Original Paper

- PRIMARY CARE NETWORK (PCN) AS A MODEL OF CARE FOR GP CHRONIC DISEASE MANAGEMENT
- REVISITING THE APPROACH TO DENGUE: THE PRIMARY CARE PERSPECTIVE

Primary Care Network (PCN) As A Model Of Care For GP Chronic Disease Management

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ABSTRACT

Objectives: The Primary Care Network (PCN), comprising small private General Practitioner (GP) clinics supported by a mobile team of dedicated nursing and allied health professionals, as well as a chronic disease register (CDR), can be an alternative model for good chronic disease management. GPs in the network manage the mobile team, set common goals for each clinic and self-evaluate. In this paper we share the data and experience of the first year of the pilot PCN in Singapore.

Methodology: Process indicators for diabetic patients seen from April 2011 to March 2012 (pre-PCN) and April 2012 to March 2013 were compared. McNemar test was performed.

Results: There was statistically significant improvement in process indicators of yearly DRP, DFS and Urine ACR screening for diabetes in the first year post-PCN compared to baseline data. Rates of regular HbA1c and LDL-C testing, as well as smoking blood pressure and weight assessment also showed statistically significant improvement.

Conclusion: The PCN has shown promise in improving quality of care for diabetes among small private GP clinics. Key challenges to the success of PCN include good clinician leadership, suitable IT support, and creating a viable business model for GPs.

Key Words: PCN; GP; Team-based Care; Mobile Team; Chronic Disease

SFP2015; 41(2): 61-64

INTRODUCTION

An urgent challenge for healthcare in Singapore today is our rapidly ageing population. The number of citizens aged 65 and above will triple to 900,000 by 2030.[1] Along with an ageing population comes an increased prevalence of chronic diseases which could pose a huge burden on our healthcare system in the near future, especially if not managed well.

"Primary health care is well positioned to have an important impact on outcomes of care for patients with chronic conditions," says Grant M Russell.[2] In Singapore, primary health care is provided through an island network of outpatient polyclinics and private General Practitioner's clinics. There are currently 18 polyclinics and about 2,400 private General Practitioner's clinics.[3] The 2010 Primary Care Survey showed that Polyclinics, despite seeing only 19% of overall primary care attendances, are managing 45% of chronic condition load. On the other hand, General Practitioners (GPs), who are seeing 81% of overall primary care attendances, are only managing 55% of the chronic patient load.[4]

The Primary Care Master Plan, announced in 2011, aims to engage the GPs to help transform the primary care landscape and enhance chronic disease management in the community. Community Health Centres (CHCs) and Family Medicine Centres (FMCs) are the care models of this master plan.[5]

The Primary Care Network (PCN), comprising small private GP clinics supported by a mobile team of dedicated nursing and allied health professionals, can be an alternative model. By providing team-based care, it can expand the amount of time available for patient care and allow physicians to focus on the more complex medical care issues.[6]

The concept of PCN is not new. It is a well-established model of care in New Zealand and Canada,[7,8] and comprises a network of GP clinics coming together to share resources in providing nursing and allied health care as well as administrative support such as care coordination. The aim is to provide more holistic care through a team-based care approach. GPs in the network lead the team, manage the shared resources, set common goals and self-evaluate.

In this paper, we share the experience of the PCN pilot project, as well as some of the preliminary findings of improvement in process indicators. This pilot project started in April 2012 and is a collaborative effort between Frontier Healthcare Group and Agency for Integrated Care (AIC).

The PCN pilot project

This pilot project started with nine clinics of Frontier Healthcare Group. The clinics are located in different parts of the island.

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The two key elements of the PCN are the provision of a mobile team comprising of nursing and allied health practitioners, and the tracking of chronic patients' clinical indicators through the chronic disease register (CDR). Services provided by the mobile team include nurse educator counselling, Diabetic Retinal Photography (DRP) and Diabetic Foot Screening (DFS).

A CDR was set up identifying the number of chronic patients being managed at each clinic and within the network as a whole. Individual clinic assistants maintained the CDR in collaboration with a centralised staff team. Patients with at least one of the following five chronic conditions were included in the register: diabetes mellitus, hypertension, lipid disorder, asthma, and chronic obstructive pulmonary disease. Only patients whose chronic conditions were being managed by the GP clinic were included in the register. Patients with the stated chronic medical condition who visited the GP for acute care only were not included in the register. We verified this by checking through the chronic medications dispensing records.

Data fields in the CDR included both process indicators and care outcomes in accordance with our national Chronic Disease Management Programme (CDMP)[9] guidelines. Indicators for diabetic patients included HbA1c, blood pressure (BP), LDL-Cholesterol (LDL-C), weight, smoking assessment, DRP, DFS, urine albumin/creatinine ratio (UACR). Smoking assessment was considered to have been performed only if there was documentation in the case-notes of the patient having been a smoker or non-smoker.

