DETERMINING MALARIA RISK FACTORS IN ABUJA, NIGERIA USING VARIOUS STATISTICAL APPROACHES

OGUNTADE EMMANUEL SEGUN

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By

OGUNTADE EMMANUEL SEGUN

Thesis Submitted to the School of Graduate Studies, Universiti Putra Malaysia, in Fulfilment of the Requirements for the Degree of Doctor of Philosophy

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DEDICATION

This thesis is dedicated to God Almighty, the giver of life and source of inspiration and wisdom.

Abstract of thesis presented to the Senate of Universiti Putra Malaysia in fulfilment of the requirement for the degree of Doctor of Philosophy

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Chairman : Shamarina Shohaimi, PhD
Institute : Institute of Mathematical Reseach

Malaria is a widespread infectious disease in the tropics with significant health threat to the inhabitants, especially, the low income earners residing in the remote areas. Studies have identified many driving factors of malaria prevalence; however, there are still missing links as malaria remains endemic in developing nations despite various interventions instituted against it especially in Sub-Saharan Africa (SSA). Previously, several decision support tools have been used to support expert-based opinion in the field of sciences for malaria modelling. However, these conventional techniques have problems of incorporating prior belief, uncertainty representation, missing values, expert judgement and hierarchical relationships among variables. These problems, however, can be overcome using belief networks, which has not been fully explored. Therefore, this current study is aimed at deriving a Bayesian belief network (BBN) for malaria epidemic in Abuja, Nigeria. A total of 384 respondents took part in the present study which is comprised of two phases: pre- and post-intervention. Participants were randomly selected based on stratified sampling according to residential areas. Data on socio-demographic characteristics, knowledge, attitude and practice (KAP) related to malaria and intervention measures were collected using validated questionnaires. The climate data were obtained from the data bank of Agricultural Development Project Gwagwalada, Abuja, Nigeria (1997-2014). Data collected were used for the multilevel analysis, Markov Chain Monte Carlo (MCMC) simulation via WinBUGS algorithm and influence diagrams for BBNs. A non-informative prior was assumed for Bayesian logistic regression and posterior samples generated at different sizes. The spatial heterogeneity in malaria incidence patterns at various sites were estimated with Moran I and semivariogram models. Using BBNs, different learning strategies were explored and compared with k-fold using negative entropy loss. The optimal model based on the parsimony principles was obtained from the hill climbing algorithm with score metrics. The results revealed a high reported cases at the baseline data collection possibly

occasioned by the observed low malaria KAP levels at the pre-intervention study. A Wilcoxon signed rank test showed a significant change in incidence scores of households in the district considered for pre- and post-test interventions. The study revealed that there was an association between level of usage of the intervention measures and malaria cases. The non-usage increases the odds of the disease by 1.79 ([95% CI: 1.06, 3.03]; $p=0.028$) and 1.67([95% CI: 1.06, 2.64]; $p=0.029$) for insecticide-treated nets (ITNs) and window and door nets (WDNs) respectively. The multilevel analysis based on logistic regression identified gender, socio-economic status (SES), household size and intervention measures as predictors while Monte Carlo study of local malaria predictors' results was comparable to logistics especially when n is large (150,000) and with a lower precision level (0.000001). The Moran I index using distance decay method to generate the weight gave a spatial autocorrelation of -0.33. The spatial outliers (a high-low and low-high outliers) of Moran I results reflected an alternation in incidence patterns. To account for spatial random effects in the models, semivariogram autocorrelation models were incorporated and Moran hypothesis tested. The results revealed that the model without autocorrelation structure has the lowest Bayesian information criterion (BIC) value of -6.31, while the highest value of 0.66 was observed with autoregressive error structure of order 1, hence, there was no spatial autocorrelation in the malaria incidence in the study area ($p=0.328$). Therefore, this was not incorporated in BBN models. Based on cross-validation analysis, the score-based algorithm outperformed the constraint-based algorithms in the structural learning. Using hill climbing from search and score algorithms, the Bayesian network analysis revealed that there were associations among the network covariates, while cofounding effects of SES were observed. The BBNs developed revealed that SES, household size and education level have the highest influence on reported cases as variations in response due to global sensitivity of network nodes. Based on the data, an empty graph (a network representing models with the usual independent assumption) was also learned and the results compared with BBNs. However, the loglikelihood and other metrics scores of an empty graph were lower than that of the BBNs. Thus, the BBNs represent the dependencies in the variables better than assuming independence of all the variables. This present study provides a detailed record on the epidemiology of malaria in the study area, Abuja, Nigeria. This in turn could be used to formulate effective control and preventive measures for malaria. The study shows that there is a significant influence of household characteristics on the incidence of malaria. The BBN is expected to contribute to the existing literature on malaria epidemic and in identifying the significant predictors of malaria at household and community levels within the study area.

