

**DEVELOPMENT AND VALIDATION OF  
QUESTIONNAIRE TO ASSESS MALAYSIAN PARENTS'  
KNOWLEDGE, PRACTICE AND PERCEPTION ON  
ACETAMINOPHEN POISONING IN CHILDREN**

**BY**

**MUHAMMAD ZHARIFF BIN MUHAMAD**

**DISSERTATION IS SUBMITTED IN PARTIAL FULFILMENT  
OF THE REQUIREMENTS FOR THE DEGREE OF  
MASTER OF SCIENCE (HEALTH TOXICOLOGY)**

**ADVANCED MEDICAL AND DENTAL INSTITUTE  
UNIVERSITI SAINS MALAYSIA**

**2019**

**DEVELOPMENT AND VALIDATION OF  
QUESTIONNAIRE TO ASSESS MALAYSIAN PARENTS'  
KNOWLEDGE, PRACTICE AND PERCEPTION ON  
ACETAMINOPHEN POISONING IN CHILDREN**

by

**MUHAMMAD ZHARIFF BIN MUHAMAD**

**DISSERTATION IS SUBMITTED IN PARTIAL FULFILMENT  
OF THE REQUIREMENTS FOR THE DEGREE OF  
MASTER OF SCIENCE (HEALTH TOXICOLOGY)**

**ADVANCED MEDICAL AND DENTAL INSTITUTE  
UNIVERSITI SAINS MALAYSIA**

**2019**

## DECLARATION

This is to certify to the best of my knowledge, this dissertation is entirely the work of the candidate, Muhammad Zhariff Bin Muhamad.

---

Dr. Husnaida Binti Abdul Manan @ Sulong

Main Supervisor

Integrative Medicine Cluster

Advanced Medical and Dental Institute, USM

## ACKNOWLEDGEMENT

First and foremost, I would like to thank Allah S.W.T for giving me the strength, knowledge, ability and opportunity to undertake this research study and to persevere and complete it satisfactorily. Without His blessings, this achievement would not have been possible. I greatly appreciate and acknowledge the support received from my supervisor Dr. Husnaida Binti Abdul Manan @ Sulong, my co – supervisor Dr. Nur Arzuar Bin Abdul Rahim and Dr. Mohd Yusmaidie Bin Aziz for the time and guidance throughout this process. They have been there providing their heartfelt support and guidance at all times and has given me invaluable guidance, inspiration and suggestions in my quest for knowledge. I would like to thank the Ministry of Health, Malaysia for giving me the opportunity to further my studies in the Master of Science (Health Toxicology) at the Universiti Sains Malaysia. I would also like to express my gratitude to my parents, my family, Puan Zakiah Binti Abdul Ghaffar, Head of Research Section, Quality Control Centre, National Pharmaceutical Regulatory Division and the staffs of Advanced Medical and Dental Institute who have been so helpful and cooperative in giving their support at all times to help me achieve my goal. And last but not least, I would like to thank my parents; Encik Muhamad Bin Haji Yusoff and Puan Zaiton Binti Mohd Shahrouron for the emotional support during the difficult times and for always being there for me.

## TABLE OF CONTENTS

<b>ACKNOWLEDGEMENT .....</b>	<b>i</b>
<b>TABLE OF CONTENTS.....</b>	<b>ii</b>
<b>LIST OF TABLES.....</b>	<b>vi</b>
<b>LIST OF FIGURES.....</b>	<b>vii</b>
<b>LIST OF SYMBOLS.....</b>	<b>viii</b>
<b>LIST OF ABBREVIATIONS.....</b>	<b>ix</b>
<b>ABSTRAK.....</b>	<b>x</b>
<b>ABSTRACT .....</b>	<b>xii</b>
<b>CHAPTER 1            INTRODUCTION .....</b>	<b>1</b>
1.1    Research Background .....	1
1.2    Benefits of Study .....	3
1.3    Justification of Study .....	4
1.4    Rationale of Study .....	5
1.5    Study Objectives.....	6
1.5.1    General Objectives.....	6
1.5.2    Specific Objectives .....	6
1.6    Research Questions.....	7
1.7    Research Hypotheses.....	7
1.7.1    Hypotheses Development .....	7
1.7.2    Hypotheses Testing.....	8
1.8    Operational Definition.....	9
1.9    Conclusion.....	10
<b>CHAPTER 2            LITERATURE REVIEW.....</b>	<b>11</b>
2.1    Overview .....	11

2.2	Acetaminophen Poisoning in Children.....	11
2.3	Practice of the uses of Acetaminophen and Management of Fever .....	14
2.3.1	Fever Phobia Phenomenon Among Parents.....	14
2.3.2	Risk of Double Dipping .....	18
2.3.3	Safety Measure in Preventing Accidental Poisoning.....	19
2.4	Basic Knowledge of Parents Regarding Acetaminophen and Fever .....	21
2.5	Perception on the Use, Dosage, and Indication of Acetaminophen .....	25
2.6	Development Phase of Questionnaire.....	27
2.6.1	Item Generation .....	28
2.7	Validation Phase of Questionnaire .....	30
2.7.1	Item Analysis .....	30
2.7.2	Content Validity.....	31
2.7.3	Face Validity.....	32
2.7.4	Construct Validity.....	33
2.7.5	Questionnaire Reliability .....	33
2.8	Conclusion.....	34
<b>CHAPTER 3                    METHODOLOGY.....</b>		<b>35</b>
3.1	Introduction .....	35
3.2	Location of Study .....	35
3.3	Design of Study .....	36
3.4	Ethical Consideration .....	36
3.5	Duration of Study .....	36
3.6	Population of Study .....	37
3.7	Subject Criteria.....	37
3.8	Sample Size Calculation.....	38
3.9	Development Phase of Questionnaire (Research Tool/Instrument) .....	40

