HORNET STINGS: FACTORS ASSOCIATED WITH SYSTEMIC REACTIONS IN CHILDREN ADMITTED IN HUSM

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LIST OF ABBREVIATIONS AND SYMBOLS

%	Percentage
<	Less than
>	More than
ALP	Alkaline phosphatase
ALT	Alanine aminotransferase
aPTT	Activated Partial Thromboplastin Time
AST	Aspartate aminotransferase
CI	Confidence interval
CVS	Cardiovascular system
DIVC	Disseminated intravascular coagulopathy
et al.	And others (Latin: *et alii)*
FDP	Fibrinogen degradation product
HUSM	Hospital Universiti Sains Malaysia
IgE	Immunoglobulin E
IgG	Immunoglobulin G
IM	Intramuscular
IV	intravascular
LLR	Large local reaction
MOH	Ministry of Health
MSR	Mild systemic reaction

NICE	National Institute for Health and Clinical Excellence, United Kingdom
OR	Odds ratio
PPSP	Pusat Pengajian Sains Perubatan
PPSP	Pusat Pengajian Sains Perubatan
PS	Power and Sample Size Software
SPSS	Statistical Package for Social Sciences
SSR	Severe systemic reaction
USM	Universiti Sains Malaysia
WHO	World Health Organization

ABSTRAK

Sengatan Tebuan: Faktor-faktor yang membawa kepada reaksi sistemik di kalangan kanak-kanak yang dimasukkan ke wad di HUSM

PENGENALAN:

Tebuan, lebah, penyengat dan semut adalah dari keluarga hymenoptera di kalangan serangga menyengat yang menyuntik racun (venom) ke dalam mangsanya. Sengatan serangga ini menjadi antara permasalahan kesihatan serata dunia. Sengatan dari serangga ini, boleh menyebabkan kesan tindak balas setempat yang ringan, hingga ke tindak balas sistemik yang teruk yang boleh membawa kepada maut. Sengatan serangga ini sendiri boleh menyebabkan kesan lansung pada tubuh, malah ia juga boleh menyebabkan tindak balas alahan sistemik yang menyeluruh. Kebanyakan kes sengatan hymenoptera yang berlaku di Malaysia, adalah disebabkan oleh sejenis vespid, iaitu tebuan.

OBJEKTIF:

Objektif utama kajian ini adalah untuk mengkaji ciri-ciri kanak-kanak yang dimasukkan di Hospital Universiti Sains Malaysia (HUSM) kerana sengatan tebuan. Kajian ini juga melihat pada kekerapan reaksi sistemik serta cuba untuk menentukan faktor-faktor terjadinya reaksi sistemik di kalangan kanak-kanak yang disengat oleh tebuan.

KAEDAH:

Kajian ini ialah kajian retropektif menyelidik rekod lampau. Semua kanak-kanak yang dimasukkan ke HUSM dari tahun 2006 hingga tahun 2011 di ambil sebagai sampel kes. Kerangka persampelan adalah rekod-rekod yang diperolehi dari Pejabat Rekod Perubatan dan semua pesakit yang memenuhi kriteria telah dilibatkan dalam kajian ini.

KEPUTUSAN:

Sebanyak 141 kes telah dimasukkan dalam kajian ini. Majoritinya adalah lelaki (61.7%), dan hampir kesemuanya adalah berbangsa Melayu (98.6%). Pesakit termuda dalam populasi kajian kami adalah kanak-kanak berumur 6-bulan dan yang paling tua berumur 17 tahun. Enam belas kes (11.3%) mempunyai sejarah alahan, 26 kes (18.4%) mempunyai sejarah *atopy*, 12 kes (8.5%) mempunyai sejarah *asthma* dan 17 kes (17.5%) mempunyai sejarah pendedahan sengatan tebuan sebelumnya. Majoriti kes adalah kemasukan langsung ke HUSM (75.9%). Yang lain telah dirujuk dari Klinik Kesihatan (19.9%), dari hospital daerah (3.5%) dan dimasukkan berikutan panggilan ambulans (0.7%). Bilangan kes kanak-kanak yang diterima di HUSM bagi sengatan tebuan adalah terendah pada musim hujan dan memuncak pada bulan April hingga Ogos yang panas dan kering. Lapan puluh peratus dari kes, telah berlaku di siang hari (0701H hingga 1900H), dengan masa min berlaku sengatan adalah pada jam 1509H ± 6.08. Lima puluh satu peratus kejadian sengat berlaku di luar kawasan rumah. Kebanyakan kes telah disengat pada kepala, muka dan leher (45.4%). Yang lain telah disengat pada anggota bahagian atas (tidak termasuk tangan) (22%), di bahagian tangan (42.6%), pada bahagian hadapan badan (10.6%), pada bahagian belakang badan (17.7%), pada punggung dan kemaluan (4.3%), pada bahagian anggota bawah (kecuali kaki) (12.8%) dan pada bahagian kaki mereka (17.7%). Sebanyak 140 kes (99.3%) mempunyai reaksi setempat dan hanya 1 kes tidak mempunyai sebarang tindak balas di semua. Reaksi setempat seperti bengkak, sakit, gatal-gatal, kemerahan atau jangkitan setempat di tempat sengatan. Sebanyak 42 kes (29.8%) telah direkodkan mengalami