Methods

Data from April 2011 to March 2012 (pre-PCN) and April 2012 to March 2013 (PCN first year) were compared. Summary statistics were given as mean and standard deviation for continuous variables and percent frequencies for categorical variables. For pre- and post-PCN comparisons of process indicators, the McNemar test was performed using a 2 x 2 table to test for statistically significant differences. All the patients on the CDR for DM were included in the analysis. Patients who were followed up for less than one year were excluded as they were not due for some of the annual requirements. Significant changes in care outcomes such as improvement in HbA1c levels and successful weight loss require a longer time horizon to manifest, and thus will not be presented in this paper.

Results

A total of 377 diabetic patients were on the CDR with at least one year follow up and thus used for analysis. Mean (SD, range) age of the patients was 57.2 (11.64, 25 to 93) years. Forty-five percent of the patients were female, 73% were Chinese, 18% were Malay, 7% were Indians, and 2% were of other ethnicities.

There was a statistically significant improvement in process indicators of yearly DRP, DFS and UACR screening for diabetes in the first year post-PCN compared to baseline data. Rates of regular HbA1c and LDL-C testing, as well as smoking blood pressure and weight assessment also showed statistically significant improvement. Please refer to Table I for the detailed analyses.

Table I: Proportion of diabetic patients (%) having done their process indicators.

Indicators (Results expressed as % achieved)	pre-PCN	PCN 1st year	P value
Diabetic retinal photography (DRP)	26.3	39.0	<0.001
Diabetic foot screening (DFS)	17.5	37.1	<0.001
Urine Albumin Creatinine Ratio (UACR)	45.1	63.9	<0.001
Body weight assessment	36.1	70.8	<0.001
Smoking assessment	30.2	50.7	<0.001
1 Blood pressure measurement	89.4	93.6	0.0356
1 HbA1c Test	68.7	80.4	<0.001
1 LDL-C Test	69.5	79.8	<0.001

Discussion

In this pilot study to evaluate the implementation of PCN in Singapore, the preliminary results were encouraging. An improvement in the process indicators among the patients with diabetes within the first year of PCN was evident.

There are several reasons for the effectiveness of a PCN.

Firstly, through the setting up of a chronic disease register, we are now able to provide, for the first time, data to reflect GP standards of chronic care (including both process indicators and care outcomes). This facilitates self-evaluation and peer review. It also allows for comparison with benchmarks that are available from the public institutions such as the Polyclinics.

The CDR also provides a systematic process for tracking of patients' disease control and care outcomes. Patients due for their regular chronic disease screenings are given telephone reminders. Patients whose chronic diseases are poorly controlled from the care indicators (i.e., HbA1c levels) are highlighted to the multidisciplinary team for discussion. Targeted interventions such as counselling by nurse educators can then be implemented. The goal of this is to translate to better control of chronic diseases, reduced complications of chronic diseases, and reduced downstream costs.

Secondly, the availability of a mobile team to provide nursing and allied health services in and within the vicinity of the clinic confers much convenience to the patients and may help to improve compliance. Having these services under "the same roof" as the GP also reinforces the concept of team-based care. The fees for such services can be deducted through national schemes such as Medisave and CHAS, to help reduce out-of-pocket payments and improve compliance to follow-up.

Thirdly, the PCN ensures relevant support for GPs to provide team-based care which is crucial in managing chronic conditions well. GPs who are managing chronic patients in isolation often do not have enough time to deliver all the preventive and chronic disease services recommended in national clinical care guidelines. The support of a dedicated nurse educator within the mobile team, as well as systemic-level support in maintaining the CDR database and initiating inter-clinic quality improvement initiatives are likely to give confidence to GPs to improve in chronic disease management.

Limitations

The GPs currently in the pilot PCN are GPs who are keen to measure and improve their care in chronic disease management. There is thus a selection bias. Whether such encouraging results can be replicated as PCN grows in size, will be dependent on the motivation of GPs that subsequently come on board.

Secondly, we acknowledge that with the general increase in affluence and health awareness in Singapore, patients are getting more aware of the need for regular monitoring of their conditions and screening for complications, improving compliance. This may be a confounder in our results.

Thirdly, while the results show significant improvement, there is still much room for improvement in process indicators. Also, due to the lack of local data on chronic disease management from the private sector we are unable to benchmark our results. We hope that more chronic disease databases can be set up in the near future to provide avenues for benchmarking and continuous quality improvement.

Challenges ahead for the PCN

From this experience, we also recognised several challenges in sustaining and expanding the PCN.