3.10	Study Variables.....	41
3.10.1	Dependent Variables.....	41
3.10.2	Independent Variables .....	42
3.11	Validation of questionnaire .....	43
3.11.1	Content validity.....	44
3.11.2	Face validity.....	47
3.11.3	Pilot Study.....	49
3.11.4	Construct validity.....	50
3.11.5	Reliability.....	52
3.12	Data Collection.....	53
3.13	Statistical Analysis .....	54
3.14	Conclusion.....	59
3.15	Study flow chart.....	60
<b>CHAPTER 4</b>	<b>RESULTS.....</b>	<b>61</b>
4.1	Introduction .....	61
4.2	Content Validity Stage.....	61
4.3	Face Validity Stage.....	66
4.4	Construct Validity Stage.....	69
4.5	Conclusion.....	84
<b>CHAPTER 5</b>	<b>DISCUSSION .....</b>	<b>85</b>
5.1	Introduction .....	85
5.2	Questionnaire Development Stage .....	85
5.3	Content Validity Stage.....	86
5.4	Face Validity Stage.....	88
5.5	Construct Validity Stage.....	90
5.6	Limitations of Study .....	96

5.7	Recommendations .....	97
	<b>REFERENCES .....</b>	<b>98</b>
	<b>appendices .....</b>	<b>106</b>



## LIST OF TABLES

	<b>Page</b>
Table 3.1 Construct validity sample size calculation .....	38
Table 3.2 Reliability analysis sample size calculation .....	39
Table 3.3 Content validity evaluation criteria .....	45
Table 3.4 Face validity evaluation criteria stages .....	48
Table 4.1 Content Validity Index for Relevance Criteria .....	62
Table 4.2 Content Validity Index Post Content Validity Meeting .....	64
Table 4.3 Face validity index (comprehensibility).....	67
Table 4.4 Socio-demographic characteristics of questionnaire respondents (n=216)	70
Table 4.5 Simplified rotated component matrix table .....	74
Table 4.6 Items with factor loading below 0.4 item after 4 rounds of analysis .....	76
Table 4.7 Summary of reliability analysis and factor loading .....	78

## LIST OF FIGURES

	<b>Page</b>
Figure 3.1: Independent Variable and Dependent Variable of the Study Processes .	43
Figure 3.2: Study flow chart.....	60
Figure 4.1 Scree plot of the Eigenvalue versus Component Number .....	72
Figure 4.2: Storage behaviour of opened blister packaging for tablet formulation...	82
Figure 4.3: Storage behaviour of opened bottle of paracetamol syrup .....	82
Figure 4.4: Storage behaviour of opened blister packaging for suppository formulation .....	83
Figure 4.5: Feared consequences of untreated fever .....	83

## LIST OF SYMBOLS

%	percentage
&	and
$\alpha$	Alpha

## LIST OF ABBREVIATIONS

AMDI	Advanced Medical and Dental Institute
Avg	Average
CITC	Corrected Item Total Correlation
CVI	Content Validity Index
EFA	Exploratory Factor Analysis
<i>et al</i>	and others
FDA	Food and Drug Administration
FVI	Face Validity Index
HSA	Health Science Authority
i-CVI	Item level - Content Validity Index
i-FVI	Item level - Face Validity Index
ICC	Intra-Class Correlation Coefficient
KMO	Kaiser-Meyer-Olkin
NEISS	National Electronic Injury Surveillance System
NSAID	Non-Steroidal Anti-Inflammatory Drug
OTC	Over the Counter
PCA	Principal Component Analysis
s-CVI	Scale level - Content Validity Index
s-FVI	Scale level - Face Validity Index
SD	Standard Deviation
SPSS	Statistical Package for Social Science
UA	Universal Agreement
USA	United States of America
USM	Universiti Sains Malaysia

**PEMBINAAN DAN PENGESAHAN BORANG SOAL SELIDIK UNTUK  
MENILAI TAHAP PENGETAHUAN, AMALAN DAN PERSEPSI IBU BAPA  
WARGA NEGARA MALAYSIA BERKENAAN KERACUNAN  
ACETAMINOPHEN DALAM KALANGAN KANAK-KANAK**

**ABSTRAK**

Pengenalan: Keracunan acetaminophen (paracetamol) mampu membawa kepada komplikasi dan kesan buruk yang serius kepada kesihatan kanak-kanak. Pengetahuan, persepsi, dan amalan penggunaan ubat yang baik adalah wajar untuk memastikan keselamatan penggunaan ubat berkenaan dalam kalangan kanak-kanak. Objektif kajian ini adalah untuk membangunkan dan mengesahkan borang soal selidik untuk menilai tahap pengetahuan, persepsi, dan amalan berkenaan keracunan acetaminophen dalam kalangan kanak-kanak.

Metodologi: Satu kajian secara keratan rentas dalam kalangan ibu bapa warganegara Malaysia yang memenuhi keperluan kriteria inklusi dan eksklusi dan telah melawat Pusat Kajian Klinikal, Institut Perubatan dan Pergigian Termaju, Universiti Sains Malaysia. Kajian ini telah mendapat keizinan peserta sebelum dijalankan. Satu borang soal selidik yang mengandungi taburan 67 item mengikut setiap domain telah dibangunkan. Borang yang diisi dalam tempoh 30 minit ini mendapat sambutan yang baik dalam kalangan responden. Pengesahan soal selidik ini merangkumi fasa kesahan kandungan, muka, dan gagasan. Penilaian pengesahan termasuk indeks kesahan kandungan aras-item (i-CVI) dan indeks kesahan muka aras-item (i-FVI). Manakala bagi kesahan gagasan, nilai Kaiser-Meyer-Olkin (KMO) dan ujian kesferaan Bartlett telah diambil kira untuk menilai kecukupan sampel manakala, analisis faktor dan komunaliti dianalisis untuk ujian analisis

faktor penerokaan (EFA). Analisa kebolehpercayaan instrumen pula melibatkan penggunaan alfa Cronbach dan *corrected inter-item total correlation* (CITC). Borang soal selidik ini dibahagikan kepada 3 domain dan mempunyai 67 item secara keseluruhan. Pembangunan borang soal selidik ini telah dibuat hasil bacaan literatur dan sesi sumbang saran dalam kalangan ibu bapa.

