies or consider the potential value of routine pneumococcal vaccination. More boys than girls were admitted with an ARI, which is similar to findings from previous studies in Viet Nam and other Asian countries [13,19]. The male predominance was most pronounced in very young children (67.0% males in children <2 years of age), but persisted in all age groups. It may be partially related to gender imbalances found in some Asian societies, the observation that girls mature quicker than boys or to preferential health seeking behaviour among parents.

The fact that children with mild disease were admitted to hospital indicates that local practices may not be aligned with new pneumonia case management guidelines [9]. The experience in Viet Nam is that clinicians often admit children to hospital, even in the absence of WHO criteria for severe pneumonia [5]. Studies in Hong Kong and China identified likely pneumonia in only 24.9% and 28.7% of patients admitted with an ARI [20,21]. A recent study in northern Viet Nam identified influenza in 18% of severe pneumonia cases tested [8]. Our study identified prolonged periods of hospitalisation that

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Table 3 Age spectrum, duration of hospitalization and outcome of children hospitalized with different acute respiratory infection disease categories in Viet Nam

Respiratory disease category	Age spectrum n (%)	Admission duration Median (mean)	Outcome n (%)
Acute URTI	<2yrs – 2,183 (38.1)	3 (3.7) days	Died: 18 (0.3)
N = 5,740	2–4yrs – 2,217 (38.6)	range 1–89 days	Discharged: 5,694 (99.2)
	5–14yrs – 1,340 (23.3)		Referred: 28 (0.5)
Influenza and pneumonia	<2yrs – 17,658 (67.9)	7 (8.8) days	Died: 249 (1.0)
N = 25,988	2–4yrs – 6,706 (25.8)	range 1–373 days	Discharged: 25,487 (98.0)
	5–14yrs – 1,624 (6.3)		Referred – 252 (1.0)
Other acute LRTI	<2yrs – 4,277 (76.4)	6 (6.2) days	Died: 11 (0.2)
N = 5,597	2–4yrs – 1,095 (19.6)	range 1–154 days	Discharged: 5,538 (98.9)
	5–14yrs – 225 (4.0)		Referred: 48 (0.9)
Tuberculosis	<2yrs – 58 (52.2)	8 (14.3) days	Died: 6 (5.4)
N = 111	2–4yrs – 15 (13.6)	range 1–87 days	Discharged: 74 (66.7)
	5–14yrs – 38 (34.2)		Referred: 31 (27.9)

Acute URTI - ICD-10 J00-J06; Influenza and pneumonia - ICD-10 J09-J18; Other acute LRTI - ICD-10 J20-J22; Tuberculosis - ICD-10 A15-19 [14].
URTI, Upper respiratory tract infection; LRTI, lower respiratory tract infection, yrs, years

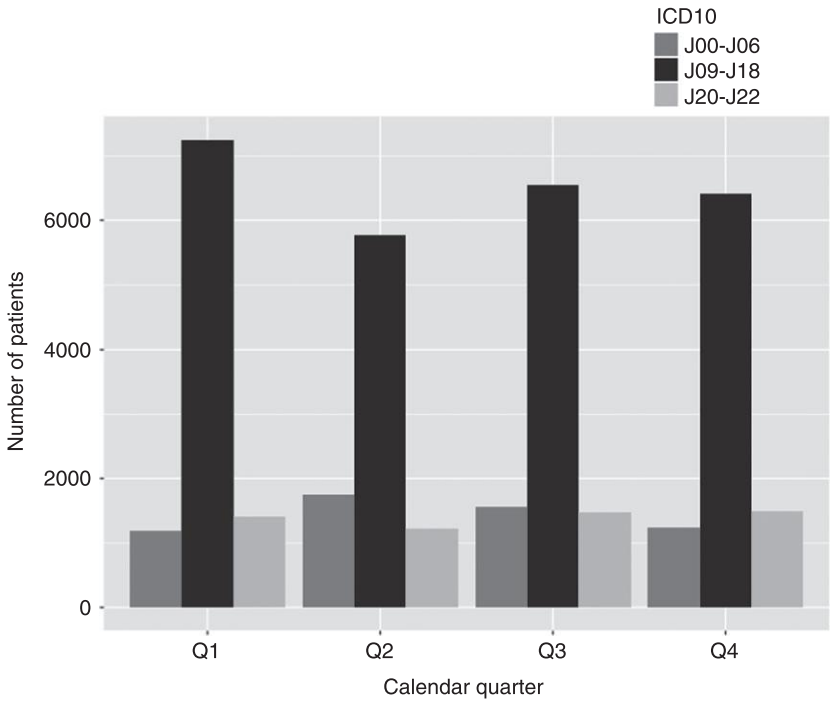

Figure 2 Frequency of acute respiratory infections by calendar quarter in Viet Nam. J00–J06 – Acute upper respiratory tract infections. J09–J18 – Influenza and pneumonia. J20–J22 – Other acute lower respiratory tract infections. Q1: January, February, March; Q2: April, May, June; Q3: July, August, September; and Q4: October, November, December.

exceeds international recommendations. This may be related to a lack of confidence to discharge young children with mild symptoms, perceived community expectations and the historical use of intravenous antibiotics in such cases [10]. Unfortunately, we were unable to extract detailed information on disease severity or antibiotic use from the electronic database. Accurate assessment of appropriate management practices will require a prospective study to document all the required variables. Lower respiratory tract infections other than influenza/pneumonia, such as bronchitis and bronchiolitis, were detected in 12.5% of children; similar to rates reported in a study that reviewed ARI admissions in Hong Kong [20]. As expected, URTIs were more commonly diagnosed at the

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district hospital level where children with mild disease generally present.