Firstly, clinician leadership is crucial. The GP leaders would need to galvanise GPs to come together to form a network, provide leadership and be held accountable for its clinical and corporate governance. This reflects a "bottom-up" approach for engaging GPs which is likely to achieve better results than the traditional "top-down" approach adopted by policy-makers.

Secondly, the current take-up of chronic disease load by the GPs is low as the business model for managing chronic cases is not attractive to the GP practice. Besides relying on GPs' goodwill to take on more chronic cases, there should be more intervention by the state in the form of funding.

Thirdly the current data collection is manual and labour intensive. A good IT system would help facilitate more efficient data collection. With a network of GP practices, sufficient economies of scale may be achieved to make this a worthwhile investment.

We acknowledge that PCN is in its early days. While improvement in process indicators may have been demonstrated, any improvement in care outcome can only be assessed later.

CONCLUSION

The PCN can be an alternative model in the Primary Care Master Plan, to enhance chronic care by the GPs. The pilot PCN has shown initial promising results. Key challenges to the success of PCN include incentivising good GP clinical leadership, providing good IT support for data collection as well as creating a viable business model for implementation of PCN by GPs.

Declaration of conflict of Interest

The authors declare that they have no conflict of interest in relation to this article.

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Revisiting The Approach To Dengue: The Primary Care Perspective

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ABSTRACT

Dengue disease has a wide clinical spectrum that spans from asymptomatic or mild infection to life-threatening disease. The approach to dengue has recently been revised and dengue can be classified in terms of disease severity. This new approach, which makes use of warning signs, is useful to the primary care physician who is often the first line of contact as it guides triaging, serves as decision support for who can be managed in the outpatient setting, and flags up those who should be sent to hospital for further evaluation and management. This review article aims to familiarise primary care physicians with the use of this new classification, provide background on its development and give an understanding of principles of this new approach.

Key Words: Dengue, Who Classification, Warning Signs, Primary Care, Singapore

SFP2015; 41(2): 65-73

INTRODUCTION

In the month of May 2013, Singapore saw the first fatality from the 2013 dengue epidemic. The patient was a 20-year-old Chinese male who was seen at a government restructured hospital's emergency department (ED) and diagnosed as having viral fever.[1,2] At the time of presentation, there was apparent lack of awareness that the patient had severe dengue. He was noted to be clinically stable, was discharged with advice to have his blood test repeated by a primary care doctor and to return to the ED if his symptoms worsened. The very next day, he returned to the ED but left without seeing the doctor. Two days later, he was admitted through the ED with fever, headache and vomiting. He tested positive for acute dengue infection, deteriorated despite maximal supportive therapy and passed away three days after admission.

The 1997 World Health Organization (WHO) classification system[3] divided dengue into dengue fever (DF), dengue haemorrhagic fever (DHF), and dengue shock syndrome (DSS). In 2009, the WHO issued a new classification[4], which divided the disease into probable dengue, dengue with warning signs and severe dengue. The new classification attempted to address the deficiencies of the old classification system and included warning signs to aid in the triaging of symptomatic dengue cases, so as to pick up patients who may need closer monitoring or admission to hospital.

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The aim of this review article is to:
(1) describe the limitations of the 1997 dengue fever/dengue haemorrhagic fever/dengue shock syndrome (DF/DHF/DSS) classification system;
(2) describe the new 2009 dengue/severe dengue (D/SD) classification;
(3) describe the process of diagnosing dengue in a suspect patient using the new D/SD classification system;
(4) describe the factors taken into consideration in triaging patients with warning signs for referral to hospital; and
(5) describe the management of dengue patients in the outpatient setting.

EPIDEMIOLOGY

Dengue is a Flaviviral illness characterised by fever, low platelets, myalgia and joint pains, which is transmitted by the mosquito vector, the principal vector being *Aedes aegypti*.[5]

The dengue vector *Aedes aegypti* is a highly domesticated mosquito which lives in close association with humans and prefers to lay its eggs in water containers commonly found in and around homes.[6] The National Environment Agency (NEA) had listed domestic and ornamental containers, and flower pot plates/trays among the top breeding habitats of *Aedes aegypti* in Singapore.[7] The peak biting period is at dawn (2 to 3 hours after daybreak) and dusk (several hours before dark), but the *Aedes* mosquito will feed all day indoors and on overcast days. The female mosquitoes prefer human blood, and are observed to take multiple feeds for each egg production cycle. As such, the mosquito may transmit the dengue virus to multiple persons in a short time.[8]

The number of dengue cases was found to be significantly correlated with weekly mean temperature.[7,9] Dengue epidemics in Singapore of years 2005, 2007 and 2013 have shown that the number of cases increase towards the mid-year.[10-12]

The vast majority of infections, especially in children, are asymptomatic or minimally symptomatic. Symptomatic infections represent only a small fraction of the full burden of dengue virus infection.[13-15] Most cases of dengue infection occur in young adults in Singapore and the proportion of severe disease in Singapore is low.[16,17]

Limitations of the 1997 DF/DHF/DSS Dengue Classification System

In the 1997 classification system[3], dengue was divided into DF and DHF.

