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- A comparison of medication adherence between subsidized and self-paying patients in Malaysia
- Achieving triple treatment goals in multi-ethnic Asian patients with type 2 diabetes mellitus in primary care
- Randomized controlled trial on the effect of Al-Quran recitation vs counseling on smoking intensity among Muslim men who are trying to quit smoking



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All correspondence should be addressed to:

Associate Professor Dr. Su May Liew

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The Malaysian Family Physician Journal

Academy of Family Physicians of Malaysia,

Unit 1-5, Level 1 Enterprise 3B Technology Park Malaysia (TPM)

Jalan Innovasi 1 Lebuhraya Puchong-Sungai Besi

Bukit Jalil, 57000 Kuala Lumpur.

Tel: +603 4041 6800 / 4041 7800

Email: journal.mfp@gmail.com

Website: <http://www.e-mfp.org>

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Local Advisors

Professor Datin Dr Yook Chin Chia (chiayc@um.edu.my)

Professor Dr Wah Yun Low (lowwy@um.edu.my)

Associate Professor Datuk Dr DM Thuraiappah (dmthuraiappah@outlook.com)

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- Books and other monographs: Corporate Author WONCA International Classification Committee. International Classification of Primary Care, ICPC-2. 2nd ed. Oxford: Oxford University Press; 1998.

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Religion in medicine

Liew SM

Editor-in-Chief

Dear readers,

It has always been interesting to me to see the juxtaposition of beliefs and scientific evidence in clinical practice. Increasingly, in my work as an academic lecturer training primary care physicians and a researcher in health behaviours, I have noted the major impact of personal beliefs and practices on a doctor's consultation. Cognitive biases that are a result of a lifetime of cultural and personal values have been shown to affect one's behaviour which translates to our own personal health beliefs and subsequently impacts on our work.¹ This may be of greater impact when the evidence in the area is sketchy and this is particularly true for primary care which is defined by breadth of clinical practice.

In this issue of the Malaysian Family Physician, there is an article regarding the effect of Al-Quran recitation on smoking cessation.² Should we allow for an overlap of religion and medicine?³ Or should we firmly separate the two in case it leads to a slippery slope towards non-evidence based medicine?⁴ It is my view that all forms of interventions should be tested, appraised by the peer review process and published for all to judge fairly. However, it can be difficult to remove bias as blinding to the religious intervention is not possible.

I would feel uncomfortable prescribing religious interventions in my clinical practice. The power dynamics of the patient physician relationship is tilted towards the health care practitioner and my concern is that there would be an element of coercion despite efforts to minimise this by shared decision-making. We would welcome further discussion on this matter with letters from our readers. As stated by our previous Chief Editor, Professor Ng Chirk Jenn, let us continue to address sensitive issues head-on.⁵

In this issue, we have 3 original articles, 6 case reports and 1 Test Your Knowledge article. We hope that you enjoy reading these papers.

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A comparison of medication adherence between subsidized and self-paying patients in Malaysia

Aziz H, Hatah E, Makmor-Bakry M, Islahudin F, Ahmad Hamdi N, Mok Pok Wan I

Aziz H, Hatah E, Makmor-Bakry M, et al. A comparison of medication adherence between subsidized and self-paying patients in Malaysia. *Malays Fam Physician*. 2018;13(2);2–9.

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Authors:

Ernieda Hatah

(Corresponding author)
PhD, MPharm (Clin), Bpharm (Hons)
Faculty of Pharmacy
Universiti Kebangsaan Malaysia
Jalan Raja Muda Abdul Aziz
50300 Kuala Lumpur, Malaysia.
Email address: ernieda@ukm.edu.my

Hamiza Aziz

Bpharm (Hons), Master of Science (Pharm)
Faculty of Pharmacy, Universiti Kebangsaan Malaysia, Jalan Raja Muda Abdul Aziz, Kuala Lumpur Malaysia.

Mohd Makmor Bakry

PhD, MPharm (Clin), Bpharm (Hons)
Faculty of Pharmacy, Universiti Kebangsaan Malaysia, Jalan Raja Muda Abdul Aziz, Kuala Lumpur Malaysia.

Farida Islahudin

Faculty of Pharmacy, Universiti Kebangsaan Malaysia, Jalan Raja Muda Abdul Aziz, Kuala Lumpur Malaysia.

Abstract

Background: Limited efforts have been made to evaluate medication adherence among subsidized and self-paying patients.

Objective: To investigate medication adherence among patients with and without medication subsidies and to identify factors that may influence patients' adherence to medication.

Setting: Government healthcare institutions in Kuala Lumpur, Selangor, and Negeri Sembilan and private healthcare institutions in Selangor and Negeri Sembilan, Malaysia.

Methods: This cross-sectional study sampled patients with and without medication subsidies (self-paying patients). Only one of the patient's medications was re-packed into Medication Event Monitoring Systems (MEMS) bottles, which were returned after four weeks. Adherence was defined as the dose regimen being executed as prescribed on 80% or more of the days. The factors that may influence patients' adherence were modelled using binary logistic regression.

Main outcome measure: Percentage of medication adherence.

Results: A total of 97 patients, 50 subsidized and 47 self-paying, were included in the study. Medication adherence was observed in 50% of the subsidized patients and 63.8% of the self-paying patients ($\chi^2=1.887$, $df=1$, $p=0.219$). None of the evaluated variables had a significant influence on patients' medication adherence, with the exception of attending drug counselling. Patients who attended drug counselling were found to be 3.3 times more likely to adhere to medication than those who did not (adjusted odds ratio of 3.29, 95% CI was 1.42 to 7.62, $p = 0.006$).

Conclusion: There is no significant difference in terms of medication adherence between subsidized and self-paying patients. Future studies may wish to consider evaluating modifiable risk factors in the examination of non-adherence among subsidized and self-paying patients in Malaysia.

Introduction

Patients with chronic diseases, such as diabetes, stroke and cardiovascular diseases, usually require long-term use of medication to control their conditions. Therefore, it is important that patients take their medication as advised since failure to adhere to the prescribed medication could lead to poor clinical outcomes, increased healthcare costs, increased hospital stays, and an increased economic burden on the country's healthcare system.¹⁻³ Despite the general knowledge that adhering to prescribed medications is important, medication non-adherence remains a major problem worldwide. According to the World Health Organization's (WHO's) 2003 report, 50% of patients with chronic diseases do not adhere to their prescribed treatment. This problem was reported to exist in both developed and developing countries. For example, in the United States of America

(USA), approximately half of the 3.2 billion annual prescriptions dispensed were not used as prescribed.⁴ Similarly, in Malaysia, approximately 46% and 56% of patients with hypertension were non-adherent in terms of their medications.^{2,5}

Adherence to long-term therapy is defined by the WHO as "the extent to which a person's behavior taking medication, following a diet, and/or executing lifestyle changes corresponds with agreed recommendations from a healthcare provider".⁶ Patients' adherence to medication can be influenced by many factors. These include health-system-related, patient-related, condition-related, socioeconomic-related, and therapy-related factors.⁶ One important factor that may influence patients' adherence to medication is medication cost. A previous study on medication adherence using the Health Belief Model reported that an increase in medication cost may decrease

Najwa Ahmad Hamdi

Bpharm (Hons)
Pharmacy Division, Ministry of
Health Jalan Universiti, Petaling
Jaya Selangor, Malaysia.

Ivy Mok Pok Wan

MPharm (Clin), Bpharm
Universiti Kebangsaan Malaysia
Medical Centre, Jalan Yaacob Latif
Bandar Tun Razak, 56000 Cheras
Kuala Lumpur, Malaysia.

patients' adherence to medication.⁷ In the study, adherence to diabetes medications was found to be influenced predominantly by the costs of or barriers to the diabetes management regimen.⁷ In addition, higher out-of-pocket spending (self-paying) and medication co-payments were also reported to increase the risk of stopping or becoming non-adherent to medication.⁸

Another previous systematic review of patients with diabetes mellitus suggested reducing an inpatient's cost share to increase medication adherence.⁹ This is in view of the fact that high patient copayments or out-of-pocket expenditures for medication had a significant association with medication nonadherence.¹⁰ Nevertheless, studies examining patient adherence to fully subsidized medications reported variable findings. In a study by Sears et al., medication adherence was reported to be low (34%) among veteran patients with medication subsidies for treatment of overactive bladder.¹¹ Meanwhile, in a study by Batavia et al., subsidized patients with Human Immunodeficiency Virus (HIV) in India were found to have significantly higher adequate adherence rate (84.6%) than self-paying patient groups who need to pay 50%, 75% and 100% of their medication costs (71.6%, 72.3%, and 79.2% respectively).¹²

In Malaysia, the major provider of healthcare services, the public health care system, is subsidized heavily by the government.¹³ Nevertheless, patients' adherence to medication is worrisomely low. Based on the Fees (Medical) Order of 1976, Malaysian public primary care services are provided nearly free of charge, and patients can receive medical care and medication at a minimal cost of RM1 per visit.¹³ However, a study by Ramli et al. found that only 53.3% of hypertensive patients receiving treatment at public primary healthcare clinics were adherent to their medication.² In addition, a study by Hassali et al. reported a high return rate for unused medication at a government hospital in Malaysia. In their study, the calculated cost of returned unused medication was about RM42.35/patient. If this cost is postulated across Malaysia, it could result in the government losing a million dollars per year.¹⁴ One of the possible reasons for the returned unused medications is medication non-adherence.¹⁴

Although medication adherence among patients

with medication subsidies was evaluated in previous studies, few have compared it with self-paying patients. In addition, to our knowledge, no study has yet evaluated and compared the potential factors that may influence subsidized and self-paying patients' adherence to medication.

Aim of the study

This study aims to compare the medication adherence of subsidized and non-subsidized patients (i.e., self-paying patients) and to identify factors that may influence patient behavior in terms of medication adherence.

Ethics approval

Ethical approval for this study was obtained from the Research Ethics Committee of Universiti Kebangsaan, Malaysia (UKM 1.5.3.5/244/ NF-056-14) and the Medical Research and Ethics Committee of the Ministry of Health, Malaysia (NMRR-14-1255-22473).

Methods

This is a cross sectional, observational study of the medication adherence of patients with and without medication subsidies. Patients were clustered into two groups based on their medication payment schemes and sampled using a convenience sampling technique. Patients who received their health consultation at public hospitals or clinics and were not required to buy their medication on their own were classified as subsidized patients. Private patients who paid medication costs themselves and/or for whom medication costs were not covered by insurance or an employer benefit scheme were classified as self-paying patients. Subsidized patients were sampled from two government hospitals located in Kuala Lumpur and a health clinic located in a rural area in Malaysia. Meanwhile, self-paying patients were sampled from one private hospital, one private clinic, and a community pharmacy in Selangor, Malaysia.

Using convenience sampling, patients who attended those facilities as out-patients were approached in the pharmacy waiting area and told about the study. Since respondents were required to use a Medication Event Monitoring Systems (MEMS) bottle, they were also told about the function of the MEMS bottle. In particular, respondents were told that the bottle cap recorded and stored patients' dosing events

in terms of the actual times that the medication container was opened and closed. Only one of the respondent's chronic illness medications, the one deemed to be the most expensive medication, was repacked into the MEMS bottle. The most expensive medication for subsidized patients was determined by reviewing the medication prices printed on the patients' medication labels. For self-paying patients, the most expensive medication was determined based on patient's information and medication bills.

Respondents were invited to participate if they agreed to use the MEMS bottle and fulfilled the study inclusion criteria, which were that they were an adult aged 18 years and above, were diagnosed with at least one chronic disease, used at least three types of long-term medication, and were on the medication therapy for at least 6 months. Patients were excluded from the study if they were terminally ill, lived in assisted living facilities, had difficulties in opening a MEMS cap (such as patients with rheumatoid arthritis), using pillbox as a medium for organizing their medication, and/or had cognitive impairment, such as dementia or Alzheimer's disease. Patients who agreed to participate were asked to sign an informed consent form and fill in the survey. Data collection was done between December 2014 and October 2015. Using the reported adherence rates for subsidized and self-paying patients by Ramli et al.² and Batavia et al.¹², respectively, as reference, the relative sample size required to detect a difference between two proportions (level of significance (α) of 0.05, power of 80%, with proportions of adherence in subsidized and self-paying patients of 53% and 80%, respectively) was 45 in each group.¹⁵

Based on common reported factors for medication non-adherence, the following demographic data and characteristics were collected from the participants during the first meeting: age, gender, monthly income, educational background, marital status, patient's location (rural or urban), experience in attending drug counseling, frequency of the medication selected to be stored in the MEMS bottle, number of health problems, and number of medications prescribed. The median household income in all states in Malaysia for 2015 was RM3000.¹⁶ Therefore, the following categories were established for patients' household incomes: 1) > RM3001 for above the countries' median household income, 2) < RM1000 for poor households, and 3) RM1001 to RM3000 for below the median

household income.¹⁷ The rurality of the facility participant attended was determined following the definition of the Department of Statistics, Malaysia, in which rural refers to a settlement with a population of less than 10,000 people. The public clinic for subsidized patients was chosen purposely, as it located in the Felda community area, which is known to be rural.

To ensure that respondents knew what drug counselling was, the respondents were provided with the explanation that it refers to a one-to-one session with a pharmacist in which the pharmacist provided information, discussed the patient's concerns, and answered the patient's questions related to their medications. With the participant's agreement, their medications were reviewed and only one medication was re-packed into a MEMS bottle for each participant. Respondents were asked to take the medication in the MEMS bottle as instructed by their healthcare provider and to open the MEMS bottle only when they actually took their medication. The MEMS bottles were collected by the researchers at the participants' homes after four weeks. The data that were stored on the MEMS cap were then downloaded to a computer.¹⁸ Medication adherence was calculated as the percentage of days in which the dose regimen was executed as prescribed (number of days of bottle openings in accordance to the number of doses prescribed). Referring to the previously cited definition, the current study used 80% as the cut-off point for medication adherence.¹⁹⁻²⁴

Data were analyzed using the Statistical Package for the Social Sciences (SPSS) Version 20. Descriptive data were presented as means and standard deviations where appropriate. Medication adherence was modeled separately for subsidized and self-paying patients using binary logistic regression with both the stepwise and backward elimination approaches. Prior to the final modeling, a univariate analysis was performed to determine which variables would be included in the final analysis. Only variables with p-values of <0.25 were included in the final model.²⁵ In the final model, only those variables with a p-value <0.05 were determined to have a significant influence on medication adherence behavior.