Keputusan: Kesahan kandungan telah dijalankan melalui sesi mesyuarat dengan panel pakar penilai (8 orang) dan panel penilaian oleh panel luar (2 orang). Kesahan muka pula dikaji dengan pra-ujian soal selidik dengan 30 orang responden. Manakala, kesahan gagasan pula dianalisis melalui analisis faktor. Sebanyak 57 daripada 64 soalan (item dan subitem) dikekalkan berdasarkan pengiraan i-CVI dan penilaian pakar penilai. Bagi kesahan muka pula, sebanyak 18 soalan (item dan subitem) disingkirkan kerana nilai i-FVI yang rendah. Bagi EFA, keputusan menunjukkan model 19 faktor dengan jumlah pengestrakan varians sebanyak 68%. Lima belas item telah dikeluarkan setelah ujian EFA dijalankan sebanyak 4 kali sehingga semua faktor muatan melebihi nilai 0.4. Nilai alfa Cronbach bagi faktor pengetahuan dan amalan melebihi 0.6 manakala bagi persepsi, nilai yang didapati adalah 0.55.

Kesimpulan: Borang soal selidik ini dianggap sah dan boleh dipercayai bagi domain pengetahuan dan amalan. Bagi domain persepsi pula, didapati faktor tersebut adalah tidak sah dan tidak boleh dipercayai. Walau bagaimanapun, borang soal selidik yang telah dibangunkan ini telah menyediakan suatu platform untuk menilai tahap pengetahuan, amalan dan persepsi ibu bapa warganegara Malaysia terhadap aspek atau faktor penyebab keracunan acetaminophen.

Kata Kunci: Pengesahan, Acetaminophen, Keracunan, Pengetahuan, Persepsi, Analisis Faktor Penerokaan

**DEVELOPMENT AND VALIDATION OF QUESTIONNAIRE TO ASSESS  
MALAYSIAN PARENTS' KNOWLEDGE, PRACTICE AND PERCEPTION ON  
ACETAMINOPHEN POISONING IN CHILDREN**

**ABSTRACT**

Introduction: Acetaminophen (paracetamol) poisoning may lead to serious complications and adverse health effects in children. A good knowledge, perception and practice is essential in ensuring the safe use of the drug among children. The objective of this study is to develop and validate a questionnaire to assess knowledge, perception and practice among Malaysian parents related to/ on acetaminophen poisoning in children.

Methodology: A cross-sectional study was conducted among volunteered and consented Malaysian parents who attended Clinical Trial Centre, Advanced Medical and Dental Institute, Universiti Sains Malaysia and fulfilled the inclusion and exclusion criteria. A self-administered questionnaire was developed consisting of 67 items that takes 30 minutes to complete and well received by all respondents. The validation of the questionnaire involved content, face and construct validity stages. The evaluation included item-level content validity index (i-CVI) and face validity index (i-FVI) for content and face validity respectively. As for construct validity, the values of KMO and Bartlett's sphericity test were taken into account for sampling adequacy as well as factor loading and communalities for the measurement of exploratory factor analysis. Reliability analysis involved the use of Cronbach's alpha and corrected inter-item correlations (CITC). This questionnaire was divided into three domains, with 67 items distributed to respective domains. The development of questionnaire was aided from literature review and brainstorming session with parents.

Results: Content validity was established through panel expert meeting (8 experts) and content reviews (2 reviewers). Face validity was examined through pre-testing (30 respondents) and construct validity was examined through factor analysis. The findings of content validation had shown that 57 out of 64 questions (items and subitems) to be retained based on the calculation of I-CVI and content expert judgement while the face validity, a total of 18 questions (items and subitems) were deducted as a result of low I-FVI. For EFA, the result showed a 19-factor model with total variance extraction of 68%. A total of four factors were determined based on visual examination of the scree plot. Fifteen items were deleted after the repetition of EFA that was made four times until all factor loadings above the cut-off value of  $>0.4$ . The Cronbach's alphas for the factors of knowledge and practice are above 0.6 but for perception the value found is 0.55.

Conclusion: This questionnaire is regarded as valid and reliable in terms of the domains of knowledge and practice. On the other hand, for the domain of perception, it is found that the factor is not valid and unreliable. However, the tool developed has provided a platform to evaluate the knowledge, practice, and perception of Malaysian parents towards the aspect or factors of paracetamol toxicity in children.

Keywords: Validity, Acetaminophen, Poisoning, Knowledge, Perception, Exploratory Factor Analysis



# CHAPTER 1

## INTRODUCTION

### 1.1 Research Background

Acetaminophen as a drug is a common type of over the counter (OTC) analgesic which is available in a variety of dosage forms and can be also used in combination with opioids (Blieden *et al*, 2014). It was first discovered in the 19th century at Germany and was commonly used in the 20th century and is regarded as generally safe drug if consumed within permissible dose (Sheen, 2002). This anti-pyretic drug has the edge over other non-steroidal anti-inflammatory drugs (NSAID) in the sense of it does not cause gastrointestinal disorder (Blieden *et al*, 2014). The drug is characterized by its pain reduction through the inhibition of prostaglandins and temperature reduction in fever via a central effect and subsequently metabolized in liver (Goldman, 2013).

Acetaminophen, or Paracetamol, or most commonly known in Malaysian societies as Panadol; a term which is not exactly referring to the brand but in a study conducted in a qualitative study conducted locally, it was reported that most of the respondents were only familiar with the term Panadol and not acetaminophen or paracetamol. They are unable to distinguish the generic products of acetaminophen despite having about 50 acetaminophen products marketed by different companies in the country. Acetaminophen is widely used as an over the counter (OTC) medicine for the treatment of fever and pain and one of the most common drugs prescribed in children (Goldman, 2013). In Malaysia, there are many different formulations and strengths of acetaminophen available as an OTC (Mohd Zain *et al*, 2006). These include the forms of

tablets, suppositories, and syrups which are commonly used in children (Goldstein *et al*, 2008). Acetaminophen is classified as over the counter non-prescription drug, in which the lack of guidance and intervention from healthcare professionals may impose a higher potential risk of adverse events as compared to prescription items (Shone *et al*, 2011).