reaksi sistemik, 37 darinya mempunyai komplikasi yang teruk. *Anaphylaxis* adalah komplikasi yang paling kerap ditemui dengan 32 kes (22.7%) diikuti oleh *coagulopathy* (7%), kecederaan buah pinggang (0.04%), *sepsis* (1.4%), masalah kardiovaskular, hati dan rhabdomyolisis dengan 1 kes setiap satu (0.7% setiap) dan terdapat 3 kes menyebabkan kematian (2.12%). Kanak-kanak dengan sengatan tebuan pada bahagian hadapan badan mereka adalah 7.8 kali lebih berkemungkinan mempunyai reaksi sistemik (95% CI 2.16, 28.14, p = 0.02). Kanak-kanak dengan sejarah atopy pula adalah 4.3 kali lebih berkemungkinan untuk mendapat reaksi sistemik ekoran sengatan tebuan (95%CI 1.63, 11.24, p=0.03).

KONKLUSI:

Memahami ciri-ciri sengatan tebuan dan melihat kepada corak hidup, serta sebab berlakunya sengatan tebuan boleh membantu mengurangkan kejadian sengatan tebuan. Reaksi sistemik berlaku pada 29.8% yang dikenalpasti dalam kajian ini. Kanak-kanak yang mempunyai sejarah atopy dan mereka yang disengat di bahagian hadapan badan adalah mereka yang paling berisiko untuk mendapat reaksi sistemik. Kemampuan untuk mengenalpasti komplikasi yang lebih teruk serta pemahaman ke atas faktor-faktor yang memungkinkan berlakunya reaksi yang lebih teruk adalah sangat penting untuk memastikan rawatan yang sewajarnya dapat diberikan segera.

ABSTRACT

Hornet Stings: Factors Associated with Systemic Reactions in Children Admitted in HUSM

INTRODUCTION:

Hornets, bees, wasps, and ants are stinging insect with venoms which all belongs under the order Hymenoptera. The stings of these insects is a health concern globally. The stings may result from a mild local reaction to a fatal severe systemic reaction. The venom itself can cause direct toxic envenomation, and may also cause systemic allergic responses. The commonest hymenoptera species that causes problems in Malaysia one of the vespids, the hornet. This study looks to the features of hornet sting among children, the prevalence of systemic reactions and the factors associated with systemic reaction.

OBJECTIVE:

The main objectives of this study is to look at the profiles of children admitted in Hospital Universiti Sains Malaysia (HUSM) due to hornet stings. This study also looks at the prevalence of systemic reactions as well as to determine the factors associated with the development of systemic reactions among children stung by hornet.

METHODOLOGY:

This study was a retrospective record review, of all children admitted in HUSM from 2006 till 2011. The sampling frame was the records obtained from the Medical Record Office and all patients fulfilling the the inclusion and exclusion criteria were recruited into the study.

RESULT:

A total of 141 cases were recruited in this study. Majority were boys (61.7%), and almost all were Malay (98.6%). The youngest patient in our study population was a 6- month old child and the oldest 17 years old. Sixteen cases (11.3%) had history of allergy, 26 cases (18.4%) had history of atopy, 12 cases (8.5%) had history of asthma and 17 cases (17.5%) had a history of previous exposure to hornet stings. Majority of cases were direct visits to HUSM (75.9%). The others were referred from Klinik Kesihatan (19.9%), from district hospital (3.5%) and was admitted following ambulance call (0.7%). The number of cases of children admitted in HUSM for hornet stings is lowest during the rainy months, and peaked in the dry months of April to August. Eighty percent of the cases occurred during daytime (0701H till 1900H), The peak time for stings to occur is at 1509H ± 6.08. Fifty-one percent of the sting events occurred outdoor. Majority of the cases had been stung at their head, face and neck (45.4%). The others were stung at their upper limbs (excluding hand) (22%), at their hand