Results

A total of 250 patients were approached, and 112 patients agreed to participate in the study. However, upon completion of the

study, only 105 participants (92.9%) returned the MEMS bottles. Patients that did not return the MEMS bottle could not be reached (n=3) or claimed to have lost the bottle (n=4). Of the 105 returned MEMS bottles, 8 patients' MEMS data were excluded as only one or two readings of the bottle being opened were available. Upon confirming with the patients, they admitted that the medication were taken out from the MEMS bottle and stored it in another container. Thus, a total 97 (86.6%) patients provided data that were suitable for data analysis. Of this, 50 patients were from the subsidized group and 47 were from the self-paying group. The demographic characteristics of the participants are presented in **Table 1**.

Table 1: Demographic characteristics of respondents (n=97)

Demographic characteristics	Total or Mean (SD)	n (%) / Mean (SD)		p-value
		Subsidized (n=50)	Self-pay (n=47)	
Age	55.26 (10.76)	52.98 (10.8)	57.68% (10.3)	0.168
<i>Gender</i>				0.265
Male	48 (49.5%)	22 (44%)	26 (55.3%)	
Female	49 (50.5%)	28 (56%)	21 (44.7%)	
<i>Monthly income</i>				0.001
<RM1000	26 (26.8%)	10 (20%)	16 (34%)	
RM1001-RM3000	39 (40.2%)	30 (60%)	9 (19.1%)	
>RM3001	32 (23.0%)	10 (20%)	22 (46.8%)	
<i>Educational Background</i>				0.171
Primary school	27 (27.8%)	17 (34%)	10 (21.3%)	
Secondary school	39 (40.2%)	21 (42%)	18 (38.3%)	
College/ University	31 (32%)	12 (24%)	19 (40.4%)	
<i>Marital status</i>				0.191
Single	5 (5.2%)	4 (8%)	1 (2.1%)	
Married	92 (94.8%)	46 (92%)	46 (97.9%)	
<i>Patient's location</i>				<0.001
Urban	74 (76.3%)	26 (54%)	47 (100%)	
Rural	23 (23.7%)	23 (46%)	0 (0%)	
<i>Attended drug counseling</i>				0.074
Yes	42 (43.3%)	24 (48%)	31 (66%)	
No	55 (56.7%)	26 (52%)	16 (34%)	
<i>Frequency of medication</i>				0.333
Once a day	44 (88%)	38 (80.9%)	82 (84.5%)	
Twice a day	6 (12%)	9 (19.1%)	15 (15.5%)	
Number of health problems	2.68(0.93)	2.72 (0.93)	2.64 (0.94)	0.678
Number of medications prescribed	4.80(1.90)	5.48 (1.91)	4.09 (1.65)	<0.001

The mean and standard deviation (SD) of the patients' ages is 55.26 (10.76). There were no significant differences in term of patients' demographic information and characteristics between the subsidized and self-paying groups except for monthly income and the number of medications prescribed ($p < 0.05$ for both). More self-paying participants had a household income of $\geq$ RM3001 than the subsidized participants ($p = 0.001$). The number of medications received by respondents was between three and 11, with subsidized patients receiving more medications than self-paying patients (mean number of medications 5.48 ± 1.91 and 4.09 ± 1.65 , respectively) ($p < 0.001$).

Common health problems experienced by respondents in this study were diabetes, ischemic heart disease, dyslipidemia, hypertension, and stroke.

The overall mean adherence rate was 78.42 ± 23.34 . When analyzed separately, the mean adherence rate of subsidized patients was 74.1 ± 27.05 , and that of self-paying patients was 83.02 ± 17.77 ($t(95) = 1.05$, $p = 0.059$). A total of 25 subsidized (50%) and 30 self-paying (63.8%) patients were adherent to their medications ($\chi^2 = 1.887$, $df = 1$, $p = 0.219$). Demographic factors for medication

adherence and non-adherence that are commonly reported were modeled. Three variables: gender, experience attending drug counseling, and payment scheme (subsidized and self-paying) were included in the final model of medication adherence, but only attending drug counseling had a significant influence on adherence to medication (AOR 3.3, 95% CI of 1.42 to 7.62, $p = 0.006$) (**Table 2**). Participants who attended drug counseling were 3.3 times more likely to be adherent to their medication than participants who did not.

Table 2: Medication adherence model for subsidized and self-paying patients (n=97)

Variables	Univariate analysis				Multivariate analysis			
	Crude OR	95% CI	Wald's χ^2 (df)	p-value	Adjusted OR	95% CI	Wald's χ^2 (df)	p-value
Age	1.00	0.97-1.04	0.01(1)	0.91	-	-	-	-
<i>Gender</i>								
Male	1.90	0.84-4.29	2.38(1)	0.12	-	-	-	NS
Female	1.00							
<i>Monthly income</i>								
<RM1000	1.29	0.48-3.50	0.26(1)	0.61	-	-	-	-
RM1001-RM3000	1.78	0.58-5.46	1.01(1)	0.32	-	-	-	-
>RM3001	1.00							
<i>Educational Background</i>								
Primary	1.55	0.57-4.16	0.75(1)	0.39	-	-	-	-
Secondary	1.71	0.60-4.85	1.00(1)	0.32	-	-	-	-
College/university	1.00							
<i>Marital status</i>								
Single	1.15	0.18-7.23	0.02(1)	0.88	-	-	-	-
Married	1.00							
<i>Attend drug counseling</i>								
Yes	3.29	1.42-7.62	7.70(1)	0.006	3.29	1.42-7.62	7.70(1)	0.006
No	1.00							
<i>Frequency of medication</i>								
Once daily	1.17	0.38-3.60	0.08(1)	0.78	-	-	-	-
Twice a day	1.00							
<i>Payment scheme</i>								
Self-pay	1.77	0.78-3.98	1.87(1)	0.17	-	-	-	NS
Subsidized	1.00							
Number of health problem	0.98	0.64-1.51	0.009(1)	0.93	-	-	-	-
Number of medications	0.95	0.77-1.18	0.21(1)	0.65	-	-	-	-

NS: Non-significant

Discussion

The current study evaluated the medication adherence among subsidized and self-paying patients. In general, the medication adherence among patients with chronic diseases included in the current study was poor. Only 50% of

subsidized patients and 63.8% of self-paying patients had medication adherence scores of 80% and above. Even when the participants received their medication at minimal cost or for free, the non-adherence rate was still found to be unsatisfactory. A similar finding was also reported in the study by Bailey et al.

in South Texas among underserved diabetes patients. In their study, patients who received medication at \$5, \$9.99, or free-of-charge had a suboptimal medication adherence rate of 44.1%.²⁶ In a different study among veteran patients in Philadelphia, USA, only 60.8% of patients who received medication subsidies (exempted from co-payment scheme) were adherent to their medications.²⁷

Although, in the current study, self-paying patients had a better medication adherence rate than subsidized patients, the difference was not significant. This finding contradicts the results from the Batavia et al. study conducted among HIV patients in India. They reported a significant difference in medication adherence between full medication subsidies and self-paying patients. The study, which assigned the payment rate according to patients' socioeconomic backgrounds, reported adherence rates of 84.6%, 71.6%, 72.3%, and 79.2% for patients who received medication free of charge, paid 50%, paid 75%, and paid 100% of the medication cost, respectively.¹² Adherence to medication was observed to be the highest among the underserved patients who could not afford to pay for their medication, i.e., free medication was found to promote a higher rate of adequate adherence. Nevertheless, among the self-paying patients, those with a higher payment rate had a higher percentage of adherence than patients who paid less. Batavia et al. perceived that, in certain cases, adherence may be improved or reduced when patients have constraints in terms of buying or obtaining their medication.¹² Similar findings were also reported by Park et al., a study that evaluated medication adherence among patients with diabetes. In their study, patients in private clinics with low incomes who received medical aid for health security had higher medication adherence than those with moderate and high incomes ($p = 0.044$).²⁸

In the current study, the difference in medication adherence between subsidized and self-paying patients not being significant may be due to the uniqueness of the public healthcare system in Malaysia. In Malaysia, public healthcare is provided at minimal costs or free-of-charge to all Malaysian regardless of their socioeconomic background or income. Patients who make a regular visit to a public primary health clinic or hospital out-patient clinic are required to pay a minimum payment of RM1 to RM5 per visit. Up to 95% of the services provided at public healthcare institutions, including consultations, lab

procedures, and medications, are provided at minimal cost or free-of-charge. Since patients may not be constrained to obtain their treatment and medications at public healthcare institutions in Malaysia, the perceived value of this service may be different from the previous reported studies. However, this may need to be investigated further in a future study.

In our attempt to investigate which patients' demographics and characteristics may influence medication adherence between subsidized and self-paying patients, only attending drug counseling by a pharmacist had a significant influence on medication adherence behavior. In a similar fashion, many studies have reported the significant influence of drug counseling service on improvements in patients' adherence to their medication.²⁹ Patients may become more adhere to their medication following drug counseling as they have gained more knowledge and understanding of the reasons for taking the medication and how to take it. During the session, a pharmacist may address the importance of taking the medication, help the patient to fit the medication into their daily routine, and overcome perceived barriers to medication adherence.³⁰

Nevertheless, other demographic factors, such as age, gender, race, educational level, and marital status, did not have a significant influence on medication adherence since they may not be truly independent factors affecting adherence.³¹ This is because demographic factors relate to socioeconomic and psychological backgrounds, as well as variations in culture.³¹ In addition, predictors of medication adherence that are cited frequently, such as age, gender, ethnicity, income, and educational status, are usually inconsistent due to variations in the sample population and study design.³¹ Consequently, studies have begun to explore more modifiable factors which may influence adherence, such as health beliefs or perceived benefits of medication.³² Hence, despite this study exploring only patients' demographic factors, future studies may wish to consider exploring and comparing modifiable factors for medication adherence among subsidized and self-paying patients.

This study was subject to a few limitations. Firstly, medication adherence was measured with the assumption that patients took their medication when the MEMS caps were opened. Secondly, since patients were conveniently

sampled from hospitals, clinics, and a dispensary area, the study may have included patients who were more motivated to participate in the study and/or take care of their health. Thirdly, the results of the study may apply only to patients who can afford to buy or obtain their medication in a healthcare setting. The researchers predict that the result may be different if the study had included patients who did not return for (in the case of subsidized patients) or buy (in the case of self-paying patients) their medication due to financial constraints. However, such a sample may be difficult to obtain since, in the current system, patients who cannot afford to pay for their medication may have their health consultation and medication fully subsidized. Finally, no self-paying patients were sampled from a rural area as there was no private healthcare institution available in a rural setting. Due to this fact, generalizing the study findings to self-paying patients in rural areas would not be appropriate.

Conclusion

In conclusion, there is no significant difference in term of medication adherence between the subsidized and self-paying patients included in this study. Only attending drug counseling

predicted the medication adherence of patients. More studies are required to understand the reasons for non-adherence among subsidized and self-paying patients. Future studies may wish to consider exploring modifiable factors that may influence patients' adherence to medication, such as patients' perceptions and beliefs concerning the value of their medications.

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Conflicts of interest

The authors report no conflicts of interest in this work.

How does this paper make a difference to general practice?

- The medication adherence rate among subsidized and self-paying patients in this study is still unsatisfactory.
- The only variable considered in this study which influences patients' adherence to medication is attending drug counseling.
- Exploring the potentials reasons for medication adherence and non-adherence among subsidized and self-paying patients may help in the understanding of the issues facing by the patients when attempting to adhere to a prescribed treatment.
- Future studies may wish to explore the reasons for medication adherence and non-adherence, such as beliefs concerning and the perceived value of the medications among subsidized and self-paying patients in Malaysia.

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Achieving triple treatment goals in multi-ethnic Asian patients with type 2 diabetes mellitus in primary care

Goh CC, Koh KH, Goh SCP, Koh YLE, Tan NC

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Authors:

Goh Chin Chin

(Corresponding author)

B Pharm

SingHealth Polyclinics

167, Jalan Bukit Merah, Tower 5

#15-10, Singapore 150167

Email:

goh.chin.chin@singhealth.com.sg

Kim Hwee Koh

M.Med (Fam Med), MRCS.

SingHealth Polyclinics

Soo Chye Paul Goh,

M.Med (Fam Med), FCFPS

SingHealth Polyclinics

167, Jalan Bukit Merah, Tower 5

#15-10, Singapore 150167

Yi Ling Eileen Koh

BSc

SingHealth Polyclinics

167, Jalan Bukit Merah, Tower 5

#15-10, Singapore 150167

Ngaiap Chuan Tan

M.Med (Fam Med), FCFPS

SingHealth Polyclinics,

Duke NUS Medical School,

Singapore

Abstract

Introduction: Achieving optimal glycated hemoglobin (HbA1c), blood pressure (BP), and LDL-Cholesterol (LDL-C) in patients mitigates macro- and micro-vascular complications, which is the key treatment goal in managing type 2 diabetes mellitus (T2DM). This study aimed to determine the proportion of patients in an urban community with T2DM and the above modifiable conditions attaining triple vascular treatment goals based on current practice guidelines.

Methods: A questionnaire was distributed to adult Asian patients with dyslipidemia at two primary care clinics (polyclinics) in northeastern Singapore. The demographic and clinical data for this sub-population with both T2DM and dyslipidemia were collated with laboratory and treatment information retrieved from their electronic health records. The combined data was then analyzed to determine the proportion of patients who attained triple treatment goals, and logistic regression analysis was used to identify factors associated with this outcome.

Results: 665 eligible patients [60.5% female, 30.5% Chinese, 35% Malays, and 34.4% Indians] with a mean age of 60.6 years were recruited. Of these patients, 71% achieved LDL-C ≤ 2.6 mmol/L, 70.4% had BP $< 140/90$ mmHg, and 40.9% attained HbA1c $\leq 7\%$. Overall, 22% achieved the triple treatment goals for glycemia, BP, and LDL-C control. The major determinants were the number of diabetic medications and intensity of statin therapy.

Conclusion: Eight in ten patients with T2DM failed to achieve concurrent glycemic, BP, and LDL-C treatment goals, subjecting them to risks of vascular complications. Primary healthcare professionals can mitigate these risks by optimizing therapeutic treatment to maximize glycemia, dyslipidemia, and BP control.

Introduction

The management of patients with type 2 diabetes mellitus (T2DM) centers on the reduction of their risks of both macro- and microvascular complications.¹ Ample and consistent evidences show that the risks of these vascular complications can be mitigated by attaining optimal control of their hyperglycemia, blood pressure and LDL-Cholesterol.² These vascular risks can be reduced by pharmacological intervention, lifestyle modification, and patients' adherence to therapy.