The first case of toxicity of acetaminophen was identified in 1966 in Aberdeen, Scotland in which liver toxicity was first reported (Sheen, 2002 and Thomson and Prescott, 1966). It is claimed by Wolf *et al* that acetaminophen poisoning is the number one cause of acute liver failure in the United States of America (USA) and has the potential to increase rate of mortality every year than any other medications. Locally, Mohd Zain *et al* has declared that acetaminophen poisoning is the most common drug associate poisoning in Malaysia (Mohd Zain *et al*, 2006). It also worth noting that in 2009, Food and Drug Administration (FDA) panel review has reached a conclusion that majority of the cases of acetaminophen toxicity is due to improper labelling and unintentional ingestion (Wolf *et al*, 2012).

Sheen has mentioned in his article that most of acetaminophen toxicity cases are secondary to intentional overdose due to parasuicidal attempt. However, a significant proportion of patients were presented with acetaminophen poisoning due to accidental ingestion, particularly in children under 5 years of age (Sheen, 2002). Sheen has also cited a study in his article that 53% of acetaminophen toxicity is due to unintentional overdose which was observed in children aging 2 months to 13 years old (Sheen, 2002). He claimed that accidental overdose patients had higher risk of coma and mortality as well as longer hospital stay (Sheen, 2002).

Based on findings from previous studies as described in the latter part of this study, one of the main causes of acetaminophen toxicity is contributed by the poor grasp of knowledge, lack of decent drug administration practice, and suboptimal level of drug perception among the caregivers especially parents. It is to our belief that at the moment, there is no instrument available that could analyze the Malaysian parents' level of knowledge, perception, and practice regarding acetaminophen poisoning in children. Therefore, as one of the most important tools used in research, we hope that a development and validation of questionnaire, designed to achieve this objective by acquiring the much-needed information in answering the research questions. This instrument is useful in assessing the level of knowledge, attitude and perception of a certain cohort pertaining any research field. In this study, a self-administered questionnaire is aimed to be developed and validated to assess the level of knowledge and perception of Malaysian parents towards acetaminophen poisoning among children.

## **1.2 Benefits of Study**

This study may benefit the public as well as healthcare professionals as it will provide guidance for implementing strategies to prevent the acetaminophen-related misuse in children which could eventually lead to toxicity. As of today, the educational tools to promote the rational use of acetaminophen in Malaysia are very scarce. Hence, it is the vision of this study to provide the baseline data of acetaminophen-related educational tool and programs for government agency, particularly the Pharmaceutical Services Division, Ministry of Health Malaysia.

Assessment of Malaysian parents' knowledge, practice and perception of acetaminophen poisoning in children is essential for safe use of this drug. Therefore, having a valid and reliable tool to measure the parent's knowledge, practice and perception is important for future planning of health education programs among the public. Thus, this study provides a valid and reliable tool for getting feedbacks from Malaysian parents. Other benefits include, this study also provide a guide to other disciplines that want to develop their own tool. On top of that, this study will be a precursor to promote further research in the future in regard to drugs toxicity.

### **1.3 Justification of Study**

A study had been done to observe the practice of acetaminophen administration in paediatric age in Italy by Lubrano *et al* (2016) in which the issues regarding fever-phobia and self-prescription among parents were investigated. However, to the best of our knowledge, there is no validated tool to explore parents' knowledge and perception towards acetaminophen poisoning in children conducted locally. It has brought to our attention to the study conducted locally by Tan *et al* (2015) which however focused more on the usage trend and knowledge of acetaminophen use among Malaysian adults. The study used qualitative tool as an instrument to achieve its objectives with a sample size of 14 subjects recruited in Penang, Malaysia. The authors had recommended that a nationwide survey should be implemented to investigate the level of knowledge on acetaminophen among Malaysian consumers.

It is also worth noting that only one parent was interviewed during the study. The data obtained was insufficient to generally assess acetaminophen administration knowledge in regard to paediatric use. In addition, the authors believed that more parents should be recruited. Hence, by incorporating a quantitative method and by specifically recruiting subjects with children and other important selection criteria, this study is anticipated to create a validated tool to explore Malaysian parents' knowledge, practice and perception regarding acetaminophen poisoning in children and the data obtained in the real study will be more representative towards a wider population subsequently.

#### **1.4 Rationale of Study**

Acetaminophen is generally the most common anti-pyretic medication used in paediatric setting. Due to the wide accessibility and the over-the-counter (OTC) nature of the drug, the practice of self-medication of acetaminophen is a common norm in the society (Lubrano *et al*, 2016). Despite of being able to purchase freely without a tighter regulation as compared to controlled prescription drugs, an unadvised use of the drug may lead to severe repercussion in the form of liver toxicity in the event of acetaminophen overdose. Children are at a high risk of acetaminophen overdosage due to the potential tendencies of unintentional ingestion due to easy drug accessibility and poor drug administration practice by their parents. These predicaments could be driven by the lack of health literacy and poor level of perception among the parents. Specifically, the issues as generally highlighted in previous study like improper medication storage (Ali *et al*, 2010), inaccurate source of drug information (Kelly *et al*, 2017), fever mismanagement

(Dawood *et al*, 2010) and the perceived harmlessness of the drug (Popa, 2011) were least explored in paediatric setting.

These parameters are particularly important as they indirectly influence the aspects and factors that may lead to acetaminophen toxicity among children in relation to the level of knowledge, practice, and perception of the caregivers. It is hugely important to incorporate all these factors to form a validated and structured questionnaire as implemented in this study. The validated questionnaire will eventually provide data to the policy makers in the future based on the findings of the real study in order to justify the need for educational programs for the public in countering the occurrence of acetaminophen poisoning in children.

## **1.5 Study Objectives**

### **1.5.1 General Objectives**

To develop a valid and reliable tool that could measure Malaysian parent's knowledge and perception towards acetaminophen poisoning in children

### **1.5.2 Specific Objectives**

- 1) To construct items that can be used as indicators to measure Malaysian parents' knowledge and perception towards acetaminophen poisoning in children
- 2) To determine the face validity of the tool based on face validity index (FVI)
- 3) To determine the content validity of the tool based on content validity index (CVI)

- 4) To determine the construct validity of the tool based on factor analysis and reliability analysis

## **1.6 Research Questions**

- What is the level of knowledge among Malaysian parent's regarding acetaminophen poisoning in children?
- What is the perception of Malaysian parent's regarding acetaminophen poisoning in children?