The criteria for DHF includes:
(1) Fever or history of acute fever lasting 2–7 days;
(2) Bleeding manifestation;
(3) Thrombocytopaenia of 100,000 cells/mm^3 or less; and
(4) Haemoconcentration which includes rise in haematocrit of 20% or greater, or evidence of plasma leakage (i.e., pleural effusion, ascites and/or hypoproteinaemia).

DHF is further divided into four levels of disease severity, grades I–IV with grades III and IV representing DSS, giving a total of five different categories of disease. In grade I of DHF, the only bleeding manifestation is a positive tourniquet test. In grade II, there is spontaneous bleeding, while in grade III there is hypotension, and grade IV is characterised by profound shock. This classification is illustrated in Figure 1.[18]

Horstick et al[18] described an evidence-based approach, which looked at the evidence for limitations in the 1997 classification. The team confirmed difficulties in its practical application, gathered regional and global expert consensus, developed a new classification system, and tested the usefulness and applicability of the new classification system.

The limitations of the 1997 DF/DHF/DSS classification system are as follows:

Most DHF criteria had a large variability in frequency of occurrence, which resulted in patients not always fulfilling the stringent criteria for DHF. This is shown in a systematic review,[19] which identified 37 papers reporting the use of this classification. The review found that occurrence of these criteria in DHF patients was variable, with thrombocytopaenia observed in 8.6–96%, plasma leakage in 6–95%, and bleeding manifestations in 22–93% of DHF patients.

The tourniquet test, which is the minimum requirement for bleeding tendencies, did not distinguish between DHF and DF. The tourniquet test is performed by applying a blood pressure cuff to the upper arm and inflating it to a point midway between the systolic and diastolic pressure for 5 minutes. The test is considered positive when this results in 20 or more petechiae per square inch. A study[20] involving more than 1000 febrile children hospitalised for suspected dengue found that the tourniquet test is not sensitive nor specific for Dengue Haemorrhagic Fever (DHF) and that the test differentiates poorly between Dengue Fever (DF) and Dengue Haemorrhagic Fever (DHF).

DF is frequently quoted as representing mild disease, DHF the severe form, and DSS the life-threatening form. Primary data was collected on dengue cases in the Dengue Control (DENCO) Study,[21] one of the largest prospective cohort studies in South-East Asia and Latin America.

Results showed that 22% of patients with shock did not fulfil the stringent criteria for DHF. On the other hand, plasma leakage, severe bleeding and severe organ involvement, as defined by specific criteria, were able to identify patients who needed major intervention. Warning signs of progression to severe dengue could also be identified, and these included persistent abdominal pain and tenderness, mucosal bleeding and thrombocytopaenia.

In clinical practice, frontline staff have difficulty applying the criteria for DHF. A study,[22] which involved several countries in Asia and Latin America, examined the variation and utility of clinical practice guidelines for dengue. The study had two

GRADES OF DENGUE HAEMORRHAGIC FEVER

		Fever	Bleeding Manifestation	Thrombo-cytopenia	Plasma Leakage	Additional Features
Grade I		✔	Only positive Tourniquet Test	✔	✔	-
Grade II		✔	Spontaneous Bleeding	✔	✔	-
Grade III	DSS	✔	Spontaneous Bleeding	✔	✔	Evidence of circulatory failure e.g. hypotension, weak pulse, restlessness
Grade IV	DSS	✔	Spontaneous Bleeding	✔	✔	Profound shock

Figure 1: Grades of Dengue Haemorrhagic Fever (DHF) in the 1997 WHO Classification of Dengue