(42.6%), at their anterior trunk (10.6%), at their posterior trunk (17.7%), at their buttocks and genitals (4.3%), at their lower limbs (excluding foot) (12.8%) and at their foot (17.7%). A total of 140 cases (99.3%) had local reaction and only 1 case had no reaction at all. The local reactions were either swelling, pain, itchiness, redness or local infection at the stung site. Fourty-two cases (29.8%) were recorded to present with systemic reactions. Among those with systemic reactions, 37 had severe complications. Anaphylaxis was the commonest reaction observed among the severe complications with 32 cases (22.7%) followed by coagulopathy (7%), renal injuries (0.04%), sepsis (1.4%), cardiovascular, liver impairment and and rhabdomyolisis with 1 case each (0.7% each), and there were 3 deaths noted (2.12%). Children with hornet sting at their anterior trunks has 7.8 times the odds of having systemic reaction (95%CI 2.16, 28.14, $p = 0.02$). Children with a history of atopy were 4.3 times at odds of having systemic reaction following hornet sting (95% CI 1.63, 11.24, $p = 0.03$) .

CONCLUSION:

Understanding the features of hornet stings and the behaviour of the insect may help in reducing its incidence. Systemic reactions occurs in 29.8% of the cases with hornet stings. children with a history of atopy and those stung at their anterior necks are the ones with the highest risks of developing systemic reactions. Recognising the features of severe reactions and the factors that may result in a more severe reaction is important to ensure early appropriate treatment is initiated.

INTRODUCTION

1.1 Title

Hornet Stings: Factors Associated with Systemic Reactions in Children Admitted in HUSM

1.2 Overview

All over the world, insect stings have been a significant health concern. It accounts for a number of admissions in hospital, even for the paediatric age group. The features of insect stings can range from a mild local reaction, to fatal systemic anaphylaxis reaction. There were reports of systemic reactions on repeated stings by other insects, however, severe systemic anaphylaxis reactions is caused almost exclusively by the insects of the order Hymenoptera. Hymenoptera sting is the only one known to cause anaphylaxis with any frequency of sting (Müller, 2008). Venom from Hymenoptera stings, being cytotoxic, not just causing local pain and inflammation, it can also cause toxic effects on important organs of the body (Sakhuja *et al*., 1988).

Hymenoptera generally includes mainly three Families, The Apidae, Vespidae and Formicidae. The Family Apidae includes honeybees (*Apis mellifera*), and bumblebees (Genus *Bombus*). The Family Vespidae is subdivided into subfamilies Vespinae and Polistinae (wasps). The three genera of Vespidae includes *Vespula* (Yellow Jackets), *Vespa* (Hornets) and *Dolichovespula* (short-headed wasps). The Family Formicidae include ants and fire ants (*Solonepsis* genus) (Golden, 2003; Bilò *et al*., 2005). All the insects that injects venom while stinging belong to this Order. They mainly sting for defense, and while stinging, injecting the the venom via an injecting apparatus at the end of their belly. Their venom contains toxic substances such as biogenic amines, peptides and proteins, which then triggers allergic reactions and local and systemic toxicity.

Post-hymenoptera sting reactions can range from mild local reactions to severe life-threatening conditions. It can be classified into; Normal Local Reactions, Large Local Reactions, Systemic Allergic Reactions, Systemic Toxic Reactions, and Unusual Reactions (Bilò *et al*., 2005). Among the identified severe reactions were; anaphylaxis, intravascular haemolysis, pulmonary injuries, renal impairments, cardiovascular complications, hepatic injuries and coagulopathies (Paudel and Paudel, 2009).

The commonest reaction following Hymenoptera stings, as reported in available literatures, is a transient local reaction that tends to spontaneously resolve. Large local reaction (swelling extending more than 5cm from the sting site) may be present in up to 85% of cases (Graft *et al*., 1984). This reaction, may last more than 24 hours and is caused by both immediate and delayed immunologic responses.

Systemic reaction is rather uncommon, and may be present in up to 3% of adult population (Golden *et al*., 1989) and are generally IgE mediated. Pruritus, flushings and angioedemas are among the commonest systemic reactions noted. Mucosal oedema and intestinal smooth muscle spasms may result in gastrointestinal symptoms such as vomiting, diarrhoea and abdominal cramps. Respiratory reactions may manifest as; bronchospasms, airway obstruction, laryngeal and pulmonary oedemas. Hypotension, arrhythmias, and thrombosis are among the observed cardiovascular manifestations. Seizures, cerebral oedema and intracerebral haemorrhages are also among the neurogenic reactions documented in literatures. Anaphylactic shock, is among the most feared outcome of Hymenoptera sting (Müller, 2008).