## **1.7 Research Hypotheses**

### **1.7.1 Hypotheses Development**

The main objective of this research is to develop a valid and reliable tool that could measure Malaysian parent's knowledge and perception towards acetaminophen poisoning in children. The objective of this study is achievable by constructing items that can be used as indicators to measure Malaysian parents' knowledge and perception towards acetaminophen poisoning in children. This study serves as a continuation and improvement of the previous study conducted locally by Tan *et al* in 2015.

In the study titled *An Evaluation of Practices, Perception and Understanding About Use of Acetaminophen (Paracetamol) Among Malaysian Consumers: A Qualitative Study*, the author had developed an instrument to measure the level of perception, understanding, and the rationality of acetaminophen use among Malaysians by conducting semi-structured interviews consisting open-ended questions which allow respondents to express their thoughts and comments pertaining the raised issues freely.

The knowledge of indication, dosage, toxicity of acetaminophen was also evaluated. In contrast, the present study primarily focuses on the knowledge and perception of Malaysian parents towards acetaminophen toxicity in children; a more specific and quantitative research with a larger scale of population.

### **1.7.2 Hypotheses Testing**

Bailey has defined hypothesis as proposition in testable form and predicts a particular relationship between two or more variables. If a researcher thinks that a relationship exists, he should first state it as a hypothesis and then test the hypothesis in the field (Bailey,1978). In contrast, Grinnell's definition of hypothesis is Hypothesis is written in such a way that it can be proven or disproven by valid and reliable data (Grinnell, 1993). On the other hand, Null hypothesis as interpreted by Mourugan and Sethuraman in 2017 is that there is no actual association or relationship between independent and dependent variables. Based on the research framework, the author had developed the hypotheses for this study as follow:

- Hypothesis 1A(H1A) : face validity index for the tool is more than 0.7
- Null hypothesis of H1A : face validity index for the tool is less than 0.7
- Hypothesis 2A (H2A) : content validity index for the tool is more than 0.78
- Null hypothesis of H2A : content validity index for the tool is less than 0.78
- Hypothesis 3A (H3A) : the tool does have construct validity and reliability
- Null hypothesis of H3A : the tool does not have construct validity and reliability



## 1.8 Operational Definition

- Knowledge** Mindfulness or experience-gained familiarity (of a person, fact, or thing); information range of a person; a hypothetical or viable understanding of a subject; dialect, the entirety of what is known, genuine, advocated conviction; certain understanding, as opposed to opinion (Biggam, 2001).
- Practice** To do or perform frequently, routinely, or regularly (Merriam-webster.com, 2019)
- Perception** The means of acknowledging (being mindful of), establishing (gathering and storing), and translating (binding to knowledge) sensory information (Ward, 2015)
- Toxicity** Harmful effect produces by a material property or properties towards biological system (Landis and Yu, 2003)
- Children** A child is defined by The Convention on the Rights of the Child as a person under the age of 18, unless the legal age for adulthood in a particular country's laws set to be younger (United Nations Children's Fund, 2018).
- Older child is defined as a person aged 6 to 9 years old while adolescents age range is 10 to 18 years old (Wang et al, 2002)

## **1.9 Conclusion**

This chapter has basically covered the research background, benefits, justification and the rationale of the study and the objectives as well as the research questions and hypotheses were thoroughly emphasized. The next chapter will further explore the current knowledge on the subject in relation to acetaminophen toxicity in relation to knowledge, practice and perception based on the previous findings.

## **CHAPTER 2**

### **LITERATURE REVIEW**

#### **2.1 Overview**

This chapter covers the current knowledge on the subjects pertaining to this study. It comprises of two main parts of information; 1) the current knowledge, practice, and perception of acetaminophen use based on previous findings and 2) development and validation phases/stages of the questionnaire

#### **2.2 Acetaminophen Poisoning in Children**

The determination of acetaminophen dosage in pediatric population is made based on individual body weight. The administration is at 10-15mg/kg at every 4-6 hour with the maximum dose per day being 90mg/kg (Lubrano *et al*, 2016). However, Goldstein *et al* (2008) states that the recommended dose for acetaminophen in pediatric patients can go up to 15mg/kg to 20mg/kg for children between 3 months to 6 years old (Goldstein *et al*, 2008). Excessive acetaminophen intake which can be due to overdosage or disproportionate frequency of administration per day in a level reaching to the toxic dose of 150mg/kg can subsequently lead to hepatotoxicity (Lubrano *et al*, 2016). This condition requires prompt treatment as any delay can result in liver impairment and death (Lubrano *et al*, 2016). The choice of treatment of acetaminophen poisoning will depend on the severity of the symptoms and the amount of exposure of acetaminophen (Blieden *et al*, 2014). This includes symptom relieving medications like laxatives and activated

charcoal and N-acetylcysteine as an antidote to acetaminophen poisoning (Blieden *et al*, 2014 and Rivera-Panera *et al*, 1997).

Due to the popularity of this acetaminophen use in children, the toxicity of this drug will remain a concern even the incident reports of the toxic effects are very low (Mohd Zain *et al*, 2006). It is identified in recent reviews of several factors that linked acetaminophen with liver toxicity in children which includes children less than 10 years of age and inappropriate dosing, symptoms onset delay after a potentially toxic ingestion, N-Acetyl cysteine treatment initiation delay, non-intentional multiple overdosing, ingestion of another hepatotoxic drug together with acetaminophen, and the use of adult preparation in children (Robert *et al*, 2001).

Liver toxicity in children has also been reported to occur at the recommended dose as well as in the setting of acute overdose. Acetaminophen-related hepatitis can potentially occur due to either chronic overdose following suprathreshold dose ingestion or too frequent administration of appropriate single doses (Kanabar,2017). There are two main factors of acetaminophen poisoning; intentional ingestion for committing suicide and unintentional consumption due to medication error which comprises of incorrect dosing for therapeutic purposes or accidental overdose (Sheen, 2002). It is mentioned by Reivera-Panera *et al* (1997) that the contributing risk factors of liver toxicity is unintentional multiple dosing of hepatotoxic drugs ingestion.