Abstrak tesis yang dikemukakan kepada Senat Universiti Putra Malaysia sebagai memenuhi keperluan untuk ijazah Doktor Falsafah

MENENTUKAN FAKTOR RISIKO MALARIA DI ABUJA, NIGERIA MENGGUNAKAN PELBAGAI KAEDAH STATISTIK

Oleh

OGUNTADE EMMANUEL SEGUN

Disember 2018

Pengerusi : Shamarina Shohaimi, PhD
Institut : Institut Penyelidikan Matematik

Malaria adalah penyakit berjangkit yang menular terutamanya di kawasan tropika dan mengancam kesihatan penduduk khasnya yang berpendapatan rendah dan tinggal di kawasan terpencil. Walaupun banyak kajian telah dijalankan untuk mengenalpasti faktor risiko malaria, ia kekal endemik di negara membangun meskipun pelbagai langkah pencegahan telah diambil terutama di sub-Sahara Afrika (SSA). Sebelum ini, beberapa kaedah sokongan keputusan telah digunakan untuk menyokong pendapat berasaskan pakar dalam bidang sains untuk pemodelan malaria. Walau bagaimanapun, teknik konvensional ini mempunyai kekurangan dari segi menggabungkan amalan sebelumnya, perwakilan ketidakpastian, nilai-nilai yang hilang, penilaian pakar dan hubungan hierarki di kalangan pembolehubah. Ini dapat diatasi menggunakan rangkaian kepercayaan yang masih belum diteroka sepenuhnya terutama berkaitan malaria. Oleh itu kajian ini bertujuan membentuk rangkaian kepercayaan Bayesian (BBN) untuk wabak malaria di Abuja, Nigeria. Seramai 384 responden telah mengambil bahagian dalam kajian ini yang melibatkan dua fasa iaitu pra-intervensi dan pasca-intervensi. Kaedah pensampelan berstrata rawak mengikut kawasan kediaman telah digunakan untuk mendapatkan responden. Data sosio-demografi, pengetahuan, sikap dan amalan (KAP) tentang malaria dan kaedah intervensi telah diperolehi melalui borang soal-selidik yang telah disahkan. Data iklim diperolehi daripada bank data Projek Pembangunan Pertanian Gwagwalada, Abuja, Nigeria (1997-2014). Data yang dikumpulkan ini digunakan untuk analisis pelbagai peringkat dan simulasi Markov Chain Monte Carlo (MCMC) melalui algoritma WinBUGS dan rajah pengaruh untuk BBN. Pengagihan sebelumnya yang tidak bermaklumat telah diandaikan untuk regresi logistik Bayesian dan sampel posterior yang dihasilkan dalam pelbagai saiz. Heterogeniti spatial dalam corak insidens skor malaria di pelbagai kawasan dianggarkan menggunakan model Moran I dan semivariogram. Melalui BBN, strategi pembelajaran yang berbeza telah diterokai dan dibandingkan dengan k-fold dengan menggunakan kerugian entropi negatif. Model optimum berdasarkan prinsip parsimoni diperolehi daripada algoritma pendakian bukit dengan skor. Hasil analisis menunjukkan jumlah kes yang dilaporkan tinggi pada pengumpulan data asas yang mungkin disebabkan oleh tahap KAP malaria yang rendah dalam kajian pra-intervensi. Ujian pangkat Wilcoxon menunjukkan perubahan signifikan dalam skor insiden isi rumah di daerah yang dipertimbangkan untuk pra-intervensi dan pasca-intervensi. Dapatan analisis menunjukkan bahawa terdapat kaitan antara tahap penggunaan kaedah intervensi dan bilangan kes malaria. Ketidakpenggunaan meningkatkan kemungkinan mendapat malaria kepada 1.79 ([95% CI: 1.06, 3.03]; p = 0.028) dan 1.67 ([95% CI: 1.06, 2.64]; p = 0.029) untuk jaring yang dirawat racun serangga (ITN) dan jaring bagi tingkap dan pintu (WDN). Analisis pelbagai peringkat berdasarkan regresi logistik mengenal pasti jantina, status sosio-ekonomi, saiz keluarga dan kaedah intervensi