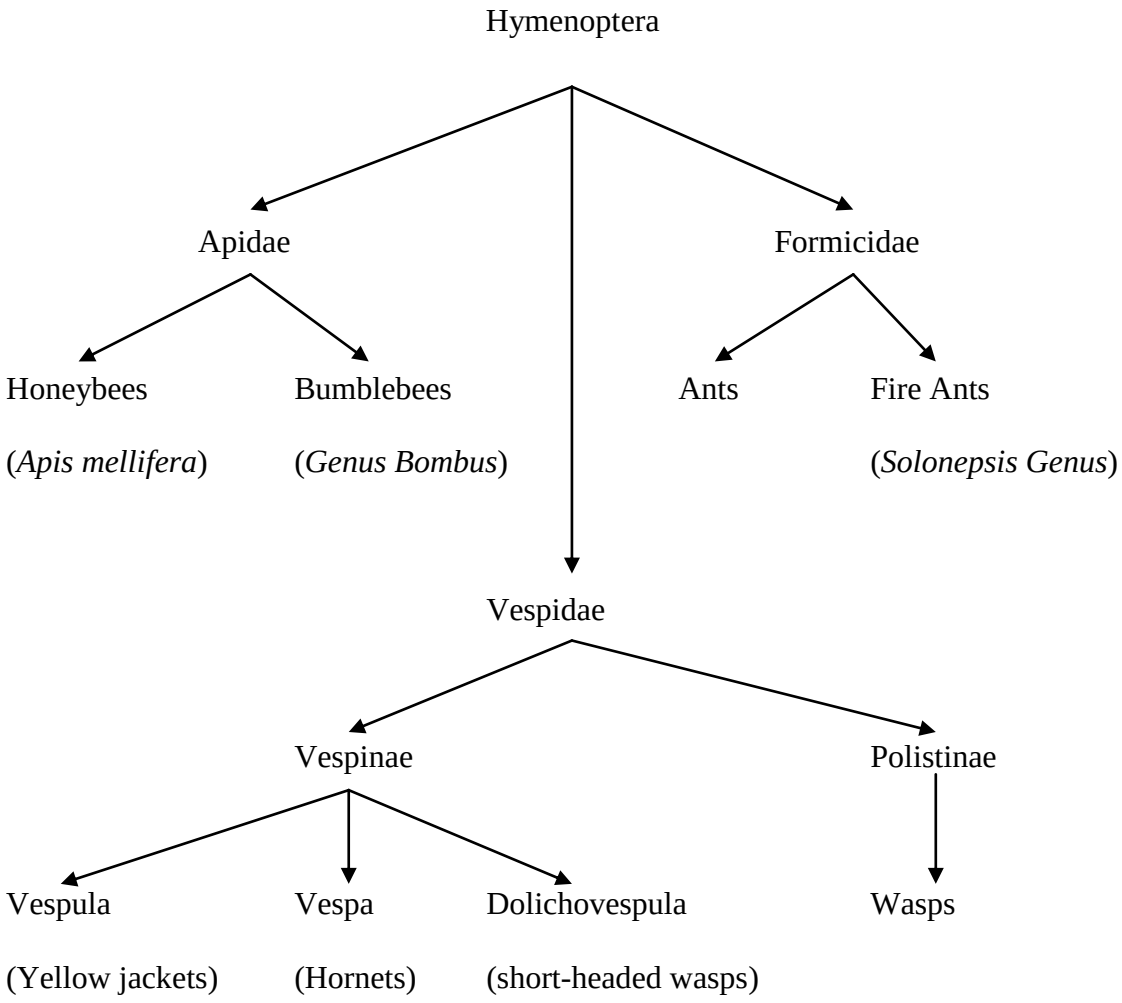
The vast range of reactions and complications to hymenoptera stings warranted urgent targeted treatment regime. Proper recognition of the signs and symptoms of severe reaction is of utmost importance. Patients presenting with anaphylaxis should receive adrenaline intramuscular immediately, delayed use of adrenaline may be ineffective and associated with fatal reactions (Bock *et al*., 2001).Those with cutaneous manifestations may benefit from the use of antihistamines, analgesics and

corticosteroids. Other symptomatic and supportive measures may also be of benefits. All modalities however, is never a substitute for adrenaline when anaphylaxis ensues. Antibiotics are rarely of use, as the venom is bacteriostatic in nature. Patients with a history of systemic reactions following insect stings may benefit from venom immunotherapy (Golden *et al*., 2011).