Achieving intensive glycemic control has shown to reduce the risk of microvascular endpoints by 25% and albuminuria at twelve years by 33%.³ In addition, a 17% reduction in events of non-fatal myocardial infarction and a 15% reduction in events of coronary heart disease were recorded.⁴ Oral anti-diabetic

agents have emerged as valuable tools for the attenuation of atherosclerotic activity and the protection of the vasculature in patients with type 2 diabetes.⁵

Tight blood pressure control of $< 130/80$ mm Hg in patients with hypertension and T2DM has been associated with a significantly lower risk of all-cause mortality (risk ratio (RR)=0.87; 95% CI of 0.78-0.96). For microvascular outcomes, a 10 mm Hg-lower systolic BP was associated with a lower risk of retinopathy (RR=0.87; 95% CI of 0.76-0.99) and albuminuria (RR=0.83; 95% CI of 0.79-0.87).⁶ As lowering BP has been associated with improved mortality and other positive vascular outcomes, the use of medications for lowering BP among patients with T2DM should be sustained.

Reduction of Low Density Lipoprotein-Cholesterol (LDL-C) further mitigates vascular

complications. A significant 21% reduction in major vascular events occurs for every mmol/L reduction in LDL-C for people with diabetes (RR=0.79; 95% CI of 0.72–0.86; $p<0.0001$).⁷ An increase of 0.38 mmol/L or 15 mg/dL in High Density Lipoprotein-Cholesterol (HDL-C) was associated with a 22% reduction in risk of coronary arterial disease.² Poor lipid profiles have been associated with poor glycemic control.⁸ L. Acuña et al. found that more than half of the patients with diabetes in their study had suboptimal LDL-C levels, while 36% had low HDL-C levels of $<40\text{mg/dl}$ ($<1.0\text{ mmol/L}$).⁹

However, attaining concurrent control of glycemia, blood pressure, and LDL-C in patients with T2DM is challenging. Data from the Asia and Greece study revealed that approximately 10% or less of patients achieved triple vascular disease control.^{8,10,11} Data from a large Japanese working population, predominantly composed of men, reported that the younger population segment had suboptimal achievements of HbA1c, BP and LDL-C treatment goals.⁸ In China, only 5.6% achieved all target goals; lower BMI (<24), higher education, and shorter duration of T2DM (<5 years) were independent predictors of better vascular risk control.¹⁰ In the USA, two study cohorts from the Kaiser Permanente (KP) and Denver Health (DH) health care institutions, achieved 33% and 16% simultaneous control of all three risk factors, respectively.¹² The difference was attributed to the population-based management system used by KP over a period of many years. The system identified targeted individuals who had not achieved simultaneous control in order to treat their elevated risk factors. More healthcare resources were directed towards this population-based intervention to increase the number of patients successfully achieving their treatment goals.

In order to adopt an approach similar to KP's, it is crucial to determine the proportion and baseline population characteristics of patients with T2DM who fail to attain triple treatment goals. The size of this at-risk population will determine the amount of healthcare resources needed to manage them. In Singapore, about 45% of the local multi-ethnic Asian population with T2DM is being managed in public primary healthcare due to accessibility, and the comprehensive and subsidized healthcare services provided by these polyclinics.¹³ The subsidies at these polyclinics cover consultation

and medications. SingHealth Polyclinics (SHP) comprises nine polyclinics, which cover half of the highly urbanized island state over the southern and eastern regions.¹⁴ SHP has also adopted a population-based management system for patients with long-term, non-communicable diseases, such as T2DM, so that resources are allocated appropriately to cater to patients at risk of vascular complications. Hence, this study aimed to determine the proportion of patients with T2DM who failed to achieve triple treatment goals for concomitant glycemic, blood pressure, and LDL-Cholesterol (LDL-C) control. The secondary objective was to identify modifiable factors associated with triple treatment goals' achievement.

Methods

The Lipid Health study was conducted from Oct 2013 to Sep 2014 at two of SHP's polyclinics.¹⁵ This questionnaire collected data pertaining to demographic and clinical profiles, laboratory investigations, and personal lifestyle information for patients with dyslipidemia. This paper is a sub-analysis of the data from the Lipid Health study, focusing on a segment of the study population with T2DM and dyslipidemia.

Subjects

The main study recruited patients with dyslipidemia, ranging in age from 31 to 80 years old, who visited two primary care polyclinics from Oct 2013 to Sep 2014.¹⁵ Three major ethnic groups, namely Chinese, Malays and Indians, were equally stratified to determine their perceptions and attitudes towards lifestyle habits such as exercise, diet, and medication. Patients who fulfilled the inclusion criteria of physician-diagnosed dyslipidemia and being Singaporean or a permanent resident (at least 3 years of residence in Singapore) were interviewed by trained research assistants to complete the survey. The subjects in this paper were patients known to have T2DM, as confirmed by the diagnostic codes in their electronic health records.

Two clinical research coordinators were hired and underwent training by the principal investigator on the study and its implementation. They were further trained in the Singapore version of Good Clinical Practice (SG-GCP). Written informed consents were obtained from the patients prior to the administration of the questionnaire.

The study excluded patients who had difficulty communicating in the local major languages and dialect or were unable to provide informed consent due to cognitive, hearing, and/or visual impairments.

Definition of treatment goals

The treatment goal for T2DM is normoglycemia, defined as HbA1c $\leq 7.0\%$, according to the Ministry of Health (MOH) Clinical Practice Guidelines on Diabetes Mellitus.¹⁶ Following the recommendations of the Eight Joint National Committee (JNC 8)¹⁷, the blood pressure goal for patients with T2DM is defined as $<140/90$ mmHg. The LDL-C treatment goals for the High Risk Group, including those with T2DM, is < 2.6 mmol/L (<100 mg/dL).¹⁸ The intensity of statin therapy, graded as low, moderate, or high, is based on the 2013 ACC/AHA guideline on the primary and secondary prevention of cardiovascular events.¹⁹

Sample size calculation

The sample size was based on the aim of the main study,¹⁵ which required a sample of at least 380 subjects for each of the three ethnic groups used in this subgroup analysis. In this paper, only those with T2DM were included in the analysis ($n=665$).

Questionnaire

The questionnaire was administered in English, the local common language of communication for the multi-ethnic Asian population. The trained clinical research coordinators, conversant in English, Mandarin, Malay, and local dialects, provided language assistance, as required, to patients filling in the questionnaire.

Clinical information, including laboratory investigations, such as lipid profiles (total cholesterol, HDL-C, Triglycerides (TG), and LDL-C), BP, HbA1c readings, and electronic medication prescriptions were retrieved from their electronic medical records. The questionnaire, targeted at patients with dyslipidemia, covered self-reported adherence to their prescribed medications and perceptions related to their understanding of and attitudes towards lifestyle modifications and pharmacological treatments. This paper focuses on the impact of modifiable factors, largely pharmacological treatments, in attaining triple treatment goals among the subset of patients with T2DM and dyslipidemia.

Statistical analysis

The analysis was done using the attainment of concurrent triple treatment goals of defined levels of glycated hemoglobin (HbA1c), LDL-C, and BP as the primary outcome. To assess the difference between those who have well-controlled glycated hemoglobin and those who do not, a Chi-square test or Fisher's Exact test was used to test independence for categorical responses. Continuous variables were tested using independent t-tests and the Mann Whitney U test.

Adjusted odds ratios (ORs) and the corresponding 95% confidence intervals (CIs) were calculated using logistic regression in which all potentially significant factors were entered. Data were coded and analyzed using IBM SPSS Statistical Software 22.0. For all of the test performed, a p-value of less than 0.05 was considered statistically significant.

In terms of the measurements used for BP, HbA1c, and LDL-C, current readings of BP were carried out twice, with an interval of 15 minutes between the two measurements, and the average of the two readings was used as the BP parameter. The most recent laboratory results (HbA1c and lipid profiles), as well as details of medications prescribed, were retrieved from the medical records.

Results

The study population comprised a total of 665 patients (402 females and 263 males) with a mean age of 60.6 years old. Table 1 summarizes the demographic characteristics of the patients included in the analysis. A total of 78.2% of the patients with T2DM and dyslipidemia failed to achieve concurrent treatment goals for HbA1c, BP, and LDL-C.

Demographic variables, such as gender, educational level, and employment status were not associated with triple goal achievement. A significant proportion of patients aged 60 years and older (26.2%) and of Chinese ethnicity (28.6%) attained better simultaneous control of the three treatment goals than those from younger age groups and other ethnic groups (Table 1). As many as 88% of the study population had a body mass index of 23 and above, yet the levels of triple-goal control were similar for the overweight and non-overweight groups. A greater proportion of patients with T2DM and other comorbidities failed to attain

concurrent treatment goals, and the association was significant among patients with renal disease (91.4%) (**Table 1**).

The patients in this study were taking an average of 2 diabetes-related medications, while the mean duration of T2DM was 6 years. Those who failed to achieve their triple control were likely to consume a higher number of diabetic

medications and had a longer duration of T2DM. The highest percentage (46%) of simultaneous control was observed among patients who were not prescribed any diabetic medications. Those who were on either oral hypoglycemic agents or insulin were more likely to achieve concurrent treatment goals compared to those on combination treatments ($p<0.01$) (**Table 1**).

Table 1: Demographic profiles of patients with T2DM in association with their glycemia, blood pressure, and LDL-Cholesterol controls

	Total	Glycated hemoglobin ¹ , BP ² and LDL ³ goals not achieved	Glycated hemoglobin ¹ , BP ² and LDL ³ goals achieved	p-value
Demographic profile	665 (100.0)	520 (78.2)	145 (21.8)	
<i>Gender</i>				0.30
Female	402 (60.5)	309 (76.9)	93 (23.1)	
Male	263 (39.5)	211 (80.2)	52 (19.8)	
<i>Ethnic Group</i>				0.01
Chinese	203 (30.5)	145 (71.4)	58 (28.6)	
Malay	233 (35)	193 (82.8)	40 (17.2)	
Indian	229 (34.4)	182 (79.5)	47 (20.5)	
<i>Age (years)</i>				<0.01
<60	287 (43.2)	241 (84)	46 (16)	
≥60	378 (56.8)	279 (73.8)	99 (26.2)	
<i>Education</i>				0.99
Secondary or below	573 (86.2)	448 (78.2)	125 (21.8)	
Diploma/ Tertiary	92 (13.8)	72 (78.3)	20 (21.7)	
<i>Employment Status</i>				0.65
Employed	300 (45.1)	237 (79)	63 (21)	
Unemployed	365 (54.9)	283 (77.5)	82 (22.5)	
<i>BMI⁴</i>				0.62
Below 23	79 (11.9)	60 (75.9)	19 (24.1)	
23 and above	584 (88.1)	458 (78.4)	126 (21.6)	
Lifestyle habits				
<i>Current Smoker</i>				0.70
Yes	37 (5.6)	28 (75.7)	9 (24.3)	
No	628 (94.4)	492 (78.3)	136 (21.7)	
<i>Alcohol</i>				0.43
Yes	9 (1.4)	8 (88.9)	1 (11.1)	
No	656 (98.6)	512 (78)	144 (22)	
Comorbidities				
<i>Hypertension</i>				0.92
Yes	604 (90.8)	472 (78.1)	132 (21.9)	
No	61 (9.2)	48 (78.7)	13 (21.3)	
<i>Ischemic Heart Disease/ Coronary Artery Disease</i>				0.94
Yes	153 (23)	120 (78.4)	33 (21.6)	
No	512 (77)	400 (78.1)	112 (21.9)	
<i>Cerebral Vascular Disease/ Stroke/ TIA</i>				0.49
Yes	30 (4.5)	25 (83.3)	5 (16.7)	
No	635 (95.5)	495 (78)	140 (22)	

	Total	Glycated hemoglobin ¹ , BP ² and LDL ³ goals not achieved	Glycated hemoglobin ¹ , BP ² and LDL ³ goals achieved	p-value
<i>Renal Disease</i>				<0.01
Yes	70 (10.5)	64 (91.4)	6 (8.6)	
No	595 (89.5)	456 (76.6)	139 (23.4)	
<i>Peripheral Vascular Disease</i>				0.76
Yes	6 (0.9)	5 (83.3)	1 (16.7)	
No	659 (99.1)	515 (78.1)	144 (21.9)	
Duration of comorbidities				
Duration of Type II Diabetes, median (IQR)	6 (3-11)	6 (3-11)	4.5 (2-9)	<0.01
Duration of Hypertension, median (IQR)	7 (3-11)	7.5 (3.3-11)	7 (3-11)	0.84
Duration of Dyslipidemia, median (IQR)	7 (3.5-11)	7 (3-11)	7 (4-10)	0.59
Medication				
Number of diabetic medications, median (IQR)	2 (1-2)	2 (1-3)	1 (1-2)	<0.01
Number of anti-hypertensive medications, median (IQR)	2 (1-3)	2 (1-3)	2 (1-3)	0.35
Number of lipid-lowering medications, median (IQR)	1 (1-1)	1 (1-1)	1 (1-1)	0.72
<i>Diabetic medication type</i>				<0.01
Not on diabetic medication	76 (11.4)	41 (53.9)	35 (46.1)	
Oral	481 (72.3)	377 (78.4)	104 (21.6)	
Insulin	11 (1.7)	9 (81.8)	2 (18.2)	
Combination (Oral and insulin)	97 (14.6)	93 (95.9)	4 (4.1)	
Statin Intensity⁵				<0.01
Low	153 (25.3)	104 (68)	49 (32)	
Moderate	377 (62.4)	305 (80.9)	72 (19.1)	
High	74 (12.3)	62 (83.8)	12 (16.2)	
Fasting Lipid Profiles (mg/dL)				
<i>HDL-C⁶</i>				0.70
Goals not achieved	103 (15.5)	82 (79.6)	21 (20.4)	
Goals achieved	562 (84.5)	438 (77.9)	124 (22.1)	
<i>Triglyceride Levels⁷</i>				0.046
Goals not achieved	77 (11.6)	67 (87)	10 (13)	
Goals achieved	587 (88.4)	452 (77)	135 (23)	

¹ Glycated hemoglobin: Goals not achieved: HbA1c > 7; Goals achieved: HbA1c ≤ 7

² Blood pressure: aged 60 years or older < 150/90mmHg; aged below 60 years < 140/90mmHg; Patients with diabetes < 140/90mmHg

³ LDL-C: For high risk group, goals achieved refers to LDL ≤ 2.6mmol/L (100 mg/dL), Goals not achieved refers to LDL > 2.6mmol/L (100 mg/dL).