sebagai peramal manakala kajian Monte Carlo mengenai hasil ramalan malaria tempatan adalah setanding dengan logistik terutamanya apabila n adalah besar (150,000) dan dengan tahap ketepatan tinggi (0.000001). Indeks Moran I global menggunakan kaedah peluruhan jarak jauh untuk menghasilkan berat memberikan autokorelasi spatial pada -0.33. Pencilan ruang hasil Moran I mencerminkan perubahan dalam pola insidens. Untuk mengambil kira kesan rawak ruang dalam model, model autokorelasi semivariogram dimasukkan dan hipotesis Moran diuji. Hasil kajian menunjukkan bahawa model tanpa struktur autokorelasi mempunyai nilai kriteria maklumat Bayesian terendah (BIC) -6.31, manakala nilai tertinggi 0.66 diperhatikan dengan struktur kesilapan autoregressive order 1, maka tiada autokorelasi spasial dalam kejadian malaria di kawasan kajian (p = 0.328). Oleh itu, ini tidak dimasukkan dalam model BBN. Berdasarkan analisis silang-pengesahan, algoritma berasaskan skor mengatasi algoritma berasaskan kekangan dalam pembelajaran struktur. Menggunakan kaedah pendakian bukit daripada algoritma carian dan skor, analisis rangkaian Bayesian menunjukkan perkaitan antara kovariat rangkaian, manakala terdapat kesan bersama SES. BBN yang dibangunkan menunjukkan bahawa status sosioekonomi, saiz isi rumah dan tahap pendidikan mempunyai pengaruh tertinggi terhadap kes malaria yang dilaporkan sebagai variasi kesan tindakbalas terhadap kepekaan global nod rangkaian. Berdasarkan data, graf kosong (rangkaian mewakili model dengan andaian bebas yang biasa) juga dipelajari dan hasilnya dibandingkan dengan BBNs. Walau bagaimanapun, log kemungkian dan skor metrik graf kosong lebih rendah daripada BBN. Oleh yang demikian, BBN mewakili kebersandaran dalam pembolehubah yang lebih baik daripada mengandaikan kebebasan semua pembolehubah. Kajian ini menyediakan rekod terperinci tentang epidemiologi malaria di Abuja, Nigeria. Hasil dapatan kajian ini boleh digunakan untuk merumuskan kawalan berkesan dan langkah-langkah pencegahan malaria. Selain itu, kajian ini menunjukkan bahawa terdapat pengaruh signifikan ciri-ciri isi rumah terhadap insiden malaria. Model BBN dijangka menyumbang kepada kajian sedia ada mengenai wabak malaria dan mengenal pasti peramal malaria yang signifikan di peringkat isi rumah dan komuniti di kawasan kajian.

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This thesis was submitted to the Senate of Universiti Putra Malaysia and has been accepted as fulfilment of the requirement for the degree of Doctor of Philosophy. The members of the Supervisory Committee were as follows:

Shamarina Shohaimi, PhD
Associate Professor
Faculty of Science
Universiti Putra Malaysia
(Chairperson)

Meenakshii a/p Nallapan, PhD
Senior Lecturer
Faculty of Science
Universiti Putra Malaysia
(Member)

Mohd Noor Hisham Mohd Nadzir, PhD
Senior Lecturer
Faculty of Science
Universiti Putra Malaysia
(Member)

____
ROBIAH BINTI YUNUS, PhD
Professor and Dean
School of Graduate Studies
Universiti Putra Malaysia

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This is to confirm that:

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Signature: ______________________________
Name of Member of Supervisory Committee: ______________________________

Signature: ______________________________
Name of Member of Supervisory Committee: ______________________________