1.3 Literature Review

1.3.1 Hymenoptera

The Order Hymenoptera generally includes three Families, The Apidae, Vespidae and Formicidae. Honeybees (*Apis mellifera*), bumblebees (Genus *Bombus*), belongs to the family Apidae. The Family Vespidae are subdivided into subfamilies Vespinae and Polistinae (wasps). The three genera of Vespidae includes *Vespula* (Yellow Jackets), *Vespa* (Hornets) and *Dolichovespula* (short-headed wasps). The Family Formicidae include ants and fire ants (*Solonepsis* genus) (Golden, 2003; Bilò *et al*., 2005). All stinging insects that injects venom while stinging belong to this Order. They mainly sting for defense, and while stinging, injecting the the venom via an injecting apparatus at the end of their belly. Their venom contains toxic substances such as biogenic amines, peptides and proteins, which then triggers allergic reactions and local and systemic toxicity.


Hymenoptera
Apidae
Formicidae
Honeybees
(*Apis mellifera*)
Bumblebees
(*Genus Bombus*)
Ants
Fire Ants
(*Solonepsis Genus*)
Vespidae
Vespinae
Polistinae
Vespula
(Yellow jackets)
Vespa
(Hornets)
Dolichovespula
(short-headed wasps)
Wasps

1.3.2 Features of Hornet stings

The rate of exposure to hymenoptera stings varies from 40% to 84% in the general population in different regions of the world (Navarro *et al*., 2004; Graif *et al*., 2006; Jennings *et al*., 2008). Hymenoptera venom allergy in the meantime, occurs in 1% to 7.6% of the general population (Settipane *et al*., 1972; Navarro *et al*., 2004; Jennings *et al*., 2008). In a study of 10,000 high school children in Israel, 56% were stung at least once; 20% of those developed large local reaction, 12% developed mild local reaction, 4% developed moderate to severe systemic reaction (Graif *et al*., 2006).

Available studies suggested that males are more susceptible for insect stings and have higher risk of having allergic reactions following hymenoptera stings, as compared to females. Males were found to visit hospitals for allergy twice more likely than female, even though female were noted to have higher incidence of anaphylaxis (Harduar-Morano *et al*., 2011). Insect stings were also noted to be higher in male schoolchildren, as reported in an observational study of 10,000 high school children (Graif *et al*., 2006). Following insect stings, males are noted to have significantly higher associations with severe reactions (Rueff *et al*., 2009). Males were noted to have larger number of positive results when tested for IgE antibodies to venom (Golden *et al*., 1989).

A 6-year study in Chicago, USA found that incidence of hymenoptera stings are seasonal. Significantly higher calls for envenomation were noted during the summer holidays, and was positively related to mean daily temperature and mean daily atmospheric pressure (Friedman *et al*., 2010). Bee stings however, may not only occur in summer and spring, but may also occur on warm winter days, as bee colonies are able to survive the cold winters. Vespids in the meantime, only the queen survives the cold, and will begin building new colonies during spring, resulting in increased number of vespid stings in the summer and fall (Müller, 2008).

Clinical presentation of Hymenoptera stings vary from individuals and the severity is broad. The reactions can can be either mild local reaction, large local reaction, systemic allergic reaction, unusual and toxic allergic reactions (Bilò *et al*., 2005). Most cases do not have any serious reactions and treatments are not usually necessary. Most only have mild local reactions, which includes mild swelling, pain, redness or itchiness at stung site, which at most, only required symptomatic treatment (Golden *et al*., 2011).

Studies observed 1% to 8 % of general population develop allergic reactions towards hymenoptera venom. Other reaction like large local reactions which may extend more than 5cm to 10cm at the site of sting, immediate IgE-mediated systemic allergic reactions like urticaria, angioedema, bronchospasm and anaphylaxis are also observed (Settipane *et al*., 1972; Navarro *et al*., 2004; Jennings *et al*., 2008).

Occasionally, delayed allergic reactions are observed. These unusual reactions include generalised vasculitis, encephalomyelitis, glomerulonephritis and serum-like syndromes, probably are IgG-mediated or cellular immunologic responses. Rarely, non-immunologic mediator are responsible. Generalised reactions and multi-organ involvement can occur due to venom toxic reactions (Müller, 2008); Golden *et al*., 2011).