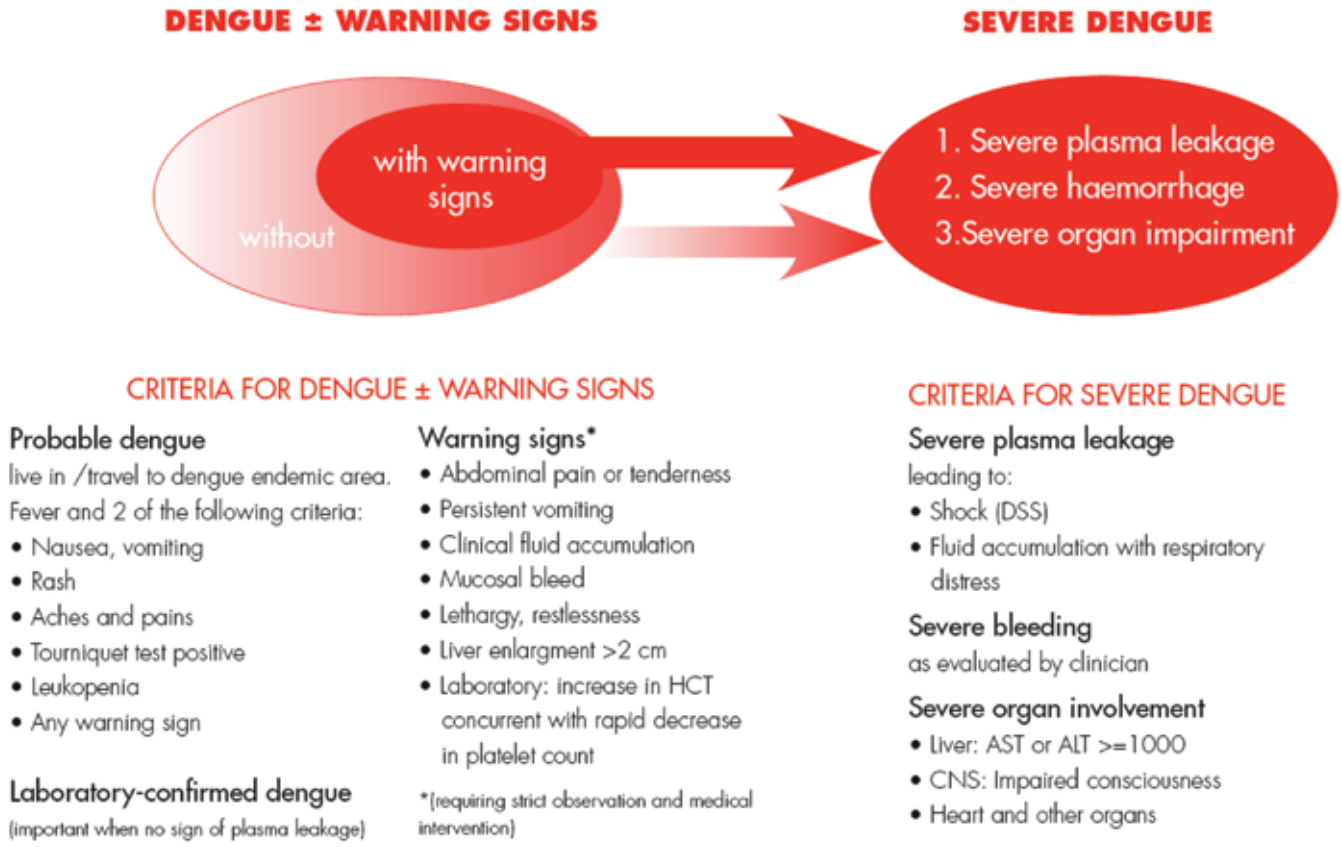

Figure 2: WHO Dengue Classification by Severity
Source: Dengue: Guidelines for Diagnosis, Treatment, Prevention & Control. WHO, Geneva

elements; the first being systematic analysis of dengue guidelines from countries involved, and the second, a field study among health care staff from seven countries using questionnaires and focus group discussions. All the guidelines studied were based on the WHO 1997[3] dengue classification. Guideline analysis revealed considerable differences regarding the classification of DHF/DSS, severity grading and management algorithms. Classification of dengue into DF and DHF as well as grading of DHF severity into grades I-IV were not uniformly applied. The field study showed that dengue clinical guidelines were not always accessible to health care staff. Frontline staff also had difficulty applying the guidelines due to lack of training, manpower and unavailability of diagnostic tests.[22]

Evidence from all the studies mentioned and subsequent expert consensus meetings led to the conclusion that the 1997 DF/DHF/DSS classification does not correlate well with disease severity.[18]

The Dengue/Severe Dengue (D/SD) Classification System

In 2009, the new D/SD case classification was introduced, replacing the 1997 DF/DHF/DSS classification. In this new approach, the disease is divided into two clear entities,

1. Dengue (D) with or without warning signs; and
2. Severe Dengue (SD).

Patients who display warning signs are at greater risk of progression to severe dengue and thus merit closer observation. But even without warning signs, any patient with dengue can progress to severe disease. Hence the term "non-severe dengue" should be avoided.

The entity of "Dengue" includes cases where the definitive diagnosis of dengue infection has been confirmed via definitive laboratory investigations (laboratory-confirmed dengue) or patients with fever plus any two of the criteria listed (probable dengue).

Warning signs, which include abdominal pain or tenderness, persistent vomiting, clinical fluid accumulation, mucosal bleeding, hepatomegaly and rise in haematocrit with concurrent drop in platelet count, predict risk of progression to severe dengue.

The entity "Severe Dengue" is characterised by severe plasma leakage, severe haemorrhage and severe organ impairment.
This approach is illustrated in Figure 2.