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LIST OF ABBREVIATIONS

ACF	Autocorrelation Function
ACT	Artemisinin Combination Therapy
AIC	Akaike Information Criterion
AR	Autoregressive Model
ARMA	Autoregressive Movind Average
BASICS	Basic Support for Institutionalizing Child Survival
BBN	Bayesian Belief Network
BDE	Bayesian Dirichlet
BDS	Bayesian Dirichlet Sparse
BIC	Bayesian Information Criterion
BLR	Bayesian Logistic Regression
BMA	Bayesian Model Averaging
BUGS	Bayesian Inference Using Gibbs Sampling
CI	Confidence Interval
CPT	Conditional Probability Table
CV	Coefficient of Variation
DAG	Directed Acyclic Graph
DDT	Dichloro Diphynl Trichloroethane
EIR	Entomological Inoculation Rate
FCT	Federal Capital Territory
FLR	Frequentist Logistic Regression
FMOH	Federal Ministry of Health
GAC	Gwagwalada Area Council
IRS	Indoor Residual Spray

ITNs	Insecticide-Treated Nets
KAP	Knowledge, Attitude and Practice
K2	Cooper and Herskovits
K-S	Kolmogorov-Smirnov
LL	Log-Likelihood
LRM	Logistic Regression Model
LSMOH	Lagos State Ministry of Health
MBDE	Bayesian Dirichlet (intervention Data)
MBR	Man Biting Rate
MCMC	Markov Chain Monte Carlo
MLE	Maximum Likelihood Estimation
MPT	Marginal Probability Table
NGO	Non-Governmental Organization
NMCP	National Malaria Control Programme
NMCPP	Nigeria Malaria Control and Prevention Program
NPC	National Population Commission
RBM	Roll Back Malaria
SANDH	South Africa National Department of Health
SE	Standard Error
SES	Socio-economic Status
SSA	Sub-Sahara Africa
SW	Shapiro-Wilk
WDNs	Window and Door Nets

CHAPTER 1

INTRODUCTION

1.1 Background

Malaria is a protozoan disease caused by a single cell parasite called *Plasmodium* and transmitted by infected female mosquitoes of the genus *Anopheles* (Afoakwah *et al*., 2018; Mohammadkhani *et al*., 2016), as it seeks blood for its egg development (Yahaya, 2012). The malaria infection is the product of interactions between the human intermediate host, mosquito vector which lives symbiotically with the *Plasmodium* agent and the immediate environment where the various interactions take place. The suitability of the various environmental factors predisposes the disease prevalence as the host vector strives well within certain favourable environmental conditions (Ssempiira *et al*., 2018; Lingala, 2017; World Health Organization (WHO), 2016; Babajide *et al*., 2015; Siraj *et al*., 2014;). Hence, the spatial distribution of the numerous strains of mosquitoes which serve as a vector of *Plasmodium* networking is enhanced. For instance, an average temperature between 18℃-30℃ favours the breeding of mosquitoes and malaria parasites (Beck-Johnson *et al*., 2013). Also, a relative humidity of 60% - 90% enhances their breeding and multiplication while a relative humidity below 60% decreases their population (Akinbobola & Omotosho, 2013).

Malaria is the most prevalent tropical parasitic disease with most of the tropical and subtropical countries endemic in recent times (Osakunor, Sengeh, & Mutapi, 2018). More than one-third of the world's population is at risk with the adverse consequences of the disease affecting children, adults and communities (Bocoum *et al*., 2014). It is the most deadly communicable disease with a mortality rate of two children per minute in Sub-Saharan Africa (SSA) (Ashikeni, Envuladu, & Zoakah, 2013; De-Castro & Fisher, 2012; WHO, 2003). In 2015, there were 438,000 deaths from estimated 214 million malaria cases worldwide (Haddawy *et al*., 2018). Only ten percent (43,800) of the global deaths occurred outside Africa while the remaining 90% (390,200) of the global deaths occurred in SSA (Adu-Prah & Tetteh, 2015; WHO, 2015). Asia has the second highest cases and deaths from malaria (Roll Back Malaria (RBM), 2012). Basically, malaria occurs in 106 countries worldwide out of which 35 countries are responsible for the majority of total annual global deaths (Andrew, 2014; ; Nyarko & Cobblah, 2014; Mohon *et al*., 2012; Kitua *et al*., , 2011; WHO, 2010). Most of these high-risk countries are in Africa and South-East Asia (RBM, 2009). While the disease has been eliminated in Northern African countries (Snow *et al*., 2012; Africa Malaria Report (AMR), 2003), the SSA countries remain in the control stage of the WHO malaria elimination continuum (control, pre-elimination, elimination and prevention of reintroduction) (Onyiri, 2015; WHO, 2007). There exists more malaria cases per thousand populations in SSA nations and in particular Nigeria where over 97% of the population are at risk of the disease (Uzochukwu, Ossai, Okeke, Ndu, & Onwujekwe, 2018).