In an observational study among school children in Ireland, at least 40% of the population were stung at least once; 5.3% of those stung had large local reaction (LLR), 3% had mild systemic reaction (MSR), and 1% developed moderate to severe systemic reaction (SSR) (Jennings *et al*., 2008). A study in Israel observed 56% of the 10,000 schoolchildren studied were stung at least once; 20.5% had LLR, 11.6% had MSR and 4.4% had SSR (Graif *et al*., 2006).

1.3.3 Complications of Hornet stings

Hymenoptera venom effects can be classified into allergic and toxic reactions. Allergic reactions, triggered by histamine release and other immunologic mediators, cause vasodilatation and increase vascular permeability, leading to anaphylaxis and shock. IgG and IgM activation results in immune complex deposition, such as seen in glomerulonephritis and serum sickness-like syndrome. Toxic reactions can either be primary reaction or direct cell toxicity, and secondary reaction which is a result of cellular destruction, and the release of chemokines. Direct cellular toxicity causes haemolysis, rhabdomyolysis, and acute tubular necrosis. Secondary reaction results in vasoconstriction, platelet and coagulation cascade activation, and thrombus formation resulting in cardiovascular events (Dechyapirom *et al*., 2011).

The commonest complication observed following Hymenoptera sting is anaphylaxis. It is a severe, potentially fatal systemic allergic reaction following exposure to an allergen (Sampson *et al*, 2006). Anaphylaxis is defined when any of the 3 criteria is fulfilled:

1. Acute onset of illness with skin or mucosal involvement, such as generalised urticaria, pruritus, flushing or angioedema, with at least one of these signs: respiratory compromise (i.e. Bronchospasm, laryngeal oedema, dyspnoea, hypoxaemia) or reduced blood pressure or symptoms of end-organ dysfunction.

2. Having any two of these reactions following a contact with allergen; involvement of skin-mucosal tissue, respiratory compromise, persistent gastrointestinal symptoms or reduced blood pressure or its symptoms.

3. Reduced blood pressure or its symptoms following contact with a known allergen.

   (Sampson *et al*., 2006)

The World Allergy Organisation categorised anaphylaxis as either immunologic or non-immunologic. Immunologic reactions are IgE-mediated and non-IgE-mediated (immune complex mediated, complement and IgG-mediated). Non-immunologic reactions are a result of sudden mast cell and basophile degranulation without the presence of immunoglobulin (Johansson *et al*., 2004).

Both immunologic and non-immunologic reactions results in sudden release of mast cell and basophile-derived mediators such as histamine, leukotrienes, and prostaglandins. Mast cell activation, releases tryptase, a neutral protease which is selectively concentrated in secretory granules of mast cells. Tryptase is a useful marker in confirming anaphylaxis (Schwartz *et al*., 1987).

Release of the immune mediators, results in vasodilatation, increased vascular permeability and smooth muscle spasm. Respiratory symptoms may be the result of increase secretion, airway oedema and bronchospasm, resulting in airway obstruction

and respiratory compromise (Arnold and Williams, 2011) other symptoms include rhinorrhoea, urticaria, flushing, angioedema, abdominal cramps with vomiting and diarhoea, uterine cramps and headaches. Cardiovascular symptoms are mainly caused by capillary leakage and decreased vascular tone, progressing into shock, arrhythmias, and myocardial dysfunction.

Barnard did a study in 400 fatalities due to hymenoptera stings. the study observed that 60% of autopsied patients had massive oedema and secretion in the respiratory tract, resulting in fatal airway obstruction (Barnard, 1973). Another 12% had reaction which was described as anaphylactic shock, in which the vascular involvement were noted to be milder and airway obstruction thought to be causing only partial obstruction.. other reactions observed were pulmonary haemaorrhage (10%), vascular pathology which included coronary occlusion, generalised haemorrhage and extracardial infarction with emboli (12%), and cerebral pathology which included cerebral oedema, haemorrhage, infarction, and necrosis (7%).

1.3.4 Factors associated with Systemic Reactions

Studies identified elderly person, especially those with existing co-morbidities such as pre-existing cardiovascular diseases or on beta-blockers or angiotensin-converting enzyme inhibitor drugs are more susceptible for systemic reactions and more severe complications following hymenoptera stings (Rueff *et al*., 2009). Post-sting

anaphylaxis is also more commonly observed among elderly cases (Harduar-Morano *et al*. 2011). Children however, with their relatively smaller body size, are noted to be more vulnerable to the toxic reaction of the dose-dependant toxic envenomation, and may result in mortality even with lesser number of stings (Müller, 2008).