Diagnosing Dengue in a Suspect Patient Using the New Classification System

Prompt diagnosis is important as it allows close monitoring of the patient for warning signs of progression to severe dengue. The

patient is identified early as a reservoir for the virus and vector control measures can be given to reduce the risk of further transmission.

In the early febrile phase, the primary care physician faces a diagnostic challenge as early dengue can be difficult to distinguish clinically from non-dengue febrile diseases.[23,24]

Many conditions, both infective and non-infective, may mimic the febrile phase of dengue. Influenza, Kawasaki Disease, meningococcal infections, measles and rubella, infectious mononucleosis and acute retroviral illness can mimic dengue.[25] Patients with dengue usually have gastrointestinal symptoms and diagnosis may be confused with acute gastroenteritis. In addition, a patient with dengue may have coinfections with other pathogens such as influenza, typhoid, chikungunya and leptospira, further complicating the clinical presentation.[26-29]

Of special mention is chikungunya, an acute viral illness, which shares the same vectors, symptoms, and geographical distribution as dengue.[30,31] There have been two outbreaks of chikungunya in Singapore, in 2008 and 2013.[12,32] The two diseases have been confused with each other, particularly when an outbreak of chikungunya occurs in a dengue-endemic region.[33] Differentiating the two diseases is important because the management and outcome of both diseases are different. While chikungunya is not generally life-threatening[34] dengue can be severe.[4]

A retrospective case-controlled study[35] compared adult patients with chikungunya with adult dengue patients who were admitted to hospital. The study noted that although there is substantial overlap in clinical presentation between the two diseases, myalgia or arthralgia featured more prominently in patients with chikungunya. Chikungunya patients also had significantly higher leukocyte counts and lesser degrees of thrombocytopaenia compared to dengue patients.

History taking should include information on symptoms, past medical history and family history. In the physical examination, the patient should have vital signs recorded. Initial evaluation should focus on the following aspects:

- Recognising that the febrile patient could have dengue (by applying criteria for suspect case of Dengue Fever);
- Recognising the early stage of plasma leakage (raised haematocrit, signs of occult hypotension such as tachycardia, narrowed pulse pressure, postural hypotension, or a recorded blood pressure that is lower than the patient's known usual blood pressures); and
- Recognising patients with warning signs who need to be referred to the hospital for admission or further evaluation.

The Ministry of Health (MOH) Singapore has come up with recommendations[36] for initial evaluation of a patient suspected to have dengue. The clinical criteria for suspect cases of dengue fever are summarised in Table I, and the recommended Initial Investigations are summarised in Table II.

When selecting an appropriate test to confirm acute infection, the diagnostic method chosen depends on the time of clinical illness.

The Non-Structural (NS) 1 antigen is a glycoprotein secreted by virus-infected cells during the acute phase of dengue.[37,38] It becomes detectable from Day 1 and up to Day 9 after onset of fever, whereas IgM becomes detectable by Day 3 to 5 after onset of illness in primary dengue and earlier in secondary dengue.[4,39]

In a patient who is seen early in the course of disease during the period of viraemia, serum can be sent for NS1 Antigen Assay for detection of viral protein. This provides an earlier definite diagnosis compared to the alternative method where serum is obtained for paired sera with the second convalescent sample taken between Days 15-21 of illness (here a 4-fold rise in titres of a pair of acute and convalescent sera is confirmatory).[25]

A small study involving hospitalised adult dengue patients[40] found that NS1 antigen positivity beyond day 5 of illness was associated with higher risk of severe disease in their cohort.

Standard Diagnostics (SD) Bioline Dengue Duo is a commercially available, point-of-care rapid diagnostic kit which combines NS1 antigen and IgM or IgG detection.[41] It has been found to be highly sensitive and specific for dengue when compared against WHO-based reference standard tests. A prospective cohort study[42] involving adult patients with acute undifferentiated febrile illness found the overall sensitivity and specificity were 93.9% (95% CI 88.8–96.8%) and 92.0% (95% CI 81.2–96.9%) respectively. The 1997 and 2009 WHO dengue case definitions were found to be just as sensitive but less specific. These findings mirrored an earlier study[43] which found that both WHO classification schemes had high sensitivity but lacked specificity.