⁴ BMI value of 23 and above indicates unhealthy weight range

⁵ Statin Intensity: Adopted from the 2013 American College of Cardiology and American Heart Association (ACC/AHA) Blood Cholesterol Guideline

⁶ HDL-C: Goals not achieved: < 1.0 mmol/L (40 mg/dL); Goals achieved: ≥ 1.0 mmol/L (40 mg/dL)

⁷ Triglyceride: Goals not achieved: ≥ 2.3 mmol/L (200 mg/dL); Goals achieved: < 2.3 mmol/L (200 mg/dL)

The triple-treatment goal attainments of the 665 patients in this study is presented in Figure 1. In this sample, 71.0% and 70.4% of patients achieved LDL-C and BP treatment goals, respectively. Among the three goals, glycemic control was least satisfactory, at 40.9%. Dual achievement of the HbA1c and BP goals was reported for 28%, 30% achieved both the HbA1c and LDL-C goals, while the combined BP and LDL-C goals had 52% compliance (**Figure 1**). Simultaneous control of blood glucose, blood pressure, and blood lipids was reported for 21.8% of patients.

Figure 1: Venn diagram showing proportion of patients with T2DM attaining their glycemia, blood pressure, and LDL-Cholesterol treatment goals (n=665)

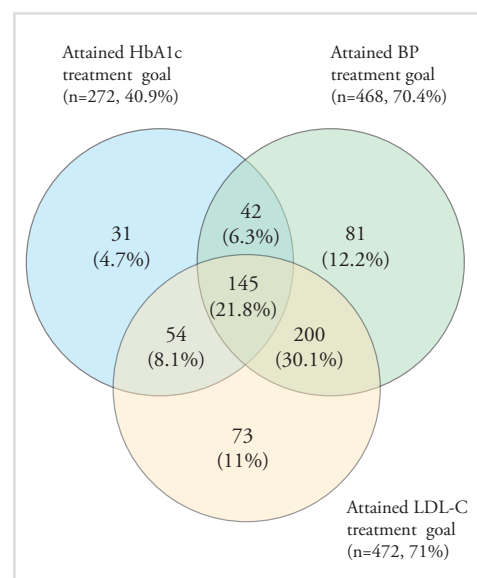


Table 2 shows the results of the logistic regression analysis of factors associated with attainment of the triple treatment goals. Patients who received moderate (OR=0.56, 95% CI of 0.35-0.91, p=0.02) to high intensity (OR =0.45, 95% CI of 0.21-0.97, p= 0.04) statin treatments were less likely to achieve concurrent treatment goals compared to the low intensity.

Table 2: Factors influencing glycated hemoglobin, blood pressure, and LDL-C goal achievement using logistic regression in patients with T2DM and dyslipidemia

	OR (95% CI)	p-value
<i>Ethnic Group</i>		
Chinese	1	-
Malay	0.72 (0.42, 1.23)	0.23
Indian	0.89 (0.53, 1.5)	0.66
<i>Age (years)</i>		
<60	1	-
≥60	1.53 (0.96, 2.42)	0.07
<i>Renal Disease</i>		
No	1	-
Yes	0.42 (0.15, 1.15)	0.09
Duration of T2DM	0.98 (0.93, 1.04)	0.56
Number of diabetic medications	0.50 (0.35, 0.73)	<0.01
<i>Diabetic medication type</i>		
Combination (Oral and insulin)	1	-
Not on diabetic medication	2.69 (0.63, 11.51)	0.18
Oral hypoglycemic agent only	2.33 (0.77, 7.02)	0.13
Insulin (of any type) only	2.63 (0.36, 19.14)	0.34
<i>Triglyceride Levels</i>		
Goals not achieved	1	-
Goals achieved	1.63 (0.74, 3.59)	0.23
<i>Statin Intensity</i>		
Low	1	-
Moderate	0.56 (0.35, 0.91)	0.02
High	0.45 (0.21, 0.97)	0.04

Discussion

Younger patients were less likely to attain triple treatment goals than those who were 60 years and above. This finding is compatible with

that of an earlier study, which postulated that younger adult patients might be less motivated to manage their diabetic conditions, as they could be busy with their jobs and, therefore, have less time to comply with healthy lifestyle

and treatment requirements.²⁰ Based on their life span, they would be more susceptible to vascular complications due to earlier onset of the disease and a longer period of time in which to develop these adverse events. Sally et al. reported that young people with T2DM felt current diabetes education programs did not cater specifically to their age group in several domains.²¹ They would appreciate clear and concise information in view of their time constraints. They desired family and peer support, as community acceptance was associated with a positive impact on their life experience with the medical condition.²⁰

One out of five patients (21.8%) in this study attained triple treatment goals, which is lower than the 33% of such patients managed by KP. Achievement of the triple goals by patients was significantly associated with their therapeutics, including the number of anti-diabetic medications and intensity of their statin regime. This requires that physicians regularly review and adjust the dosages of these medications, which can be time and resource intensive. Instead of being heavily dependent on physicians and the primary healthcare team, the population-based management (PBM) model used by KP can be used as an alternative approach. Featured in the WHO European integrated care models,²² the PBM leverages the stratification of the population and design of healthcare services to cater to the needs of the patient population. The majority of their patients with chronic diseases receive support for self-management of their illnesses, and high-risk patients are empowered by a combination of self-management and professional care.

PBM was adopted by and adapted to SHP in early 2013 and continues to evolve to cater to the growing population of patients with T2DM in Singapore. The institution collates monthly clinical data and laboratory reports of patients with specific disease codes (such as T2DM, hypertension, and dyslipidemia) in their electronic health records and stratifies their risk status according to their diseases based on clinical practice guidelines and indicators of their disease control. Nonetheless, the current IT system only permits the reporting of single indicators of disease control. This study presented the first ever accounting of patients who attained the triple treatment goals, setting the stage for further research and quality improvement projects to better the current benchmark.

Fewer medications and a shorter duration of T2DM were significant factors in triple control. This finding was comparable to a multinational survey in which predictors of glycemic control included short disease duration and the use of fewer anti-diabetic medications.²³ Increasing the number of medications may be required to optimize control as the disease progresses, but doing so may adversely increase the risks of poor medication adherence and side effects. Disease progression is thus associated with an increasing challenge in terms of attaining the triple goals. A longer-term strategy to curb this seemingly inevitable rise in disease burden from T2DM will be to move upstream to manage the an institutional approach, a multi-faceted national healthcare program has been launched in Singapore to fight a “war against diabetes.”²⁴ Interventions can be designed to target the disease at the micro- (individual), meso- (healthcare system), and macro- (national) levels to enable more patients to achieve these simultaneous goals.

Strengths and limitations

Unlike most studies which reported results relating to solo glycemic control, this paper provides an examination of triple quality indicators for a highly urbanized Asian population with T2DM. The concurrent triple goal attainment is a more comprehensive mitigating measure to reduce risks of both macro- and micro-vascular complications. The results of this paper provide baseline data to trigger qualitative improvement initiatives to raise the proportion of patients with T2DM attaining this target.

However, the study population was recruited from two typical polyclinics in northeastern Singapore. Caution should be used in extrapolating the results to the entire local population. A prospective study of these patients would allow the quantification of the risk factors and identification of key measures which would optimize success in attaining triple treatment goals.

The study did not include other potential factors which may hamper the achievement of the triple treatment goals, such as patients' physical activities; social habits, such as alcoholic intake; thyroid status and possible renal impairment; genetics and local gut hormonal responses to diet and medications; and interference from gut microbiomes.

Conclusion

Simultaneous control of glycemia, hypertension and dyslipidemia was achieved by 21.8% of the study population with T2DM. Younger patients of less than 60 years of age were less likely to attain triple treatment goals. The number of diabetic medications and the intensity of statin treatment were significant factors associated with successful triple treatment goal achievement.

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Declaration of Conflicting Interests

The authors declare no conflict of interest as they are not members of the Singapore Heart Foundation, which is the independent sponsor of the study.

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Randomized controlled trial on the effect of Al-Quran recitation vs counseling on smoking intensity among Muslim men who are trying to quit smoking

Aida Maziha Z, Imran A, Azlina I, Harmy MY

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Authors:

Aida Maziha Zainudin

(Corresponding author)
MD, MMed Family Medicine
Department of Pharmacology
School of Medical Sciences
Universiti Sains Malaysia
Kubang Kerian, Kelantan
Malaysia.

Imran Ahmad

MD, MMed Family Medicine
Department of Family Medicine
School of Medical Sciences
Universiti Sains Malaysia
Kubang Kerian, Kelantan
Malaysia.

Azlina Ishak

MBBS, MMed Family Medicine
Department of Family Medicine
School of Medical Sciences
Universiti Sains Malaysia
Kubang Kerian, Kelantan
Malaysia.

Harmy Mohd Yusoff

MD, MMed Family Medicine
Faculty of Medicine, Universiti
Sultan Zainal Abidin, Kuala
Terengganu, Terengganu
Malaysia.

Abstract

Introduction: Nicotine cravings and withdrawal symptoms are associated with higher rates of relapse. It has been shown that combining behavioral therapy and pharmacotherapy leads to a higher long-term abstinence rate in those who quit smoking. Al-Quran recitation has been proven to reduce anxiety among athletes before tournaments and pulse and heart rates among patients awaiting cardiac operations. As most of the patients who wish to stop smoking experience high-anxiety states, we postulate that Al-Quran recitation will also able to reduce craving among smokers attempting to quit smoking.

Methods: Fifty smokers from an outpatient clinic were randomly assigned to control and intervention groups. They were taught different ways of coping with smoking urges, i.e., counseling using the 12'M' method (control group) versus Al-Quran recitation (intervention group). They met for four consecutive weeks of counselling and to fill out a withdrawal scale. Carbon monoxide (CO) levels were tested at baseline and at week 4. At week 12, the number of cigarettes smoked was measured again.

Results: The reduction in the number of cigarettes smoked was 7 cigarettes in the counselling group and 9 cigarettes in Al-Quran recitation group over 12 weeks duration. There was a statistically significant difference in the number of cigarettes smoked between the groups. There was also a statistically significant difference in the change in cravings between the groups at week 4 (p -value= 0.005). However, the difference in the changes in CO levels between the two groups was not statistically significant.

Conclusion: Al-Quran recitation produced a statistically significant reduction in cigarette smoking at week 12 and a significant change in cravings at week 4 among smokers attempting to quit. Difference in smoking abstinence rates was not measured in this study.

Introduction

It is estimated that there are currently five million smokers in Malaysia. The prevalence of smoking among Malaysians aged 18 and over is 22.6%.¹ There are approximately 10,000 smoking-related deaths each year in Malaysia, and this total is estimated to increase to 30,000 per year by 2030 if the current smoking trends continue.² However, quitting smoking is not an easy task. The chance of success in a single, unaided attempt to quit smoking is approximately 1 in 100, and 98% of smokers relapse within a year.² The relapse rate is high due to the addictive nature of nicotine. Withdrawal symptoms occur when the nicotine level in the blood declines. Pharmacological agents proven to improve the chances of

successfully quitting smoking include nicotine replacement therapy, varenicline, bupropion, cysteine, and nortriptyline.³ It has been shown that combining a pharmacological agent with behavioral therapy is more beneficial than the pharmacological therapy alone in helping those who are trying to quit smoking.³

At present, patients attending clinics for smoking cessation in health care facilities are given counseling on how to stop smoking. This includes setting up a date to quit and getting rid of cigarettes, ashtrays, and other items that induce smoking. Counselling on the 12'M' method is given to control smoking urges. 12'M' stands for 'Melengah-lengahkan' (delay), 'Menarik nafas dalam-dalam' (take a deep breath), 'Minum air' (drink some

water), 'Membuat sesuatu' (do something), 'Mengunyah sesuatu' (chew something), 'Mandi' (take a shower), 'Membasuh tangan' (wash your hands), 'Melakukan senaman regangan' (do stretching exercises), 'Membaca doa' (say a prayer), 'Menjauhkan diri' (avoid), and 'Meditasi' (meditation).² The 12'M' method, in conjunction with pharmacotherapy, has been shown to be beneficial. The cessation rate for this combination (6 month's abstinence) ranges from 31.8%⁴ to 52.5%.⁵ There is no available data for 12'M' used as a single therapy.

A study among Muslims in Malaysia and Buddhists in Thailand suggests that a religious factor is independently associated with successful attempts to quit smoking in both countries; over 90% of participants reported that their religion guides their day-to-day behavior, in which smoking is discouraged. A logistic regression model suggests that the religious factor had a clear independent association with attempts to quit and translated into success for Malaysian Muslims.⁶ A few studies have shown that Al-Quran recitation can reduce anxiety and improve vital signs. A study in Iran showed a significantly reduced level of anxiety among athletes who recited the Al-Quran before tournaments.⁷ It also reduced anxiety in women awaiting a cesarean section⁸ and significantly reduced the pulse and respiratory rates of patients before heart surgery.⁹ Another study showed reduced anxiety, blood pressure, and pulse rates among patients awaiting abdominal surgery.¹⁰ These studies provide evidence that Al-Quran recitation has relaxation effects and brings calmness to the reciter. Taking into account that practicality is an important factor in adherence, four short chapters in the Al-Quran were chosen for this study because they are memorized by almost all Muslims and easily recited and reproduced. Till now, there has been no available data on the effect of Al-Quran recitation on smoking cessation or withdrawal symptoms. Therefore, in this study, the researchers tested the effects of Al-Quran recitation and 12'M' counseling on smoking intensity among Muslim smokers. The study also collected withdrawal symptoms scores and carbon monoxide levels from the participants to test for any changes that occurred as the result of the interventions.

Methods

A randomized controlled trial was conducted

among 50 smokers between June 2013 and June 2014 at the Outpatient Clinic, Universiti Sains Malaysia (USM) Hospital, a tertiary teaching hospital in Malaysia. This study was approved by the Human Research Ethics Committee of USM on the 29th of November, 2012. Its FWA registration number is 00007718, and its IRB registration number is 00004494. Current smokers, i.e., those smokers smoking ≥ 10 cigarettes per day, more than 18 years old, Muslims able to recite the Al-Quran, and intending to quit smoking, were included. Familiarity with Al-Quran recitation was necessary as those unfamiliar with the recitation would find it difficult and be unable to comply with the protocol. Those who had difficulty attending interventions, were participating in other interventions, or using pharmacotherapy to quit smoking were excluded. The investigator ensured the eligibility of the participants. A computer-generated randomization list of participants was obtained. The investigator randomized the patients according to the list into either the counselling group or Al-Quran recitation group.