To date, despite interventions and control initiatives globally, the malaria trend persists and there exist uncertainties regarding the disease trend in near future (Usman & Adebayo, 2011; Alaba & Alaba, 2009). Malaria trend, however, hangs on the influence of weather variability with other ecological factors, socio-cultural and human related factors which continue to play a major role in the dynamism of the disease transmission. Such environmental impact is enormous and remains an open subject for consideration.

1.2 Problem Statement

Malaria endemicity leads to economic loss, poverty and lack of longevity for the populace in endemic nations (Afoakwah et al., 2018). Malaria is commonly associated with poverty since the prevalence trends observed in low gross domestic product (GDP) nations were high (Gimba, 2014; WHO, 2006). Therefore, predictions and target interventions are vital elements in effective control of malaria (Eunice *et al*., 2017; Mohammadkhani *et al*., 2016; WHO, 2012). There is a need to study the framework and methodology to further understand the disease causes, trends and influencing variables so as to enhance early warning, disease epidemiology, effective measures and interventions (Evans & Adenomon, 2014). There are a number of techniques used and documented in literature on modelling malaria incidence (Eunice *et al*., 2017; Adigun *et al.*, 2015; Zinszer et al., 2015; Zinszer et al., 2012). However, there exist gap in literature as some of the proposed paradigms were insufficient in selecting best variant of malaria risk factors as preliminary analysis is not capable of capturing the spatial-temporal random effects (Andrew, 2014; Yadav, Dhiman, Rabha, Saikia, & Veer, 2014) and cannot account for uncertainty in the model parameters (Berger, 1980). Also, issues of assuming known dependencies between response and covariates of interest in the classical models instead of actual dependencies among variables serve as another open problem in the conventional approaches (Haddawy et al., 2018; Landuyt, Broekx, & Goethals, 2016; Nguefack-Tsague, 2011).

Due to local movement of the disease vectors and variations in the climate conditions across communities, spatial autocorrelation or heterogeneity in incidence patterns need be incorporated into such models for effective design of interventions towards disease control (Ssempiira *et al*., 2018). Most notable literature focused on preliminary analysis or used predetermined variables (Andrew, 2014) while others purposely excluded some natural risk factors which are paramount in scaling up interventions possibly due to paucity of reliable data (Amoran, 2013; Noor, Omunbo, Amin, Zurovac, & Snow, 2006). There is a need for a more accurate tool to identify malaria risk factors that compensates the inadequacies of existing models. This study, therefore explored the potential of Bayesian belief networks (BBNs) in malaria modelling.

To date, in Nigeria, there is inadequate information regarding the exact number of incidences and deaths due to malaria in rural areas where there are so many unreported cases (Uzochukwu et al., 2018; Eunice *et al*., 2017). Also, shortage of geostatistical data on basic meteorological variables such as temperature, humidity, precipitation and land covered among others constitute a great problem in malaria epidemiological research. Additionally, weak and fragmental nature of existing health information systems and variation in weather condition leads to sporadic change in malaria incidence (Adu-Prah & Tetteh, 2015; Badaru, Adejoke, Abubakar, & Emigilati, 2014). The malaria trend constitutes a problem which the present study seeks to answer through the following questions:

(1) What are the risk factors responsible for the prevalence of malaria?
(2) What are the individual, group or collective effects of the risk factors on the prevalence of malaria?
(3) Does the existing intervention cause any significant change or reduction in the prevalence of malaria?
(4) Does altering some of the parameters of the Bayesian network nodes produce a significant effect in mitigating the epidemic of malaria?