The accidental and therapeutic poisoning of acetaminophen has become one of the most important causes of morbidity and mortality among pediatric patients due to the vast availability and use of the drug in the United States of America (Kapasi *et al*, 1980).

Sheen reported that while the majority of the cases of acetaminophen poisoning is caused by the intentional dosing of supratherapeutic levels for suicidal attempts, a significant proportion of the patients were under 5 years of age. The ingestion of toxic substances by those pediatric patients were mostly unintentional; with the drugs commonly belonged to other family members (Sheen, 2002). It is also noted that the incorrect measuring containers or devices have attributed to drug poisoning in children (Rivera-Panera *et al*, 1997). As recorded by National Electronic Injury Surveillance System (NEISS), which analyzed the emergency department medical records of 63 hospitals in 2006 and 2007 in USA, had estimated that 44% of unintentional overdoses were because of unmonitored and accidental consumption of acetaminophen by children under 6 years old (Blieden *et al*, 2014).

The US hospital discharges (The Nationwide Inpatient Sample) had found that acute liver failure had occurred more in unintentional overdose (16.7%) as compared to intentional overdose (7.7%) in which a similar trend was seen in children (Blieden *et al*, 2014). In a retrospective study of medical charts review between 1988 and 1987 of children below the age of 18 years old, conducted in the USA, it was determined that 53% of acetaminophen overdoses cases were unintentional ingestion and 3% was because of dosage error (Sheen, 2002).

Elsewhere, in the UK, there was an increase of proportion of overdoses which was from 14.3% in 1976 to 42% in 1990 involving paracetamol containing drugs (Sheen, 2002). In Malaysia, it is reported by Mohd Zain *et al* that 10.3% of cases of acetaminophen poisoning in 2006 were involving children below the age of 15 years old.

While the study has shown that cases of acetaminophen poisoning was predominantly caused by intentional ingestion among 16-30-year-old patients, the study does not rule out the significant possibility of accidental administration of the drug by children (Mohd Zain et al, 2006).

Ever since the authorization of acetaminophen by the United States Food and Drug Administration (FDA) in 1951, numerous researches have been conducted on the drug, with an extravagant number of reports publishing its toxicity and adverse reactions (Goldman,2013). A study conducted locally in Penang, Malaysia has revealed that poisoning due to acetaminophen is extraordinary; which accounted for the highest number of drug related poisoning in the country (Mohd Zain *et al*, 2006).

One of the causes accidental acetaminophen poisoning as reported by Arena (1959) is due to exploration, questioning, sampling, trial, and error phase which are formed as part of children developmental process. The attractive and bright colour, shape, packaging, taste of the drug could well influence the children to ingest the medication themselves without parental supervision (Arena, 1959).

## **2.3 Practice of the uses of Acetaminophen and Management of Fever**

### **2.3.1 Fever Phobia Phenomenon Among Parents**

Fever can be defined as a homeostatical increase of temperature and is one of the most common medical conditions in children (Kelly *et al*, 2017). It was stated that fever

occurs at the temperature of 38-degree Celsius and above. However, this condition does not necessitate urgent treatment as the current guidelines only recommend the use of antipyretics when the children are in pain or to reduce discomforts (Kelly *et al*, 2017).

On the other hand, Lubrano *et al* has mentioned that the current guideline has indicated that the treatment of anti-pyretic should only commence when the temperature reaches 39 or 40 degree Celsius. (Lubrano, 2017). A study has indicated that fever is the usual reason of why children are brought to a clinic for medical consultation (de Bont *et al*, 2015). This is in line with the claim made by Lagerlov *et al* that fever is the most common chief complaint as it represents more than 30% of admittance to pediatric clinic (Lagerlov *et al*, 2003).

It has been reported in recent years that the phenomenon of fever phobia has been recognized among parents. Many parents perceive fever as a health threat and not as a crucial element of homeostatic response of defense mechanism against infection (Lubrano *et al*, 2016). This predicament is normally associated with the unnecessary increase use of anti-fever drugs as mean of self-medication with the most common one being acetaminophen. In addition, Lagerlov *et al* has also indicated that the practice of acetaminophen administration among parents are hugely influenced by their perceptions about fever (Lagerlov *et al* 2003). The great concerns of serious fever complications such as febrile status epilepticus and heat stroke are extremely rare and is therefore not justified (Schmitt, 1980). Schmitt *et al* has discovered that 85% of the subjects in his study has treated their children's fever aggressively by giving antipyretic medication even before the temperature reaching 38.9-degree Celsius (Schmitt, 1980).

The drive of this phenomenon is triggered by the additional symptoms that may appear in the children which is namely lethargic, tearfulness, insomnia, lack of fluid intake, and abnormal behaviour (de Bont *et al*, 2015). The parents were then developed anxiety and fear of going to sleep as they would not be able to monitor their children (de Bont *et al*, 2015). This finding is supported by Kelly *et al* (2017) as they have found that majority of the parents developed anxiety in regards of the effects and outcomes of fever (Kelly *et al*, 2017). However, parents with more experience in managing their children have shown to be less anxious possibly due to previous encounter with uncomplicated infections with other children and may have perceived them as a normality in childhood (de Bont *et al*, 2015). In contrast, Barrett and Norton has recommended that patients with a single child to be given extra attention when being prescribed or counseled towards acetaminophen dosing as they are regarded as inexperienced and lack of acetaminophen dosing knowledge (Barrett and Norton, 2000).

De bont *et al* have also mentioned in their study that the level of fear among parents are proportional to the temperature level of their children during fever when in fact, the temperature alone is not the exclusive indication of illness severity (de Bont *et al*, 2015). This claim is in line with the study performed by Lubrano *et al* in which 74% of caregivers had started antipyretics for their children at a temperature below 38.4 degree Celsius when other guidelines have indicated that pharmacological intervention should be only begun in temperatures exceeding 40 degree Celsius or more than 39 degree Celsius if the child has shown signs of discomforts (Lubrano *et al*, 2016 and Schmidt, 1980). Schmidt has however claimed that discomforts do not usually occur until the temperature reaches 39.5-degree Celsius as many active and cheerful children may tend



to have a high body temperature in which it may reach as high as 40 degree Celsius (Schmidtt, 1980). This sort of increase in body temperature should not be regarded as life threatening (Schmidtt, 1980).