Potential participants were screened at visit 1 (V1). The smokers who fulfilled the inclusion criteria were given an explanation concerning the study, and those who agreed to participate gave their informed consent. The participants were then allocated into two groups based on the randomization list. The participants were also asked to set a date to quit. They were scheduled to make visit 2 (V2) one day prior to their quit date. A week before V2, all participants were called as a reminder of their quit date.

At V2, the participants were required to fill out a questionnaire which contained three parts: demographic information, smoking characteristics (including a Fagerstrom score), and a religiosity scale. The baseline religiosity score was obtained in order to see if a direct relationship could be found between the piousness of the participant and the likelihood of success in quitting smoking. The score was obtained through the use of a validated scale, the Muslim Religiosity-Personality Inventory.¹¹ The baseline number of cigarettes smoked was recorded, and each participant's carbon monoxide (CO) level was tested using a carbon monoxide analyzer, microCO monitor model 36-MC02-STK. The validity of the tool was checked by the supplier a month prior to the start of the study. The same analyzer was

used for all participants. Participants were taught techniques to quit smoking, which included setting a date to quit, getting rid of cigarettes and ashtrays, and telling family and friends about their attempt to quit. They were also coached on ways to cope with smoking urges. The counselling group was taught the 12'M' method, and the Al-Quran recitation group was taught to recite four chapters of the Quran while concentrating on the meaning of the verses. The four chapters used were: Al-Fatihah, An-Nas, Al-Falaq, and Al-Ikhlas. The same investigator delivered the content for each group, guided by PowerPoint slides. A question and answer session was held during each group meeting or visit. Participants were asked to practice the methods and record their practices in a diary.

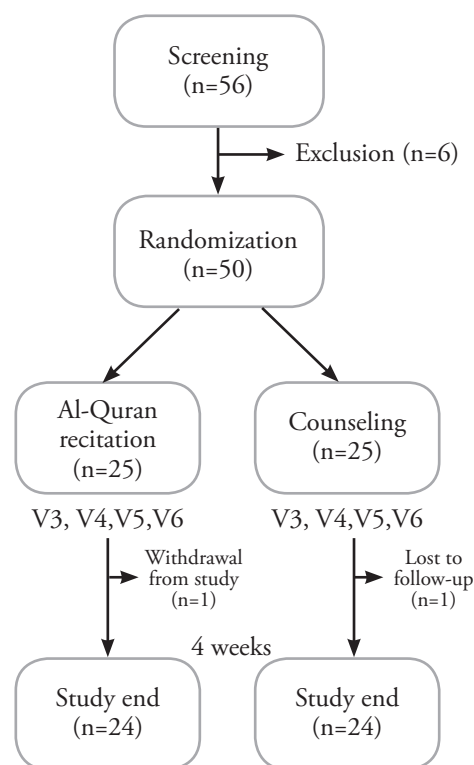
Participants were seen at visits 3 (week 1), 4 (week 2), 5 (week 3), and 6 (week 4). At each visit, counseling and Al-Quran recitation were emphasized, depending on the group participants were assigned to, and the Malay version of the Wisconsin Smoking Withdrawal Score (WSWS) (12) was filled out by the participants. At week 4, CO levels were assessed. At visit 7 (week 12), the number of cigarettes still being smoked per day was obtained via a phone call.

The primary outcome for this study was smoking intensity in term of the reduction in the number of cigarettes smoked per day at the end of study period, i.e., the difference in cigarettes smoked per day between week 1 and week 12. The secondary outcomes were the changes in withdrawal symptoms scores based on the WSWS and changes in CO levels from week 1 to week 4. The WSWS has 28 items, which are rated on a 5-point scale with 0 being totally disagree and 4 being totally agree. Low score signifies low withdrawal symptoms and high scores signifies high withdrawal symptoms. It contains seven domains, which are anger, anxiety, concentration, craving, hunger, sadness, and sleep. For analysis, the withdrawal symptoms score was calculated according to domain. The total score for each domain was then entered into the SPSS. The anger domain was covered by questions 13, 15 and 18; the anxiety domain by questions 3, 6, 8 and 10; the concentration domain by questions 4, 23 and 27; the craving domain by questions 9, 11, 20 and 26; the hunger domain by questions 1, 14, 16, 21 and 28; the sadness domain by questions 7, 12, 19 and 24; and the sleep domain by questions 2, 5, 17, 22

and 25. Questions 1, 2, 4, 10, 17, 22, and 24 had reverse scoring. The higher the total scores signifies the higher symptoms experienced by the patient.

The sample size was calculated using the Power and Sample Size Calculation (PSSC) software. The first objective was to compare the change in withdrawal symptoms score among group at 4 weeks intervention. The standard deviation (SD) value for "craving for a cigarette now" was adapted from a study conducted by Shahab et al.¹⁴ The second objective was to compare the change in carbon monoxide level among groups at 4 weeks intervention. The third objective was to compare the change in number of cigarette smoked among the intervention group compared to control group at 12 weeks intervention. The SDs for the CO level and number of cigarettes smoked were adapted from Lee et al.¹³ The detectable mean was based on expert opinion. Based on the sample size calculations for each objective, the largest sample size required was 21 (for objective 3). After factoring in a 20% drop out rate, the sample size calculated was 25 per group.

Figure 1. Study overview and design



Data was analyzed using SPSS for Windows 21.0. Non-parametric tests were used due to skewed distributions on boxplots charting (not shown). Independent t-tests were used for comparison of baseline characteristics, differences in withdrawal scores from baseline, differences in CO levels from baseline, and a difference in the number of cigarettes smoked between groups. The paired t-test was used to analyze the differences in withdrawal scores from baseline to endpoint in the same group. Data are reported as medians + Interquartile Range (IqR) unless otherwise stated, and a p-value of less than 0.05 was used to indicate a significant difference.

Results

A total of 56 potential participants were screened. Of these, 50 met the inclusion criteria and were randomized to the counseling group (n=25) and Al-Quran recitation group (n=25). One participant from Al-Quran

recitation group withdrew from the study at V4 since he could not comply with the Al-Quran recitation when he had smoking urges. In addition, one participant in the counseling group was lost to follow-up in V4-V6. Thus, 48 participants completed the study (response rate of 96%). Compliance with the counseling sessions and Al-Quran recitation sessions was 100%. All participants returned their diaries and achieved more than 70% compliance with the protocol (practicing 70% or more of the methods taught for coping with smoking urges as attested to in their diary).

Baseline characteristics

There were no statistically significant differences in baseline characteristics in terms of marital status, employment, income, education level, health status and religiosity between the two groups (results not shown). Baseline smoking characteristics are shown in **Table 1**.

Table 1: Smoking characteristics of participants at baseline

Variables	Al-Quran recitation Median (IqR)	Control group Median (IqR)	p-value
<i>Smoking characteristics</i>			
Number of cigarettes per day	14.5 (6)	12.5 (8)	0.238 ^a
Smoking duration (years)	22.5(21)	26.5 (15)	0.439 ^a
Fagerstrom score	4.00 (5)	4.00 (4)	0.761 ^a
Carbon monoxide level	10.0 (5)	8.5 (6)	0.407 ^a
<i>History of attempts to quit</i>			
Yes	22 (91.7) n (%)	21 (87.5) n (%)	1.000 ^b
No	2 (8.3) n (%)	3 (12.5) n (%)	
<i>Religiosity score</i>	124 (24)	120 (26)	0.391 ^a

Median (IQR) for numerical variable, n (%) for categorical variable,

^a Mann-Whitney Test

^b Fisher's Exact Test

Change in the number of cigarettes per day at week 12 and carbon monoxide levels at week 4.

There was a statistically significant difference in the reduction in the number of cigarettes smoked at 12 weeks between the two groups, as shown in **Table 2**. There was no statistically significant difference in the change in CO levels between the groups.

Table 2: Change in the number of cigarettes smoked at 12 weeks and CO levels measured at week 4

Variable	Group		Z-stat	p-value
	Al-Quran recitation Median (IqR)	Counseling Median (IqR)		
Number of cigarettes	- 9 (5.75)	- 7 (4)	-2.746	0.006^a
CO level	- 5 (4)	- 3 (3)	-1.001	0.317 ^a

^a Mann-Whitney Test

Group effect: withdrawal symptoms score between counselling and Al-Quran recitation groups

There was a statistically significant difference in the change in craving between the counseling and Al-Quran recitation groups at week 4, as shown in **Table 3**. Changes in other domains were not statistically significant.

Table 3: Changes in withdrawal symptoms scores by domain at week 4

Domain	Group		Z-stat	p-value
	Al-Quran recitation Median (IqR)	Counseling Median (IqR)		
Anger	5(3)	5 (3)	-0.358	0.720
Anxiety	6 (1)	6 (5)	-1.276	0.202
Craving	6 (2)	7 (1)	-2.823	0.005*
Concentration	7 (3)	8 (2)	-1.100	0.271
Hunger	7 (2)	7 (1)	-0.053	0.958
Sadness/ depressed	5 (3)	5 (3)	-0.272	0.786
Sleep	5 (2)	5 (3)	-0.333	0.739

^a Mann-Whitney Test

Time effect: withdrawal symptoms scores within groups

Within group analysis showed that there were statistically significant changes in anger, anxiety, and cravings at week 4 in the Al-Quran recitation group. However, in the counseling group, a significant change was seen only in the anxiety domain. Results are depicted in **Table 4**.

Table 4: Changes in withdrawal symptoms scores within group at week 4

Parameters	Al-Quran recitation group				Control Group			
	Week1	Median (IqR) Week4	Change (CI)	p-value ^a	Week1	Median (IqR) Week4	Change (CI)	p-value ^a
Anger	5(2)	5(3)	-3.345	0.001*	5 (4)	5 (3)	-0.868	0.385
Anxiety	7 (3)	6 (1)	-2.384	0.017*	8 (3)	6 (5)	-2.481	0.013*
Craving	8 (2)	6 (2)	-3.234	0.001*	7 (1)	7 (1)	-0.723	0.469
Concentration	7 (2)	7 (3)	-0.846	0.398	10 (4)	8 (2)	-1.244	0.214
Hunger	8 (3)	7 (2)	-1.042	0.297	8 (2)	7 (1)	-1.425	0.154
Sadness/ depressed	6 (1)	5 (3)	-1.496	0.135	5(3)	5(3)	-0.744	0.457
Sleep	5 (3)	5 (2)	-1.329	0.184	5 (2)	5 (3)	-0.086	0.931

^a Wilcoxon Signed Ranks Test

Discussion

Abstaining from smoking for more than three months is a predictor of success in quitting. It is suggested that self-reported cessation for more than three months should be considered an intermediate criterion for success in the evaluation of community interventions.¹⁴ Therefore, we called participants to determine the number of cigarettes smoked at 12 weeks. Our results showed a statistically significant difference in the number of cigarettes smoked at week 12 in the Al-Quran recitation group compared to the counseling group. An

alternative outcome measure is the abstinence rate, which measures the proportion of patients who totally quit smoking. However, this rate is usually computed at least 6 months after the end of the intervention. It was not possible to follow these participants for this length of time as the researcher had a time restriction.

When chronic tobacco consumers abstain from tobacco, they develop withdrawal symptoms. Tobacco withdrawal symptoms include cravings, hunger, anger, anxiety, depression, difficulty concentrating, impatience, insomnia, and restlessness. These symptoms peak within

the first week and last for two to four weeks.¹⁵ Therefore, in this study, a withdrawal score was taken at four weeks post intervention. Our results showed a statistically significant difference in only the change in craving scores at week 4 in the Al-Quran recitation group in comparison to the counseling group; differences in the changes in other withdrawal symptoms were not statistically significant.

In this study, participants were instructed to recite four short Al-Quran chapters, namely Al-Fatihah, An-Naas, Al-Falaq, and Al-Ikhlās. These chapters comprise a few long verses each that required the participants to take a deep breath in order to recite the verse completely. When reciting these verses, they were unintentionally practicing deep breathing. Our results are consistent with using yogic breathing exercises¹⁶ and controlled deep breathing.¹⁷ A study by Shahab¹⁶ investigated the effect of breathing exercises on cravings and withdrawal symptoms and revealed a statistically significant reduction in smoking urges but not for any other withdrawal symptoms. Reciting Quranic phrases has been proven to reduce anxiety among athletes and women awaiting caesarean sections and also reduces the pulse rate among patients awaiting open heart and abdominal surgery. These physiological changes could reduce the cravings among those who recite the Al-Quran.

CO levels were examined at baseline and four weeks' post intervention. There was no significant difference in the changes noted between the two groups. This non-significant difference can be explained by a few factors. First, a number of patients exhibited poor exhalation technique. At baseline, there were already readings of less than 10ppm, which did not correlate with their smoking status. In particular, this occurred among patients who had asthma and/or heart disease, explaining their poor efforts to exhale completely, which causes lower CO levels to be

recorded. Another factor was high variability in smoking technique. Some of the smokers inhaled the cigarette smoke more deeply than others. The participants who inhaled 'lightly' had lower carbon monoxide levels, according to the CO analyzer. Another possible reason was that patients had reduced cigarette smoking a day before the orientation day, as the researcher informed them of the date ahead of time. This would result in lower CO readings. Therefore, when compared to levels at week 4, there was no significant change.

From this study, it was discovered that Al-Quran recitation led to a significant difference in the change in the number of cigarettes smoked at 12 weeks compared to counseling with the 12'M' method. This finding suggests that the Al-Quran recitation approach is a potential method with which to improve smoking cessation efforts. This is due, in particular, to its ability to reduce cravings, as a higher degree of craving is associated with relapse. Because Al-Quran recitation is shown to reduce stress, it can reduce cravings, and this is reflected in the lower number of cigarettes smoked. This study was limited by the small sample size. It may not be able to represent all Muslim men who are trying to quit smoking. The same investigator delivered the content to both groups to reduce systematic bias. Ideally, the counseling and Al-Quran recitation groups would have different counselors. It is also important to note that self-reported measures of withdrawal symptoms are more vulnerable to differential misclassification bias, which can make interpreting the results difficult.

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We would like to acknowledge the cooperation of all the participants and staff involved in this project. We would also like to acknowledge the questionnaire's authors—Steven Eric Krauss and Ahmed Awaisu—for giving us permission to use the questionnaire.

How does this paper make a difference to general practice?