The male gender is observed to more commonly associated with systemic reactions following a field sting (Rueff *et al*., 2009). Certain race are also observed to be more susceptible for venom-induced allergy. Whtites are noted to be more susceptible than the blacks, and Arabs are observed to have more systemic reactions compared to Jews (Graif *et al*., 2006; Harduar-Morano *et al*., 2011).

The patients with a history of atopy and allergy were also noted to have a significant risk to develop systemic allergic reactions to hymenoptera stings (Celikel *et al*., 2006). Interesting to note, several studies found no correlation between severity of sting reactions with history of atopy or allergy (Settipane *et al*., 1972; Birnbaum *et al*., 1994; Kalyoncu *et al*., 1997).

Golden noted that subjects with a previous history of large local reactions are more likely to progress into systemic reactions in subsequent exposures to hymenoptera stings. patients with a history of severe systemic reacions had a greater probablilty of deveoping severe complications in future exposures (Golden, 2003). This observation is however not found as such on children. Less than 2% of stings in children with previous large local reactions resulted in systemic reactions (Graft *et al*., 1984).

1.4 Reasons for this study

From above discussion and literature review, these are the reasons for pursuing the study on “Hornet stings: factors associated with systemic reaction in children admitted in HUSM”

1) There are not enough data worldwide on the prevalence and features of children stung by hornet
2) There is a need to study the factors associated with development of systemic reaction among children stung by hornets.

Almost all previous study studied about hymenoptera sting, with none concerns hornets alone. In Malaysia, our experience suggest that hornet stings accounts for a majority of insect sting admissions.

CHAPTER 2

OBJECTIVES

2.0 Objectives

2.1 General Objectives

To describe the profiles of children bitten by hornet admitted in HUSM

2.2 Specific Objectives

1. To describe the profiles of children bitten by hornet admitted in HUSM from January 2006 to December 2011.

2. To determine the prevalence of systemic reaction in children bitten by hornet admitted in HUSM from January 2006 to December 2011

3. To describe the factors associated with systemic reaction after hornet sting among children admitted in HUSM in January 2006 to December 2011.

CHAPTER 3

METHODOLOGY

3.1 Research Questions

3.1.1 What are the features of hornet stings in children admitted in Hospital Universiti Sains Malaysia from 2006 to 2011?

3.1.2 What are the outcomes of hornet stings and the prevalence of systemic reaction among these cases?

3.1.3 What are the factors associated with systemic reactions among the children bitten by hornet, admitted in HUSM?

3.2 Study Design

This study was designed as a retrospective record review study of secondary data of children admitted in HUSM for Hornet Sting from 2006 to 2011. It is a retrospective record review of all case notes of children diagnosed with hornet stings who were admitted from 2006 to 2011. Hospital USM is a tertiary centre that received referrals from district hospitals and a referral centre for sub specialty by two other

tertiary centers, Hospital Raja Perempuan Zainab II (HRPZ II) in Kota Bharu, Kelantan and Hospital Sultanah Nur Zahirah (HSNZ) in Kuala Terengganu, Terengganu. Hospital USM is also a teaching hospital for school of medical sciences, Universiti Sains Malaysia.

3.3 Study Location

This study was carried out in Hospital Universiti Sains Malaysia, Kubang Kerian, located in the State of Kelantan, which is located in the East Coast of Peninsular Malaysia.

3.4 Study Population and Sample

Records of all children aged 18 years and below admitted in HUSM within the study period were included in the study for review.

- Reference Sample
    - All children aged 18 and below in Kelantan
- Source Population
    - All children aged 18 and below admitted in HUSM for hornet sting
- Sampling Frame

* All children admitted in HUSM fulfilling the inclusion criteria

3.5 Inclusion and Exclusion Criteria

3.5.1 Inclusion Criteria

- Children aged 18 years and below, admitted in HUSM and diagnosed with Hornet Stings from the year 2006 to 2011

3.5.2 Exclusion Criteria

- Patients admitted for unknown stings, other insect stings, or unsure stings or bites.
- Patients with missing records or those with very poor documentation regarding the stings

3.6 Calculation of Sample Size

The sample size for objectives 1 and 2, were calculated using single proportion sample size calculation formula (Daniel, 1999):

$$n = \left(\frac{Z}{\Delta} \right)^2 P(1 - P)$$

n : sample size

p : anticipated population proportion

Δ : absolute precision

z : confidence interval

Objective 1 : To determine the profiles of children bitten by hornet admitted in HUSM from January 2006 to December 2011.