The (SD) Bioline Dengue Duo has advantages; it can be performed by the clinician and is therefore a useful test particularly in healthcare facilities where laboratory services are not readily available. The results can be read in 15 minutes.[41] A positive test with compatible clinical findings would reduce the

Table I: CLINICAL CRITERIA FOR SUSPECT DENGUE (36)
A suspect case of dengue fever (DF) is defined as an acute febrile illness with two or more of the following features:
- Headache - Eye pain - Myalgia - Arthralgia - Rash - Haemorrhagic manifestations - Leukopaenia

Table II: Recommended Initial Investigations[36]
- FBC for Thrombocytopaenia, leucopaenia, raised haematocrit; - Dengue Serology, e.g., paired sera (acute and convalescent); - PCR for dengue virus within five days of onset may give a more rapid diagnosis; and - NS1 antigen assay for detection of the dengue NS1 protein within the first week of onset.

urgency for testing or empirical treatment for other aetiologies of acute undifferentiated febrile illnesses such as typhoid or leptospirosis.[42]

For children, however, test results should be interpreted carefully. A study involving hospitalised children with undifferentiated febrile illness[44] showed the assay to have a low sensitivity of 57.8% (95% CI 45.4, 69.4). The authors explained that the apparent low sensitivity could be due to the broad inclusion criteria for their study cohort, which was deliberate so as to capture the breadth of dengue infection in children. Another factor contributing to low sensitivity could be the high incidence of other co-infections. Specificity of the assay was 85.3% (95% CI 80.3, 89.5), but the authors found high prevalence of co-infections with other pathogens in their cohort and suggested the need for broad microbiologic assessment in children with acute undifferentiated febrile illness.

Triaging Patients with Warning Signs for Referral to Hospital

It has been shown that the commonest reason for admission to hospital was for thrombocytopaenia rather than symptomatic disease.[45]

Thrombocytopaenia level of 50,000/mm^3 or less at 5 to 7 days after onset of illness has been found to be associated with increased risks of haemorrhage and shock in adults with DF.[46-48]

MOH Singapore[36] has recommended that when making referral decisions, platelet count should be interpreted together with significant clinical signs and symptoms, which may include bleeding, change in mental status, abdominal pain, hypotension and narrowed pulse pressure.

The challenge for the primary care physician then is to find that delicate balance between sending a patient to hospital unnecessarily and missing a potentially severe case of dengue. The seven warning signs,[4] proposed by WHO as predictors of severe dengue and criteria for hospitalisation, may typically appear towards the end of the febrile phase. They include abdominal pain or tenderness, persistent vomiting, mucosal bleeding, hepatomegaly, rise in haematocrit and drop in platelets, and clinical fluid accumulation in the form of pleural effusion or ascites. Clinical fluid accumulation may only be detected if plasma loss is significant or after treatment with intravenous fluids.

Table III: Signs and symptoms to look out for when considering referral to hospital[36]
(1) Persistent feverain or tenderness (2) Dizziness; (3) Lethargy, restlessness or altered mental state; (4) Abdominal pain or tenderness; (5) Persistent vomiting; (6) Clinical fluid accumulation; (7) No urine output for 4 to 6 hours; (8) Signs of bleeding (e.g. mucosal bleeding or internal bleeding such as melena); (9) Liver enlargement >2 cm; (10) Increase in haematocrit concurrent with rapid decrease in platelet count; and (11) Platelet count of <60,000 cells/mm3 in adults and <80,000 cells/mm3 in children.

A local retrospective study of 1507 laboratory-confirmed dengue inpatients[49] assessed the usefulness of these warning signs for predicting dengue haemorrhagic fever (DHF) and severe dengue (SD) in adult dengue patients and found that no warning sign was highly sensitive in predicting subsequent DHF or SD in their cohort of confirmed dengue patients. Taken individually, no single warning sign alone had sensitivity above 64% in predicting severe disease.

Less common warning signs such as persistent vomiting, hepatomegaly, haematocrit rise, rapid platelet drop and clinical evidence of fluid accumulation were highly specific for DHF or SD. Common warning signs such as lethargy, abdominal pain or tenderness, and mucosal bleeding were less specific for severe dengue compared to the less common warning signs.

The median duration between onset of warning signs and DHF or SD was two days, which allowed a window of opportunity for intervention.

The authors noted that while having any one of the seven warning signs was associated with 95% sensitivity and 96% negative predictive value, its specificity of 18% may result in over-hospitalisation if this were to be used as a criterion for hospital admission. As all the patients were hospitalised and dengue diagnosis was laboratory-confirmed, the study did not assess the utility of warning signs as admission criteria,[4] nor usefulness for diagnosis[4] of probable dengue.

In addition to the seven warning signs proposed by WHO,[4] MOH Singapore[36] had included persistent fever, dizziness, altered mental state and platelet thresholds as additional factors for consideration when referring a patient to the hospital for further evaluation and management. Signs and symptoms to observe for when considering referral of a dengue patient to the hospital are summarised in Table III.