1.3 Significance of the Study

The results of this study will delineate the causes, transmission and prevention of malaria coupled with solving problems relating to attitude and cultural beliefs about the epidemics in the study area. The research will also help policy makers to improve decision-making process in public health services related to malaria. A graphical probability network, a BBN template for local malaria risk factors in Nigeria will also be created. Likewise, assist the government, support health groups and organizations both locally and internationally to access level of effectiveness of various measures employed to circumvent malaria epidemics. Add value to the growing body of knowledge and provide community data on key malaria indicators in Nigeria. Finally, it will provide a BBN template that can be used for other vector-borne diseases in Nigeria.

1.4 Objectives

The general objective of this research is to build a hierarchical model depicting complex inter-relationships of malaria risk factors capable of identifying key malaria predictors in the Federal Capital Territory (FCT) Abuja and by extension Nigeria. Such a model, when developed is capable of incorporating uncertainty in the parameter of interest and makes valid inferences which can help policy makers formulate intervention measures to curtail the disease prevalence. Also, a Bayesian probability network is developed to incorporate expert opinions and prior belief regarding the network nodes in the formulated belief network.

Specifically, the study intends to:

(1) To compare pre- and post-intervention knowledge, attitude and practice (KAP) on malaria awareness at local communities and determine its efficacy
(2) To identify climate risk factors, demography and socio-economic characteristics as well as control/prevention intervention variables associated with malaria infections in Abuja using two different approaches: logistic regression model and Monte Carlo Markov Chain (MCMC) simulation using Gibbs sampling.
(3) To assess spatial heterogeneity in incidence patterns across Abuja
(4) To derive a Bayesian belief network (BBN) for malaria epidemics in Abuja.

1.5 Scope of the Study

This study covers Gwagwalada Area Council (GAC), Abuja, Nigeria. The study respondents are the household heads in the selected sites in GAC. The study sites are: Dobi, Dagiri, Ledi and Tunga Maje. The focus of this study is divided into a malaria survey study, determination of malaria incidence based on self-reporting and determination of the complex interrelationships between target variable (incidence) and human-related malaria risk factors alongside climate variables for Gwagwalada and its environment. Therefore, this study is relevant to be applied on the subjects at household levels in identifying significant predictive factors of malaria using Bayesian graphical probability model and Monte Carlo simulation analysis. Also, it can be applied on subjects when spatial autocorrelations are involved in prevalence scores and such dependency measured with semivariogram models.

1.6 Organization of the Thesis

This dissertation examines and identifies malaria risk factors in Abuja, Nigeria using Bayesian frameworks. There are eight chapters in this thesis. The chapters are grouped into three parts. The first part (Chapters 1 to 3) consists of the general introduction to the study, review of related literature and research materials and methods. Chapters 4 to 7 are results and discussions based on the stated research objectives. Chapter 8 gives the summary and conclusion of the study.

Chapter 1 is the introduction to the current study. It comprises the background to the study and highlights on the problem statement, significance of the study, research objectives along with the scope of study and structure of thesis. Chapter 2 examines and appraises related literature on malaria epidemiology, environmental related risk factors and malaria control interventions. It also outlines and reviews Bayesian approaches and spatial models on disease modelling. Chapter 3 gives the general materials and methods to all the stated objectives in Chapter 1 of this study. It outlines data collection procedures and management, model formation and development.

Chapters 4 till 7 are results and discussion based on individual objectives stated in Chapter 1. Thus, each chapter begins with a brief introduction and review of related study on the subject of interest under consideration for the chapter. The method section contains the specific details of the variables of interest and explicit data analysis procedures used in obtaining the desired research outcomes. The theoretical framework is as detailed in chapter 3 but additional analysis procedures are provided for some chapters when necessary and captioned under data analysis. The summary of the study findings based on the statistical analysis conducted is provided by the results. The last section for each of the result chapters is the discussion section, whereby comparison of the findings of this present study and previous related studies reported in literature are made and detailed explanations based on the present study documented. The last chapter of this study is Chapter 8 which discusses the general conclusion and recommendations based on the research findings.

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