Dawood *et al* (2010) has mentioned that there are two factors that influence the parents' response towards children during illness; sense of situational control when faced with their children's ailments and the perception of danger that may be inflicted by the said illness. A study by Lagerlov *et al* (2003) has found that inexperienced parents may feel anxious and helpless due to their lack of knowledge in judging their children's illness. They believe acetaminophen has the healing power and the administration of the drug will somehow help them mastering the situation as they feel that they do not have to be solely dependent on the healthcare professionals anymore (Lagerlov *et al*, 2003).

The study by Allotey *et al* (2004) on the use of OTC products among Australian children corresponds to the finding as they have found that parents are prone to give medications to manipulate the behaviour of their children which are seemingly testy and vexing especially for children below 5 years old. They have regarded acetaminophen as a calming, sedating, or mood boosting solution for their children (Allotey *et al*, 2004). As a consequent to fever phobia, parents may prone to administer aggressive fever therapy by giving higher doses of acetaminophen or excessive frequency of daily administration which will in turn lead to a daily overdose of more than 90mg/kg/day (Lubrano *et al*, 2016). This predicament is especially dangerous as excessive doses or intake frequency may yield an increase acetaminophen serum concentration with the toxicity being associated with levels above 120 µg/ml (Lubrano *et al*, 2016).

Schmidtt has recommended that it is important to educate parents that it is unnecessary to treat low-grade fevers with anti-fever medications except with light clothing and encouragement of fluid intakes. The sole reason of treating low-grade fever is only to reduce discomfort in children (Schmidtt, 1980). He has also stressed on the need of taking temperature prior to each administration dose of antipyretic to children in order to avoid pointless fever therapy. Schmidtt has also noted that parents need to be educated on observing the child's signs and symptoms more rather than just looking at the temperature. The sign and symptoms that should be of great concern are dyspnoea, difficult or painful urination, delirium, whimpering, irritability or pain. Barret on the other hand recommends that parents need to be made aware of the possibility of hepatotoxicity might occur instead of rapid relief if parents administer acetaminophen to their children in excessive dose (Barret and Norton, 2000). The need for education is essential as Gilbertson *et al* (1996) mentioned in his study that only 10% of the respondents were aware that paracetamol may lead to hepatotoxicity and death.

### **2.3.2 Risk of Double Dipping**

The misuse of acetaminophen containing product in children is divided into three category; inappropriate dosing out of a single ingredient acetaminophen containing product, exceeding 90mg/kg/day dose of acetaminophen, and the perception of it would be harmless to administer two or more acetaminophen containing products in combination with the latter is described as “double dipping” (Wolf *et al*, 2012). The findings from the study by Wolf *et al* has concluded that more than half of the subjects would overdose by administering two over the counter products with acetaminophen

being the active ingredient. The findings have also suggested that the subjects were unable to identify the active ingredient in their medications and did not comply to the packaging label and instructions causing a significant increase of threat to public health. Wolf has also suggested that one of the factors causing the tendency of double dipping phenomenon is the variation of symptom relief description among products which could be suggestive that the products (even though in reality containing acetaminophen) may contain different medication and that the use in combination might be harmless. In order to avoid double dipping, Wolf has recommended that the public needs to be educated on the need of knowing and checking the active ingredient of any medications and to comply with instructions and precautions that come with the packaging insert (Wolf *et al*, 2012).

### **2.3.3 Safety Measure in Preventing Accidental Poisoning**

Shone *et al* (2011) has recommended that the safe self-administering age of children should begin at a minimum of 11 to 12 years old as children are perceived as mature enough to take medications on their own at that age. However, Allotey *et al* (2004) have mentioned in his study that parents are promoting the self-medication trend for their children at even a younger age. It was found that 67% of subjects aged 6 years old were reportedly self-consumed their medications which were taken from another person at their home without adult consultation. This behaviour is not commendable as Arena (1959) has explained in their study that the nature of exploiting, questioning, sampling, and trial and error in younger children are the ones of many reasons of accidental drug poisoning.

The nature of certain medications which are characterized by their bright colour, attractive shape and packaging, sweet taste due to sugar coating are the factors of accidental ingestion among children (Arena, 1959). This predicament can be avoided with precautionary labeling and safety packaging measures which should be of the responsibility of the manufacturers and suppliers (Arena, 1959). This statement is supported by Kapasi *et al* in which they have claimed that child resistant packaging has contributed to a significant decrease in a total number of accidental poisoning cases with acetaminophen (Kapasi *et al*, 1980).

In a study conducted in Malaysia by Ali *et al*, it is a common practice that the subjects to share or consume left-over medications from their siblings or friends; a habit most commonly adopted by women (Ali *et al*, 2010). This unsafe medication administration behaviour should be explored among subjects in this study as the dosing for children are determined from their individual body weight and any discrepancy of dosing might result in inappropriate dose.

It is noted in a study conducted locally by Ali *et al* that only half of the respondents would check the expiry date of medications before administration (Ali *et al*, 2010). Post expiry date, most of the respondents would end up throwing the drugs into a rubbish bin; an act regarded as non-environmentally friendly as well as increasing the risk of accidental ingestion due to drugs being easily reachable by children (Ali *et al*, 2010).

In 2010, the Ministry of Health Malaysia has implemented “Return Your Medicines” program in the hope of practicing safe disposal of medications. The ministry

has noted that among the factors that contribute to the excess of medications are; 1) change of treatment regiment, 2) cessation of treatment regimen, 3) medications non-compliance, 4) deceased patients, and 5) medications obtained from multiple sources that cause polypharmacy. The return policy has stated that medications that are no longer used may be returned to the pharmacy counter or medicine return box provided at all pharmacy facility in MOH hospitals and health clinics (Pharmaceutical Services Programme, 2019).