Management of dengue patients in the outpatient setting

A small retrospective study in Singapore[45] has shown that a great majority of dengue patients who were hospitalised did not progress to severe dengue and it has been shown that with careful patient selection, it was safe to monitor patients daily in an outpatient setting unless bleeding was present, platelet count was below 50,000/uL, or haematocrit rose above 50%.[50,51]

MOH Singapore has recommended[36] that outpatient management should emphasise the following points:

(1) Medical practitioners should monitor patients on a daily

basis with regards to hydration state and vital signs(especially blood pressure) so as to detect any deterioration in clinical condition early.

(2) The complete blood count and haematocrit should be monitored closely.

(3) Patients should be educated on how to recognise the warning symptoms (Table III) and to seek medical attention early should any develop.

(4) If dengue is suspected, non-steroidal anti-inflammatory drugs and intramuscular injections are to be avoided due to the risk of bleeding.

(5) Precautionary measures to prevent mosquito bites should be taken by patients to prevent ongoing transmission of dengue (e.g., use of mosquito repellent).

Advice on vector control is important, even in dengue patients who do not have disease severe enough to be hospitalised. Ambulatory dengue cases had lower viraemia levels compared with hospitalised dengue cases but, nonetheless, at levels predicted to transmit disease.[52]

Measures to prevent mosquito bites may also lessen the risk of being infected by a different serotype with the understanding that disease severity could worsen with subsequent infection by a different serotype.[13,53]

(6) Referral to hospital for further medical evaluation should be considered more strongly in patients with any of the following co-existing conditions, as they have a higher risk of complications from dengue fever.

a. Pregnancy;
b. Co-morbid conditions (e.g., diabetes mellitus, hypertension, peptic ulcer, haemolytic anaemia, congestive cardiac failure, chronic renal failure, chronic liver failure, chronic obstructive lung disease, immunocompromised state and others);
c. Obesity (BMI > 28);
d. Infancy; or
e. Old age (≥ 65 years old).

A systematic review[54] of published data had shown that there is a risk of vertical transmission of dengue virus but was inconclusive with regards to adverse pregnancy outcomes, even though case reports examined had shown high rates of caesarean deliveries and preeclampsia.

A retrospective study of 2285 DF and DHF patients in Singapore[55] had shown diabetes mellitus and diabetes mellitus with hypertension to be independent risk factors for DHF.

Making a diagnosis of dengue may be challenging in elderly patients as clinical recognition of dengue becomes more difficult. A 5-year prospective study[56] showed that the 2009 WHO dengue classification scheme is significantly less sensitive as a diagnostic tool with increasing age. Elderly dengue patients were less likely to report classical symptoms such as myalgia, arthralgia, retro-orbital pain and mucosal bleeding. Hence a lower threshold for referral to hospital should be considered. The authors proposed that older adults who present with fever and leukopaenia should be tested for dengue, even in the absence of other symptoms.

DISCUSSION

Thre are certain requirements that an ideal classification system should satisfy. Firstly, the various categories within the classification system should correspond to the nature of what is being classified. While the old DF/DHF/DSS emphasises haemorrhagic symptoms, the general consensus is that the critical phase of dengue is determined by plasma leak, not haemorrhage. In other words, DHF does not correspond to the nature of the thing being classified. With the new D/SD classification, there is a shift in focus from bleeding to plasma leak.

Secondly, all cases of dengue should fit into the classification system. This is not the case with the DF/DHF/DSS system as discussed earlier.

The third requirement is that the classification should be useful. The criteria for DHF in the DF/DHF/DSS classification requires repeated measurement of platelet count and is of limited applicability in areas with poor access to laboratory facilities,

The fourth requirement is that the classification should be simple to use. Evidence has shown that there was difficulty and inconsistency in applying the DF/DHF/DSS system, which consists of five categories.[18]

The ability to differentiate D and SD gives the new classification a distinct advantage over the previous one.[57] In an expert consensus meeting,[58] it was concluded that the new classification is helpful for diagnosis and follow-up of dengue. Warning signs help in early identification of patients who are at risk of shock and organ failure. The new classification is not only useful for management of individual cases but also for outbreak management. Furthermore, it more accurately defines the severity of disease,[59-61] considers its dynamic nature and is therefore useful for clinical studies.

Limitations

There is need for further experience with the use of the new classification system. In terms of future development, more evidence will be needed on the usefulness of warning signs and their ability to pick up severe dengue patients early. From the epidemiological viewpoint, there is currently no update of the International Disease Classification10 (ICD10) to include the new classification of dengue (D/SD); as such there is paucity in terms of reporting experience.

CONCLUSIONS

Triage and management decisions at the primary care level where patients may first be seen and evaluated are critical in determining the clinical outcome of dengue.

The D/SD classification system not only provides a structure with symptoms and signs that the primary care physician can use to pick up the suspected dengue patient, it also provides a system of warning signs of impending severe dengue, which signals the need for closer monitoring or referral to hospital.

DISCLAIMER

The author declares that he has no conflict of interest in relation to this article.

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