- Al-Quran recitation had been shown to reduce anxiety among athletes before tournaments and pulse and heart rates among patients awaiting cardiac operations.
- There is no prior study which has assessed the influence of Al-Quran recitation on reducing nicotine withdrawal symptoms and smoking intensity.
- Our study revealed that Al-Quran recitation exerted a moderate effect on smoking intensity.
- Our study also revealed a significant difference in the change in cravings in the Al-Quran recitation group compared to the counseling group. This study did not demonstrate a difference in smoking abstinence rates which was not measured.

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A forgetful and angry old lady

Mah SL, George P

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Authors:

Mah Sue Lynn

(Corresponding author)
PhD Student
(University of Nottingham)
Archdiocesan Office for
Human Development KL
Malaysia.
Email: suelynmmah@hotmail.com

Philip George

Consultant Psychiatrist & Addiction
Medicine Specialist
International Medical University
Malaysia.
Email: drphilgeorge@gmail.com

Abstract

Dementia is typically characterized by the deterioration of cognitive abilities and is a common disorder among the elderly in Malaysia. However, behavioral and psychological symptoms are also present in approximately 90% of dementia patients.¹ We report the manifestation of these symptoms in an elderly woman with dementia and the treatment thereof.

Introduction

The behavioral and psychological symptoms of dementia refer to the independent group of non-cognitive symptoms and behaviors observed regardless of the subtypes of dementia¹. Examples include aggression, disrupted mood, and changes in personality, thoughts, appetite, and sleeping patterns. The aim of this case report is to highlight these symptoms and show how they cause distress to the patient and family and affect quality of life.

Case summary

A 90-year-old female has been showing changes in her behavior and personality as her dementia progresses. These changes began about 10 years ago. The symptoms are insidious and getting worse progressively.

In the past, she was a very active woman and busied herself with gardening, house chores, and cooking. She travelled a lot and enjoyed watching vernacular shows and world news. She has lost interest in all of these things. She stopped reading more than 6 years ago. She is suspicious of her surroundings and believes that someone has been locking her in her room and refuses to go out into the garden for fear of perpetrators. She is convinced that the maids are out to get her and stealing all of her belongings, although most of her valuables are in a safe deposit box. She hits the maids and throws things at them to make them quit working to look after her. She has also started hitting her head against the wall in frustration at times when challenged with her persecutory thoughts. These symptoms seem to be worse in the evening and her sleep pattern have changed, whereby she sleeps more during the day and stays awake at night.

She cannot bathe and dress by herself, but she can eat on her own. She lives with her eldest daughter (main caregiver), but and does not speak to her grandchildren as she does not recognize them. Her physical status revealed a fairly well-groomed elderly lady in a wheelchair. She had poor eye contact and looked suspiciously at her surroundings and the clinician. She was irritable and gave single word answers to most questions. She had poor immediate and five-minute recall and poor recent memory. Her remote memory was intact. She believed that there was nothing wrong with her and it was her daughter who needed treatment. Her Mini Mental State Examination score was 12 out of 29 (removing the question on season).

The patient had no pre-existing medical illness. A diagnosis of moderate to severe dementia, which was most probably Alzheimer's type, was made. As the patient lacked mobility, her family were not keen on her being reviewed and treated by other healthcare professionals (e.g., occupational therapist/psychologist), but she is regularly reviewed by a physician.

The patient was started on Memantine 5mg nocte, Escitalopram (an antidepressant) 5mg nocte, and Quetiapine (an antipsychotic) at 12.5mg nocte, slowly increasing the dosage to 25mg nocte. There were no side effects reported.

In subsequent follow-ups, she was more communicative, cheerful, and less paranoid. Her sleep pattern was improving, and her daughter and other children were happy to spend more time with her. The main caregiver has also reported feeling less stressed after her mother underwent treatment.

Discussion

In the 1980's, the total Malaysian population was 13.7 million. Over the next 30 years, the total population more than doubled to 28.3 million by 2010.² The latest population statistics, as of July 2012, report a total Malaysian population of 29.2 million, of which 5.1% represents those aged 65 years and above.³ Together with a larger number of elderly, life expectancy is also increasing. Based on the Mental Health and Quality of Life of Elderly Malaysians Survey, the overall prevalence of dementia is 14.3%. The prevalence rates showed a clearly increasing trend by age group, doubling every 10 years, from 9.5% in the 60–69 age group up to 26.3% in those aged 80 and above. Women showed a higher prevalence rate (19.7%) than men (8.8%).⁴ In terms of disabilities faced in routine and instrumental daily life activities, the prevalence rate for older women (31%) is double that of older men (14%).⁴ These daily activities would then be assisted by a caregiver, and it has been found that female caregivers tend to report greater stress.⁵

In the case we report, a family member of the patient reported that the patient's short-term memory is poor, a defining symptom of dementia. This symptom includes problems with recalling recent events, remembering names, and repeating questions.⁶ However, the patient felt that there was nothing wrong with her. She presented with the behavioral and psychological symptoms of dementia, which includes disturbances in emotional experiences, delusional and abnormal thoughts, disinhibition, disrupted circadian rhythms, and aggression.¹ Patients with

dementia often have false beliefs that include: i) suspiciousness, ii) fear of abandonment/institutionalization, and iii) seeing malicious/discriminatory intents on the part of others towards oneself.¹ These beliefs can be confusing and frightening to patients, potentially leading to aggressive behaviors⁷.

Although psychiatric comorbidity or symptoms are common, most patients and their caregivers suffer in silence. This is largely due to the stigma of seeking psychiatric help and getting the elderly to agree to see a psychiatrist. Moreover, family members are unsure as to whether or not the symptoms exhibited are signs of normal aging. The stress that caregivers and families undergo can be significant, sometimes leading to depression and anxiety in them, as well.

In managing patients with this condition, it is always important to do a risk benefit analysis. Very often the benefit of being on a low-dose antipsychotic can outweigh the risks. Of course, there is a need to be mindful of the Lewy Body type of dementia, in which antipsychotics can worsen the patient's condition.

Funding & Conflict of Interest

None

Ethics

An ethical challenge was getting the patient to take medication for a condition that she does not believe she has. In fact, our patient felt her daughter should be on medication and not her.

How does this paper make a difference to general practice?

- Conditions such as dementia are becoming more common in a Family Physician's setting as the population of the nation is aging rapidly.
- Therefore, an understanding of the behavioral problems associated with dementia and challenges of caregivers in managing these problems is vital in order to raise public awareness.

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Chest discomfort in a patient with dengue – is it an acute myocardial infarction?

Koh KC, Hong HC

Koh KC, Hong HC. Chest discomfort in a patient with dengue – is it an acute myocardial infarction? . *Malays Fam Physician*. 2018;13(2);29–31.

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Authors:

Koh Kwee Choy

(Corresponding author)

FRCP (Lond), MMed, MBBS

BSc (Hons)

Department of Medicine

International Medical University

Malaysia.

Hong Hooi Chuen

MRCP, MBBS

Department of Medicine

Hospital Tuanku Ja'afar Seremban

Negeri Sembilan, Malaysia.

Abstract

Cardiovascular symptoms presenting in a patient with dengue fever may pose a diagnostic dilemma. We describe a case of dengue myocarditis mimicking an acute myocardial infarction in a 56-year-old woman.

Introduction

Myocarditis is an inflammation of the myocardium. Viral infection is one of the most common causes of myocarditis. Although rare, dengue has been reported to cause myocarditis.¹ The exact pathophysiology of myocardial cell injury in dengue remains unknown, although it is thought to be from direct viral invasion of the cardiac muscles, a cytokine-mediated immunological response, or both.^{2,3}

Diagnosing myocarditis is challenging due to its polymorphic presentations with no pathognomonic signs or symptoms, which can range from asymptomatic subclinical presentation to mild fatigue, lethargy, chest pain, or even complications such as heart failure, cardiogenic shock, cardiac arrhythmias, and death. We describe a woman who presented with typical angina chest pain following an uneventful bout of dengue.

Case Report

Madam MLC, a 56-year-old woman, presented with complaints of chest discomfort, progressive shortness of breath, leg swelling, abdominal fullness, and decreased effort tolerance for one day. There was an absence of chest pain and profuse sweating. Other than being post-menopausal, she had no other cardiovascular risk factors. Six days prior to the onset of these symptoms, she had presented with a high-grade fever at a private hospital and been diagnosed with dengue fever (positive NS1 antigen). She was hospitalized and, following an uneventful stay, allowed to return home after six days.

At presentation, she was conscious, alert, and afebrile. Her blood pressure and pulse rate were 100/60 mmHg and 120 /min, respectively. Her oxygen saturation was 99 % with room air. Her jugular venous pulse was raised, and there was bilateral pedal oedema. Precordial examination was unremarkable but crepitations were audible at the lung bases.

An electrocardiogram (ECG) revealed sinus tachycardia with a rate of approximately 100/min; saddle-shaped ST-segment elevation greater than 2mm in leads II, aVF, V4, V5, and V6 without reciprocal ST depression, and diminished QRS amplitude in several limb and chest leads (**Figure 1**). A chest radiograph confirmed the presence of minimal bilateral pleural effusion. Echocardiography revealed minimal pericardial effusion with no evidence of cardiac tamponade and an ejection fraction of 60%. The chamber sizes were normal with no hypokinetic areas. Her troponin I level was elevated (10.51 ng/ml; reference < 0.04 ng/ml) along with the other cardiac markers. A summary of relevant laboratory results is shown in **Table 1**.

A clinical diagnosis of dengue myocarditis with acute left heart failure was made. She was administered supplemental oxygen and an intravenous diuretic (furosemide) and advised to have complete bed rest. Serial ECGs done up to 12 hours post-admission showed similar ST-segment elevations with no Q wave formation. Serial aspartate transaminase (AST) showed a downward trend to normalization by day 7 of hospitalization. She was discharged after 12 days of uneventful hospitalization with the advice to avoid strenuous exercise till her next review at the outpatient clinic.

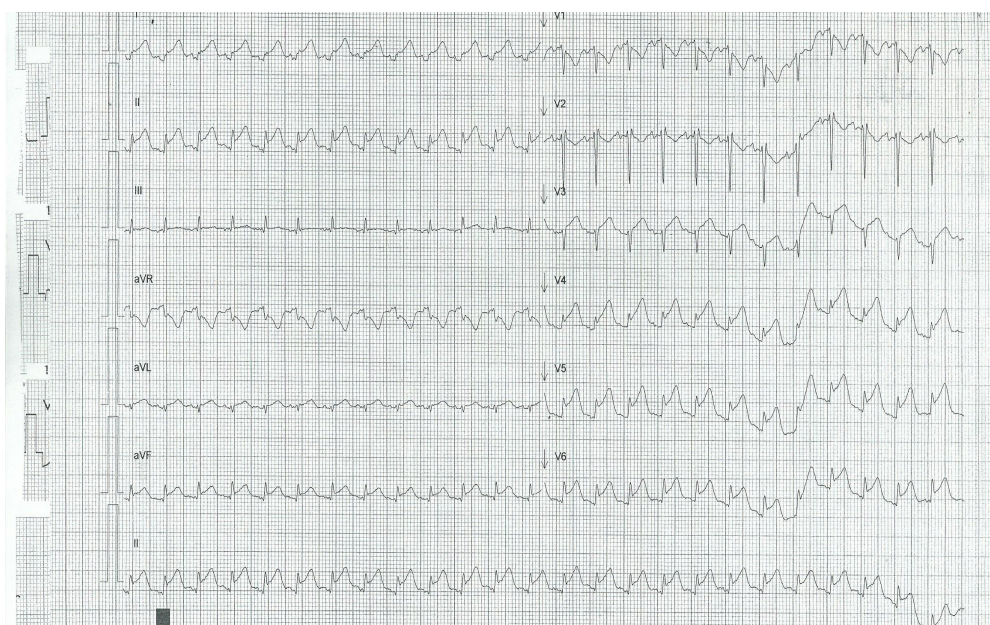


Figure 1: ECG showing ST segment elevation revealed greater than 2mm in leads II, aVF, and V4 to V6.

Table 1: Laboratory results

Laboratory parameter	Reference	Day of hospital stay						
		1	2	3	4	5	6	7
White blood cell ($10^9/L$)	4.5 – 11	12.6	14.1		10.6		7.7	7.5
Hemoglobin (g/L)	12 – 16	13.5	13.3		11.7		10.2	10.3
Hematocrit (%)	36 – 46	40.9	39.8		35.2		30.2	31.0
Platelet ($10^9/L$)	150 – 400	171	237		269		304	343
Aspartate transaminase (AST) (U/L)	8 – 20	206	219	150	105	79	51	41
Lactate dehydrogenase (U/L)	45 – 90				520			
Creatine kinase (U/L)	10 – 70				254			
Troponin I (ng/ml)	< 0.04	10.51						
Dengue IgM		equi-vocal						

Discussion

The clinical presentation of myocarditis is highly variable, often mimicking other non-inflammatory cardiac disorders. Our patient presented with features of acute heart failure (AHF) at the tail end of an uneventful dengue infection. The differential diagnoses would include acute myocardial infarction (AMI) and dengue myocarditis. A high level of clinical suspicion is required to diagnose the latter.

Laboratory markers of myonecrosis, such as creatine kinase (CK-MB), troponin I or T (cTI or CTT), lactate dehydrogenase (LDH), alanine transaminase (ALT), and aspartate transaminase (AST), are elevated in myocarditis. Troponin I (cTI) is often markedly elevated in the early phase of the

disease and is suggestive of acute myocarditis. However, the magnitude of cTI elevation is not related to survival.⁴ AST is considered the most sensitive marker of myocarditis with a sensitivity of 85%, although its specificity is relatively low.^{5,6} In addition, C-reactive protein (CRP) and erythrocyte sedimentation rate (ESR) are typically elevated with leukocytosis. In our patient, cardiac markers were elevated, with raised AST and leukocytosis (Table 1).

ECG changes characteristic of myocarditis include saddle-shaped ST-segment elevations, which are usually diffused. This diffusion is typically absent in lead VI without the reciprocal ST depressions usually seen in ST-elevation myocardial infarction (STEMI) and diminished QRS amplitudes.⁷ In addition, the ST elevation is typically < 4mm high and

does not occur simultaneously with T-wave inversions, unlike STEMI. Other ECG changes associated with myocarditis include abnormal Q waves, transient second- or third-degree heart block, prolonged QRS or QT, ventricular arrhythmias, and AV conduction defects.⁷

Although the ECG changes and raised troponin I level in our patient were in favor of AMI, the preceding history of a viral infection and absence of chest pain and profuse sweating prompted consideration of the alternative diagnosis of dengue myocarditis. The lack of Q-wave formation in serial ECGs in this patient provided another vital clue that she did not suffer an AMI.