#### **2.4 Basic Knowledge of Parents Regarding Acetaminophen and Fever**

Biggam has cited in his article the definitions of knowledge (Biggam, 2001);

- a) the awareness or familiarity acquired from involvement of a person, event, or fact
- b) range of information of a person.
- c) a practical understanding or a theoretical know-how of a subject
- d) the sum of what is known.
- e) factual, justified idea; certain understanding, in contrast to opinion.

Other definitions of knowledge which can be taken from the Merriam-Webster Online Dictionary is the factual information or condition of knowing something with familiarity gained through involvement or affiliation. The very same source has further defined knowledge as the truth or state of being conscious of something, the range of one's information or understanding, and the entirety of what is known: the body of truth, information, and principles obtained by humanity (Merriam-webster.com, 2018).

In a study conducted by Tan *Et al* in 2015 on the evaluation of practices, perceptions, and understanding about use of acetaminophen among Malaysia consumers, has claimed that there is lack of knowledge among interviewed respondents pertaining acetaminophen syrup dosing; commonly consumed by children (Tan *et al*, 2015). Another correlated finding by Kelly *et al* (2017) as their team has found that the lack of ability in defining and identifying the occurrence of fever in children among parents in Ireland. It was found that the knowledge of fever among parents is deficient as they have mostly defined febrile temperature as either below or above the correct level (Kelly *et al*, 2017).

Locally in Malaysia, it was concluded in a study conducted by Dawood *et al* (2010) that most parents have insufficient knowledge and misconception on how to manage fever among their children. The misinterpretation of fever may lead to the inappropriate use of antipyretics and hence putting the consumers at risk of sub-therapeutic doses and even worst; acetaminophen poisoning (Kelly *et al*, 2017).

In this study, the knowledge of Malaysian parents pertaining the toxicity of acetaminophen will be assessed. Kelly *et al* in her study has found that the main source of information for fever and anti-pyretic related issues regarding their children are from the internet which constitutes more than 50% of the parents. It was also shown in study conducted locally by Dawood *et al* that educated parents would have better fever treatment management for their children as they tend to obtain information from reliable sources such as the advice from doctors and pharmacist (Dawood *et al*, 2010). This study has also indicated that most parents tend to read the labels of medication prior to administration of antipyretics to children when they are having fever. However, other

sources of information that can be ambiguous such as friends, family, magazines and the internet may also enter the frame (Dawood *et al*, 2010). Hence, it is important to explore the reliability of the information obtained (Kelly *et al*, 2017).

One of the key factors that could improve medications related knowledge among Malaysian parents is a quality healthcare and communications between physician and patients or in this case, the parents or guardians of the patients. It is deduced that poor communication between parents and physician may increase the risk of adverse events as it is important that both parties share equal responsibility towards improving the lines of communication in order to ensure that an open, truthful, and two-way communications achieve (Popa, 2011). Lagerlov *et al* has mentioned in his study that physicians seldomly provide a comprehensive information on the side effects of acetaminophen when prescribing and that the parents were not overly concerned pertaining that matter (Lagerlov *et al*, 2003).

Barrett and Norton has however claimed that even when a doctor has prescribed a proper dose for a child, there studies that indicated that parents would not comply with the instructions at home as only 38% were able to remember on how to give the medications accurately with only 24% can recall the medication's name. This sort of knowledge deficiency may pose a significant threat to their children's health (Barrett and Norton, 2000).

In a study conducted in the USA, which was participated by 266 adolescents and young adults, it was found that lack of health literacy was the main reason of poor

understanding and inappropriate use of acetaminophen containing products. The lack of knowledge may lead to susceptibility to misinterpretation of product label which might potentially cause overconsumption of acetaminophen (Tan *et al*, 2015). As reported in a previous study, a study in Penang which focused on self-medication behaviour amongst female students had discovered 8.3% of accidental drug poisoning was due to poor knowledge on medications consumed (Ali *et al*, 2010). However, Håkonsen and Hedenrud (2017) had mentioned that women were found to be more knowledgeable in terms of acetaminophen content and dose as compared to their male counterpart. Furthermore, it was also noted in their study that women were able to predict overdose of acetaminophen better than men and besides of proving to be more cautious in administering the drug (Håkonsen and Hedenrud, 2017). Hence, it is worth studying a comparison between acetaminophen administration knowledge and perception between both genders locally.

Another factor influencing dosing error is the level of education and literacy of the parents (Chang *et al*, 2012). This was evident in a study conducted by Chang *et al* (2012) in which the subjects who had not completed high school would misinterpret the labelling instruction more often. It was also mentioned in the article that the limitation of English proficiency could be a stumbling block to comprehension of medications label and would increase the adverse effects risk towards the medication (Chang *et al*, 2011). In contrast, in the study conducted by Shone *et al* (2011), the misinterpretation of label information even by the English speakers can be due to several factors; label information being misread, comprehending the label instruction but misremember the details later,



and the subjects are not accustomed with reading the label information given (Shone *et al*, 2011).

Tan *et al* mentions in his study that based on the research conducted in Brazil, Canada, and Saudi Arabia, it was reported that more than half parents and caregivers have given the wrong dose of acetaminophen to their children. In comparison with his study conducted in Malaysia, the respondents are mostly not aware with the dosing of the pediatric acetaminophen syrup. In addition, the results have also indicated the lack of understanding towards acetaminophen poisoning. This predicament also evident in a study conducted in Australia and United States of America as more than half of the parents did not know the outcome of acetaminophen poisoning which would cause liver, stomach, and kidney injury (Tan *et al*, 2015). As part of the effort in increasing the public knowledge on the dangers of OTC painkillers, The U.S. Food and Drug Administration (FDA) had moved to implement a new labelling requirement which comprised of the warnings of side effects and potential toxicity namely gastrointestinal bleeding and hepatotoxicity (Popa, 2011).

## **2.5 Perception on the Use, Dosage, and Indication of Acetaminophen**

Perception on the other hand occurs as a result of perceiving. It is defined by Angell (1910) as the realization of specific material things present to sense. In contrast, Online Oxford dictionaries define perception as the ability to see, hear, or become aware of something through the senses and further defined as the way in which something is interpreted (Oxford Dictionaries | English, 2018).