Although tuberculosis is not classically considered an ARI, observations from tuberculosis endemic areas have demonstrated that young children frequently present with acute respiratory symptoms [22–25] and tuberculosis can be a cause or comorbidity in children diagnosed with pneumonia [22]. It is well established that young children are highly vulnerable to develop progressive disease following primary *M. tuberculosis* infection [26]. Given the high tuberculosis incidence among adults (197/100 000 population) [27] and evidence of ongoing tuberculosis transmission in Viet Nam [28,29], one would expect a relatively high number of children to be diagnosed with tuberculosis. The fact that the vast majority of cases were diagnosed at the tertiary referral hospital and not a single case was diagnosed at Hoa Vang District Hospital may indicate a lack of awareness among primary clinicians and limited diagnostic options at the district hospital level. Service delivery channels for children with tuberculosis are poorly developed in most tuberculosis endemic areas, as it requires close collaboration between paediatricians, maternal and child health (MCH) services and national TB control programmes [30]. Only 1% of reported TB cases in Viet Nam occurred in children during 2014 [31], which is well below the estimated global average of 10%. Of 103 paediatric (<15 years) TB cases reviewed in northern Viet Nam, most were in the 5–14 years age range [32], which suggests gross underdetection in young children as in many other TB endemic settings [33].

A study on 'out of pocket' expenses for ARI treatment in rural Viet Nam found that only 2% of patients benefited from health insurance in 2001 [34]. The fact that direct medical expenses were covered by health insurance in 62.2% of children in our study is a great improvement. The Viet Nam Ministry of Health launched a policy to provide universal health insurance to children <6 years of age in 2005, and the penetration of this scheme has been excellent [35]. Only 51.5% of admissions to Ha Noi National Hospital of Paediatrics were covered by health insurance, which probably reflects inappropriate presentation to the national referral hospital. It is not uncommon for children with mild disease to be brought directly to the Ha Noi National Hospital of Paediatrics by their parents, instead of first presenting to their local district hospital. These patients' expenses are not covered by the health insurance scheme. We found the average direct cost per ARI admission in Da Nang Hospital for Women and Children (157.5 USD) to be comparable to previous estimates of the hospitalisation cost associated with severe pneumonia in Viet Nam (176 USD) [8]. This study also reported an indirect impact of 10 caregiver days lost per pneumonia admission [8]. The cost of ARI care places a major strain on the Viet Nam health care system [7, 36], considering that the annual per capita health expenditure in Viet Nam was 142.4 USD in 2014 [37], which indicates the importance of primary pneumonia prevention and the need to limit unnecessary hospital admission.

The overall death rate (0.8%) was very low compared to children with severe pneumonia in other settings [38,39]. All deaths occurred at secondary and tertiary level hospitals reflect appropriate referral of the most severe cases. The overall low death rate may be explained by the low rate of vertical HIV-infection in Viet Nam compared to sub-Saharan Africa, a very low threshold for ARI admission and possible reclassification of the most complicated cases as sepsis or 'shock'. In general, re-admission within 2 weeks of discharge may reflect delayed recovery, poor treatment response or a nosocomial infection acquired in hospital. We were only able to identify ARI re-admissions, which excludes nosocomial infections that may result in diarrhoea, fever or other common childhood illnesses. Among children re-admitted with an ARI, those admitted with a different ARI compared to the first admission may represent a new infection acquired in hospital. Although the available data are limited and there are many caveats to consider, the risk and detrimental impact of nosocomial infections are rarely considered when children are admitted to hospital with relatively mild disease. A previous study identified high rates of influenza and respiratory syncytial virus (RSV) during the rainy season in Viet Nam, but no difference in the overall ARI rate [40]. Similarly, we could not find a clear indication of seasonal variation in disease patterns, which may be explained by the fact that Viet Nam does not have a temperate climate with pronounced temperature variations.

Our study is limited by its retrospective nature and the absence of disease verification, which introduce a risk of misclassification bias. The extracted data had to be meticulously cross-checked, as electronic databases have only recently been introduced to Hoa Vang District Hospital, and the system at Ha Noi National Hospital for Paediatrics was upgraded during the study period. In addition, we were unable to assess management practices in detail; as clinical observations, disease severity evaluation and antibiotic use could not be assessed. Discharge diagnoses were mostly based on clinical symptoms and response to treatment with limited microbiological evaluation, as is the case in most Asian countries. Despite these limitations, the study presents

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important 'real-life' data that provide a comprehensive overview and enhanced insight into the paediatric ARI disease spectrum and outcomes achieved at different levels of health care in Viet Nam.

Conclusion

ARI is a common reason for children to be admitted to hospital in Viet Nam, especially in those <2 years of age. Potentially, hospitalisations for mild disease that are unnecessary could place a huge financial burden on the health care system and increase the risk of nosocomial disease transmission. Our findings indicate that more should be done to improve primary pneumonia prevention, tuberculosis case detection and ARI case management. Prospective studies are required to better elucidate case management practices and potential inappropriate use of intravenous antibiotics.

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Supporting Information

Additional Supporting Information may be found in the online version of this article:

Table S1. Disease categories and associated outcome in infants hospitalized with acute respiratory infection in Da Nang provincial hospital, Vietnam.

Figure S1. Disease patterns by dry (May-Oct) and wet (Nov-April) season in Da Nang province, Viet Nam.

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