Nevertheless, the diagnosis of dengue myocarditis is challenging due to its non-specific clinical presentation and the lack of a safe and sensitive non-invasive diagnostic test. Endomyocardial biopsy remains the 'gold standard' diagnostic test, but the procedure is invasive and not commonly done. Post-viral myocarditis should be considered when a patient presents with or without

cardiac symptoms and signs, such as raised cardiac markers, ECG changes suggestive of acute myocardial injury, and arrhythmia or cardiac function abnormalities on an echocardiography, with a history of viral illness.⁸

Treatment of dengue myocarditis depends on its presentation. General measures in this patient included heart failure therapy through judicious use of diuretics; oxygen supplementation, as hypoxia may, at least in in vitro studies, aggravate myocarditis⁵; and prolonged rest, as in vitro studies have shown exercise to be associated with increased viral replication in the myocardium. Nonsteroidal anti-inflammatory drugs are not recommended and have been shown to exacerbate myocarditis.⁹

The ability to recognize dengue myocarditis is valuable in avoiding misdiagnosis. The abnormal ventricular function in dengue myocarditis generally resolves rapidly, and patients generally have good outcomes, although fatal complications have been reported.³

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Kimura Disease: A differential diagnosis in a nephrotic child

Aziz A, Mohamad I, Zawawi N

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Authors:

Azliana Aziz

(Corresponding author)
MB Bch BAO
Department of Otorhinolaryngology-
Head & Neck Surgery, School of
Medical Sciences, Universiti Sains
Malaysia, 16150 Kota Bharu
Kelantan, Malaysia.
Email: az.aziz21@yahoo.com

Irfan Mohamad

MMed ORL-HNS
Department of Pathology, School
of Medical Sciences, Universiti
Sains Malaysia, 16150 Kota Bharu
Kelantan, Malaysia.

Norzaliana Zawawi

MPath
School of Dental Sciences, Universiti
Sains Malaysia, 16150 Kota Bharu
Kelantan, Malaysia

Abstract

Kimura disease presents as benign lesion and is commonly present among the Asian population. It is a disease with a favourable prognosis and a peak age of onset in the third decade. It is a chronic inflammatory disorder of unknown etiology that involves the lymph nodes and subcutaneous tissues of the head and neck region. We report a case of a 15-year-old boy with multiple Kimura lymphadenopathies involving the left posterior auricular region as well as the anterior and posterior triangles of the neck.

Introduction

Patients with head and neck lesions can present to primary care for initial investigation and are commonly referred to otorhinolaryngologists. The involvement can be a single or multiple and painful or painless enlarging pathology. The most common neck mass is a cervical lymphadenopathy for which a variety of causes or disorders including infectious, autoimmune, and allergic diseases as well as benign and malignant neoplasms have been reported. Others may present with masses such as keloids, osteomas and cysts. Less commonly, a Kimura lymphadenopathy case may present. Kimura lymphadenopathy most typically affects young Asian males with an incidence of coexisting renal disease ranging from 10% to 60%.¹

Case report

A 15-year-old boy, with an underlying steroid-resistant nephrotic syndrome, was referred to us for a painless left posterior auricular lesion of more than 5 years in duration. The lesion was gradually increasing in size with rapid enlargement within the past 2 months. There was no history of otalgia, otorrhoea, hearing impairment, trauma or insect bites to the area. He had no significant nose or throat symptoms, no constitutional symptoms or contact with any tuberculosis patients. He was diagnosed with nephrotic syndrome at the age of 7. However, he developed a resistance to steroid treatment and had a number of relapses prior to referral to our clinic. The renal biopsy done was inconclusive. He was treated with high dose of oral prednisolone and oral

Cyclosporin A. The patient was non-compliant to medications. Prior to his referral to our service, he had an excisional biopsy done by the Surgical Department for a similar lesion at the left posterior triangle of the neck.

On examination, there was a smooth-surfaced left posterior auricular lesion measuring 4cm x 2cm in size, which was non-tender, fixed and fluctuant in consistency. On neck palpation, there were also multiple small lymph nodes present in the anterior and posterior triangles of varying sizes. The largest node was at posterior triangle measuring 1cm x 2cm. Examination of the ears was normal.

An ultrasonography of the neck revealed multiple cervical lymphadenopathies in the left posterior auricular region, and the anterior and posterior triangles with the left posterior auricular nodes homogenously hyperechoic. It also demonstrated increased vascularity. Other enlarged nodes in the anterior and posterior triangles varied in sizes contained multiple target signs and showed increased vascularity.

Subsequently, an excisional biopsy of the left posterior auricular swelling was done. A 4cm x 3cm mass was completely excised. The histological examination revealed lymph nodes composed of variable sizes of lymphoid follicles with prominent germinal centers. The parafollicular cortex (**Figure 1**) area was heavily infiltrated by eosinophils with areas of eosinophilic abscess formation. Interstitial fibrosis and hyalinized vessels were present however no Warthin-Finkeldey polykaryocytes or folliculolysis were noted (**Figure 2**). Features of Hodgkin's lymphoma are not readily identified either

morphologically or immunohistochemically. This finding is consistent with Kimura Disease. A similar pathology was reported from the excisional biopsy done earlier by the surgical team. The patient was reviewed for the next 6-month period and no recurrence was noted at the site of the excision. However, after approximately a year, the patient developed a similar new lesion on the neck but further surgical intervention was not contemplated. The patient continues to attend his regular pediatric medical follow-ups and reviews.

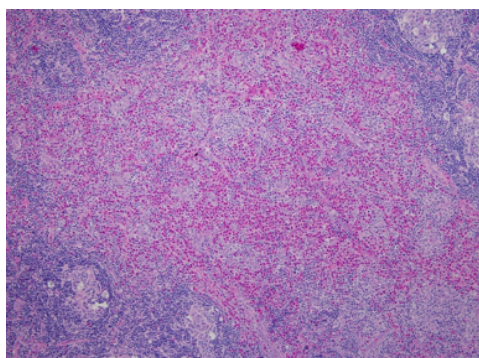


Figure 1: The parafollicular cortex area shows intense infiltration by eosinophils and capillary hyperplasia with reactive lymphoid follicles seen at the periphery of this figure. (Hematoxylin and eosin, 10X)

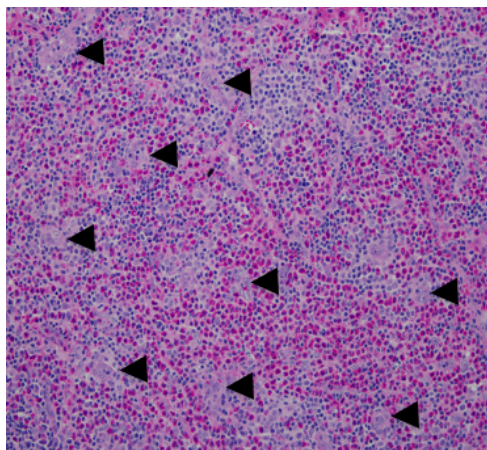


Figure 2: Eosinophilia and capillary hyperplasia (arrows). (Hematoxylin and eosin, 20X)

Discussion

The general presentation of head and neck masses in the primary care setting may vary, ranging from benign lesions to nodal metastasis. Other common head and neck lesions may include cervical lymphadenopathy caused by infections such as tuberculosis, lymphoma and allergic and autoimmune diseases.

Kimura disease, which was first reported in 1937² by Kimm and Szeto, is a cause of cervical lymphadenopathy which most often involving the cervical and posterior auricular lymph nodes. It is a common disease in the East Asian population with a higher preponderance of the disease in males. It also has a favorable prognosis and a peak age of onset in the third decade.³

Kimura disease is characterized by painless subcutaneous masses in the head and neck region occurring commonly in the pre-auricular area. In our case, the patient presented with a painless site in the left posterior auricular region. It is not known why the disease commonly occurs at this site. It may also affect axillary, epitrochlear and inguinal lymph nodes, as well as submandibular salivary glands.⁴ Rarely does it involve nasal sinuses, the oral cavity, the orbit and median nerves or the lacrimal glands.

It is an inflammatory condition which is often associated with elevations in serum immunoglobulin E levels and eosinophilia.⁵ In our case, there was the presence of tissue eosinophilia. The tissue obtained was heavily infiltrated by eosinophils with areas of eosinophilic abscess formation present. This is consistent with a study done in the United States involving a series of 21 cases of Kimura disease in which the majority had eosinophilia. Other histological features include follicular hyperplasia, eosinophilic infiltrates and the proliferation of post-capillary venules.⁶

Interestingly, 12 percent of patients with Kimura disease have proteinuria⁷ and nearly half of the cases have nephrotic syndrome. A steroid-resistant nephrotic syndrome associated with Kimura disease has been reported. Hung et al also reported a case similar to ours in which a 3-year-old boy with Kimura disease-associated nephrotic syndrome initially responded well to steroid treatment.

However, he suffered frequent relapse until finally, he became steroid resistant and a progressive decline in renal function occurred.⁸ In our patient, the nephrotic syndrome was diagnosed earlier than the Kimura disease and was treated with high doses of oral prednisolone and oral Cyclosporin A. Non-compliance with medications can also lead to the recurrence of the Kimura lymphadenopathy despite recent evidence showing a positive result with low-dose Cyclosporin A.⁸

The approach to the clinical problem involves a complete history and examination. The features that are strongly suggestive of Kimura disease include a painless, subcutaneous mass in the pre-auricular region, a patient of East Asian descent and a male in his third decade.

For further workup, blood tests, a radiological investigation and a biopsy are required.

A definitive diagnosis is based on the histopathological evaluation of the resected lesion. It should be noted that no pathognomonic features have been recognized for Kimura disease.⁹ The most common histological features found in Kimura disease include reactive follicular hyperplasia, eosinophilic infiltration and postcapillary venules proliferation were found in the presented case. Other features which are frequently present such as fibrosis, polykaryocytes, eosinophilic abscesses and vascularization of the germinal centres as described by Hui et al¹⁰ were not identified in our case.

Multiple treatment methods have been proposed for Kimura but surgical resection is the most common. However, the recurrence rate remains high at approximately 60 percent after local excision of the lesion. Recurrence has been reported in one of the five cases which have undergone complete resection.¹¹ Our patient also had a recurrence of the disease at location other than the excision site.

Particularly for a recurrence of the disease, some case reports suggest benefit from corticosteroids, the usage of the selective H1 receptor antagonist cetirizine¹² or radiotherapy.¹³ Others propose the use of low-dose Imatinib for an excellent outcome in Kimura disease treatment.⁴

However, it was found that tumor recurrence is common after the cessation of steroid therapy¹¹. The successful complete remission with cetirizine for 6 months has been reported. Cetirizine in this case acts as anti-inflammatory agent apart from inhibiting eosinophil chemotaxis and adhesion to endothelial cells.¹²

As for radiotherapy, its promising role has been highlighted when compared to local excision and systemic steroid therapy. A study showed

local response rates of 64.3% and 22.2%, respectively, for the two types of treatment. There were no side effects with a mean time of 65 months of follow-up in the radiotherapy group.¹³ The effectiveness of radiotherapy has been supported by a few case studies using an effective total dose of radiation between 20 Gy to 45 Gy of radiotherapy. There were no adverse effects observed during a mean follow-up period of 65 months¹⁴ and there have been no documented malignant transformations to date.

In selected cases, conservative management may be an option. It may be wise to leave the lesion alone due to frequent tumor recurrence, and the difficulty in obtaining a complete resection due to the infiltrative nature and multiplicity of the tumor and the associated draining lymphadenopathy.¹¹ We opted for surgical excision in this case, as the lesion was accessible and could be excised safely for histopathological confirmation of the diagnosis. The patient was spared from the potentially harmful side effects of radiotherapy or cytotoxic therapy.

Currently, there is no proposed duration of follow up. However, a tumor recurrence four years after resection has been reported¹¹. No case of malignant transformation of the Kimura Lymphadenopathy has been reported in the literature.

Conclusion

Diagnoses of head and neck masses are challenging to the Primary Care Practitioner as there can be multiple differential diagnoses. Occasionally, rare diseases such as Kimura Lymphadenopathy may be present. In such instances, referral to a specialist is in order. Strong indications of Kimura disease include a painless, subcutaneous mass in the pre-auricular region involving a male patient of East Asian descent in his third decade. Apart from a clinical determination, the diagnosis of Kimura disease can be made from radiological and most importantly histopathological examinations. Challenges remain in the management and treatment of the disease. However, the disease is fortunately benign as no malignant transformation has yet been described.

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Metallic hair pin aspiration into the left tertiary bronchus

Noh KB, Salim R, Abdullah MS, Mohamad I

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Authors:

Khairul Bariah Noh

(Corresponding author)
Department of Otorhinolaryngology -
Head & Neck Surgery
School of Medical Sciences
Universiti Sains Malaysia Health
Campus, 16150 Kota Bharu
Kelantan, Malaysia.
Email: siskik85@gmail.com

Rosdan Salim

Department of Otorhinolaryngology -
Head & Neck Surgery
School of Medical Sciences
Universiti Sains Malaysia Health
Campus, 16150 Kota Bharu
Kelantan, Malaysia.

Mohd Shafie Abdullah

Department of Radiology, School of
Medical Sciences, Universiti Sains
Malaysia Health Campus, 16150
Kota Bharu, Kelantan
Malaysia.

Irfan Mohamad

School of Medical Sciences,
Universiti Sains Malaysia Health
Campus, 16150 Kota Bharu
Kelantan, Malaysia.

Abstract

Foreign body aspiration is commonly described in infants and children. However, recently, a new high-risk group was identified among young women, especially those from the Muslim population who wear the traditional hair scarf. This is due to the habit of holding the scarf pin in between the lips to free hands to adjust the scarf more easily. Talking, laughing, or coughing while fixing the scarf may result in inadvertent inhalation of the pin into the tracheobronchial tree. We present a case of scarf pin inhalation and the challenges encountered in managing this patient during the successful removal of the pin via flexible bronchoscopy under fluoroscopy guidance. This particular case was technically challenging for us as the sharp tip of the needle was pointing upward and piercing the bronchial mucosa.

Introduction

Tracheobronchial foreign body aspiration is a nightmare and can result in life-threatening complications, especially among children. Although it is rare in adults, the incidence is known to increase with advancing age.¹ This is due to the failure of airway protective mechanisms as an adult age.