Objective 2 : To determine the prevalence of systemic reaction in children stung by hornet admitted in HUSM from January 2006 to December 2011

A national survey of 10,000 junior high school children in Israel 56.3% of the population had been stung by insects at least once (Graif *et al*., 2006).

$$n = \left(\frac{1.96}{0.1} \right)^2 0.56 (1 - 0.56)$$

n = 95

Taking the Z score as 1.96 (for 95% confidence level), anticipated population proportion of hornet sting at 56.3%, and absolute precision at 0.1, the sample size calculated is 95. Considering drop out rate of 20%, the total sample required, N is:

N = 95 + 20% drop out

= 114

Therefore, the total sample required is 114

Objective 3 : To determine the factors associated with systemic reaction after hornet sting among children admitted in HUSM in January 2006 to December 2011.

Sample size was calculated using PS Power and Sample Size Calculation Software, version 3.0.

A study in New York, showed that 26% of patients with no prior history of allergy to insect stings developed anaphylaxis, and 40% of patients with prior history of insect sting allergy developed anaphylaxis (Clark *et al*., 2005). The model for calculations were as below:

$\alpha = 0.05$,

power = 0.8,

m = 1

P_0 = proportion of children developing anaphylaxis after exposure with insect sting with no prior history of insect sting allergy = 0.26,

P_1= proportion of children developing anaphylaxis after exposure with insect sting with prior history of insect sting allergy = 0.40,

Sample size calculation (n = 176) for each group

So total sample size = 352 + 70 (20% drop out) = 422

3.7 Duration of Study

The study was conducted within two months (from April 2015 until May 2015).

3.8 Data Collection

The data were derived from retrospective record reviews of all children admitted in HUSM with hornet sting. A computer generated list was obtained from the Medical Record Office. The cases were identified according to the T-Codes of the International Classification of Disease – 10th Revision (ICD-10). Keywords used when retrieving records included; hornet sting, hymenoptera sting, insect sting. The medical records were traced from the Medical Record Department. Details of each case were recorded using the standardised proforma (Appendix B).

3.9 Definition of Terms

i. **Hymenoptera stings:** Any sting or bite caused by the order Hymenoptera which includes bees, wasps, yellow jackets, hornets and ants (Müller, 2008).

ii. **Local reaction:** Includes normal reaction and large local reaction, affecting the site of the sting or bite. Normal reactions include redness, swelling, itching and pain. Large local reactions is swelling up to more than 5 to 10cm in diameter contiguous to the site of the sting and usually increase in size for 24 to 48 hours, lasted 5 to 10 days (Golden *et al.*, 2011).

iii. **Systemic reaction:** Includes a spectrum of manifestations not contiguous with the site of the sting, ranging from mild to life-threatening. These include cutaneous responses (urticaria, angioedema), gastrointestinal involvement (nausea, vomiting, diarrhea, and abdominal pain), respiratory involvement (tongue or laryngeal eodema, bronchospasm), cardiovascular involvement (hypotension, arrhythmia) and neurological (seizures) (Golden *et al.*, 2011).

iv. **Mild systemic reaction:** Systemic reaction developed after exposure to allergen which is limited only to the skin and consists of flushing, urticaria and angioedema (Pawankar *et al.*, 2011).

v. **Severe complication of hymenoptera sting:** Includes life-threatening condition associated with the stings. It can be anaphylaxis and its complication, cardiovascular complications, rhabdomyolysis, neurologic complication, multi-organ failure, related bacterial sepsis and death(Pawankar *et al.*, 2011)(Barnard, 1973).

vi. **Anaphylaxis:** Reactions developed acutely after hymenoptera sting among those patients, with any of the 3 criteria:

a. skin or mucosal involvement with at least one of these: respiratory compromise or reduced blood pressure or symptoms of end-organ dysfunction
b. having any two or more of the following: involvement of the skin-mucosal tissue, respiratory compromise, reduced blood pressure or associated symptoms, or persistent gastrointestinal symptoms
c. having reduced blood pressure. In infant: low systolic blood pressure (age specific) or greater than 30% decrease in systolic blood pressure. In adults: systolic blood pressure of less than 90 mmHg or greater than 30% decrease from that person's baseline (Sampson *et al.*, 2006).

vii. **Cardiovascular complication:** includes cardiac complications like arrhythmia, and vascular complications which include coronary event, haemorrhage, stroke, and emboli. Hypotension is not considered as cardiovascular complication if diagnosed as anaphylaxis (Barnard, 1973).