However, nowadays, incidences are being reported in young Muslim women which involve the aspiration of hair scarf pins as a result of careless handling.²

Clinical presentation may vary depending on the site the foreign body has embedded in. Removal of a sharp foreign body is technical challenging and needs urgent attention. Locating the sharp end of the hair scarf pin is the key to removing this type of foreign body.³

Case Report

A 35-year-old lady was referred from a private hospital for further management of a foreign body lodged in the bronchus. She had held a scarf pin between her lips in order to have both hands free while fixing her head scarf, but she allegedly accidentally aspirated the foreign body after coughing suddenly. A few minutes after that, she started to have mild discomfort on the left side of her chest, especially while talking and taking a deep breath. Otherwise there was no hoarseness,

fever, shortness of breath, dysphagia, or other obstructive symptoms.

Clinically, the patient was comfortable with stable vital signs. On auscultation, air entry was equal for both lungs.

A chest radiograph (AP view) revealed a radio-opaque foreign body measuring 4 cm in length, which was vertically located in the left lung field (**Figure 1**). No pneumothorax was detected.

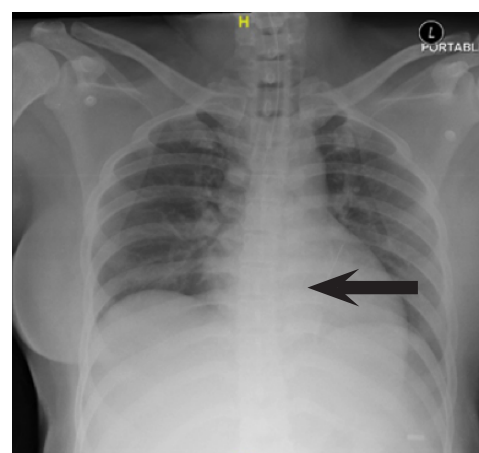


Figure 1: Radio-opaque foreign body, approximately 4 cm in length, towards left side of lung field (see arrow)

Patient was posted for emergency foreign body removal under general anesthesia (GA). Rigid and flexible bronchoscopy was performed. Intraoperative findings showed that the metal pin was located at

the left lower tertiary bronchus and was half-embedded in the bronchial wall. As the tip of the pin was embedded in the mucosa, multiple attempts to remove the pin were fruitless. After struggling for many hours, the procedure was abandoned.

Computed tomography (CT) of the thorax was then arranged after discussion with a team of interventional radiologists to locate the tip of the pin and rule out migration of the foreign body. The CT scan revealed that the tip of the pin was embedded approximately 1 cm into the bronchial septum. The head of the pin was pointed inferomedially at the left tertiary bronchus, making the attempt to grab the distal end extremely very difficult (Figure 2).

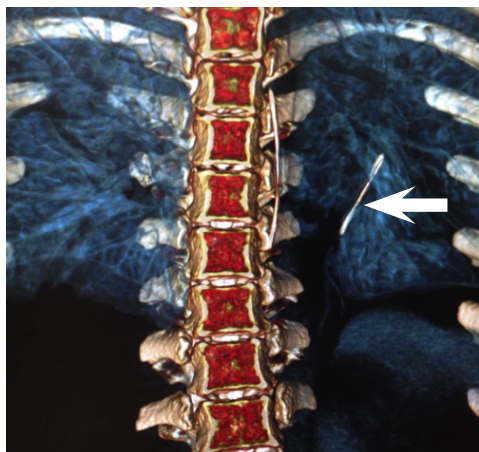


Figure 2: Computed tomography image reconstruction of thorax. Note the head of the pin pointed inferomedially at the left tertiary bronchus.

We proceeded with flexible bronchoscopy and foreign body removal under GA with a combined otorhinolaryngology (ORL) and radiology team and a cardiothoracic surgeon standing by. An angiocatheter was inserted through the flexible bronchoscopy side port under fluoroscopy guidance. An attempt to remove the pin using a snare was unsuccessful. The tip of the pin was accidentally dislodged by manipulation of the angiocatheter, then later grabbed by flexible optical forceps and removed as a whole together with the bronchoscopy without any significant trauma. A chest radiograph was performed after the procedure and showed no evidence of pneumothorax.

The procedure was uneventful, and the patient was discharged home after 48 hours of observation. Further follow-up reassured us that the patient was well.

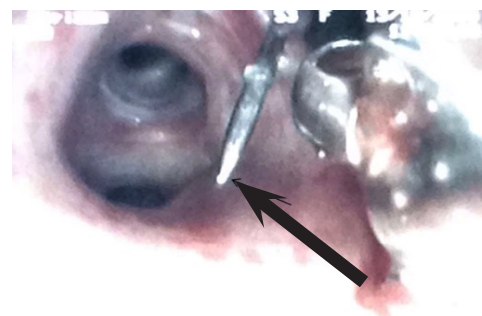


Figure 3: Endoscopic view of the tip of the pin after it was dislodged by the angiocatheter

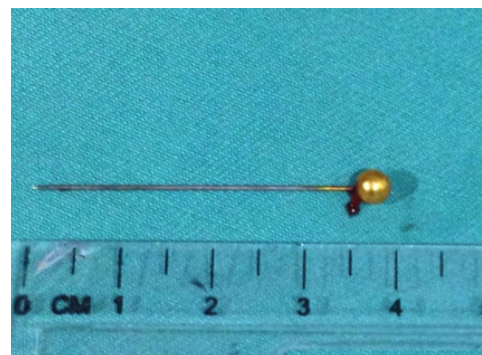


Figure 4: The scarf pin, approximately 4 cm in length, that was removed.

Discussion

Tracheobronchial foreign body aspiration is uncommon among the adolescent population. Head scarf pin aspiration is more common in the Middle Eastern population. To our knowledge, this is first reported case of head scarf pin aspiration in Southeast Asia. A few cases of scarf pin inhalation have been previously reported in Jordan, Egypt, and Turkey.

The most important thing in the diagnosis of foreign body inhalation is the history. The presenting symptoms depend on the location of the foreign body. Most of the cases of tracheobronchial foreign body inhalation are asymptomatic. The most common site of aspiration is on the right side, which covers approximately 70% of all cases in view of its anatomical structure, which is more vertical.⁴ However, in our case, the foreign body was located on the left side. The preference of this particular pin to lodge on the left side can be explained by the Bernoulli phenomenon.⁵ Negative pressure after laughing, coughing, or speaking, along with the relatively narrow diameter of the left bronchus compared to the right, allows more negative suction pressure to be gained in the left bronchial tree, which, in this case, allowed the pin to travel to the left side.

The other problem encountered in our case was the difficulty in locating the tip of the pin, which was embedded in the mucosa of the bronchus. Failure to grab the tip of the pin led to the failure of our multiple attempts. The embedded tip of such a sharp end can cause complications, such as erosion of the mucosal wall leading to a mucosal tear. Other complications of embedded head scarf pin previously reported are obstructive emphysema (2%), bronchiectasis (4%), pulmonary abscess (2%), pneumothorax (1%), mediastinitis (2%), hemorrhage (1%), and arrhythmia (3%).^{6,7}

Plain radiograph is a diagnostic tool for radiopaque foreign bodies or pneumothorax. However, CT scanning demonstrated a better anatomical image, showing the characteristics of the foreign body and suggesting possible means of collection.⁸ Thus, it became a very significant imaging modality in our case.

The choice between using a flexible or a rigid bronchoscope is still controversial, although the rigid variety is in wider use. Rigid bronchoscopy provides excellent visualization and allows for continuous ventilation of the patient. However, for the past few decades, flexible bronchoscopy has been advocated as the primary diagnostic and therapeutic modality for management of tracheobronchial foreign body aspiration, with reported success rates exceeding 90%.⁹ In our case, the use

of flexible bronchoscopy with fluoroscopy guidance was preferred in view of the location of the pin in the tertiary bronchus. We would have been unable to reach the site of the foreign body using rigid bronchoscopy. Using rigid bronchoscope in tertiary bronchus is an intrusive examination that can contribute additional complications.¹⁰

Multidisciplinary teamwork between the ORL surgeon, anesthetist, radiologist, and cardiothoracic surgeon was needed in our case. Sharing knowledge and experiences contributed to the successful removal of foreign body and shortened the operative time. Failure to remove this foreign body would have resulted in increasing morbidity for this patient, possibly requiring a thoracotomy with a lobectomy.¹¹

Conclusion

It is important to advise all women to avoid holding a pin between their lips while fixing their head scarf to prevent inhalation. A CT scan is a gold standard procedure for identifying the nature, position, and orientation of a pin. A multidisciplinary approach is important when managing this type of case in order to remove the foreign body as early as possible to prevent possible complications.

Conflict-of-interest statement: All authors have no conflict of interest in this case report.

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Non-specific skin purpura

Shalihin SE, Harun Z, Osman IF

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Authors:

Mohd Shaiful Ehsan Shalihin

(Corresponding author)

MBBS UIAM

Family Medicine Trainee Lecturer

DU51p, Department of Family

Medicine, International Islamic

University of Malaysia, Kuantan

Malaysia.

Email: shaifulehsan@iiu.edu.my

Zulkifli Harun

MD UKM

Department of Family Medicine

Universiti Kebangsaan Malaysia

Malaysia.

Iskandar Firzada Osman

MMed Family Medicine USM

Klinik Kesihatan Jaya Gading

Kuantan, Malaysia.

Abstract

Essential thrombocythemia is one of the myeloproliferative neoplasms. Palpable purpura is a rare manifestation that may delay diagnosis and treatment. We report a case of essential thrombocythemia in a 50-year-old man, who presented with recurrent thigh pain for the past one year with nonspecific localized purpura. His full blood count revealed isolated thrombocytosis of 880,000/ μ L with an impression of myeloproliferative disorder from peripheral blood film. He was referred urgently to the hematology team, which proceeded with a venesection. His condition improved with hydroxyurea. This was a rare case of chronic presentation of myeloproliferative neoplasm detected at a primary care clinic.

Introduction

Essential thrombocythemia is a nonreactive, chronic myeloproliferative disorder in which sustained megakaryocyte proliferation leads to an increase in the number of circulating platelets. Its incidence is less than 3 per 100,000 in population per year, and it occurs mainly in older age groups. The majority of patients are asymptomatic until an incidental blood count finding or presenting with a thrombotic event. It is characterized by a persistently elevated platelet count of greater than 450,000/ μ L, megakaryocytic hyperplasia, and the presence of splenomegaly. Morbidity includes large-vessel or microvascular thrombosis and bleeding. A localized, palpable skin purpura is, in fact, a rare manifestation for which other differential diagnoses need to be considered at the first visit.

Case Report

A 50-year-old man, with an underlying, reducible internal hemorrhoid under surgical follow-up, presented to our clinic at Jaya Gading with recurrent symptoms of right thigh pain for the past one year. The pain had been increasing in severity for the past six months, with skin changes on the right thigh. The pain had no specific aggravating or relieving factors and was radiating to his toes. Physical examination revealed mild hepatosplenomegaly. No other mass or lymph nodes were palpable. There were no neurological deficits or musculoskeletal

deformities detected. However, there was a localized, palpable purpura skin lesion over his right thigh; it was non-blanching, non-tender, and was not warm on palpation. Peripheral pulses were palpable and equal. He denied any similar skin lesions or pain elsewhere. He denied any history of falls, atopy, recurrent fever, or bleeding tendencies.



Figure 1: Non-specific, palpable purpura skin lesion on patient's thigh during patient's clinic visit.

An urgent full blood count revealed isolated thrombocytosis of 880,000/ μ L. His hemoglobin and leukocyte counts were normal. Peripheral blood film showed thrombocytosis with the presence of megakaryocytes with an impression of myeloproliferative disorder. He was referred and admitted to the hospital immediately after the blood film result came out. The pre-venesection platelet count was 943,000/ μ L, and the post-venesection count was 798,000/ μ L after removing 450 ml of blood. He was started on aspirin and hydroxyurea. His next platelet count during regular follow-up was 501,000/ μ L. He was otherwise asymptomatic, and his localized skin lesion had improved. He is positive for the JAK 2 mutation, which is evidence that supports the presence of the disease.

Discussion

Purpura is a non-blanchable discoloration of the skin or mucous membrane which is related to disorders of small blood vessels or a disorder of their intravascular components.¹ Palpable purpura is a sign of inflammation of underlying blood vessels in which the purpura can be felt. During the first encounter, differential diagnoses related to platelet disorders, such as vascular disorders or infections, need to be ruled out.^{2,3} Our patient did not present with any history suggestive of hematological malignancy, such as bleeding tendencies, recurrent fever, or anaemic symptoms. There were no symptoms of autoimmune diseases, such as multiple joint pain or back pain. He denied any neck swelling or masses elsewhere. There was no relation to drugs. Absence of those histories would cause difficulty in narrowing down the possible diagnosis.

In fact, our patient presented with the nonspecific symptom of localized thigh pain, which may cause the treating doctor to mistakenly attribute the disease to localized inflammation or trauma. The pain our patient suffered differed from thrombotic pain as he denied any intermittent claudication induced by activity or heat. There was no distal numbness. He described the pain as dull aching and not disturbing his quality of life. This sinister disease would have been definitely missed if the treating physician had not inspected and examined the thigh thoroughly or had assumed it to be a non-related benign soft-tissue injury, such as a muscle strain.

Another issue is the appearance of the skin lesion, which is not typical of the flat brownish-red spots of purpura. His skin lesions were raised, with papular- to nodular- like features, but they still had a similar brownish-red background color, although not to the extent of being red-purplish. This could be due to the long duration of the presentation. Nevertheless, they were non-blanchable, as expected in purpura. Overall, these skin lesions, described as “palpable purpura,” are more common in vasculitis than in myeloproliferative disorders, such as essential thrombocytopenia.^{4,5,6}

Essential thrombocythemia is one of four myeloproliferative disorders manifested by overproduction of platelets by the megakaryocytes in the bone marrow.^{7,8} Even though it is rare, it may develop into acute myeloid leukemia or myelofibrosis. Most

patients are asymptomatic and might present incidentally with isolated thrombocytosis during a blood investigation for another disease. Meanwhile, in a symptomatic patient, the most common presentation is with thrombotic features that cause burning pain, numbness, or dusky discoloration of the extremities. The pain is typically aggravated by exposure to heat and improves with cold exposure.^{7,8,9} Patients may also present with neurological disorders, such as migraine headaches, dizziness, or even transient ischemic attacks. However, none of these features are associated with our case, except the intermittent localized pain.

At a primary care level, a thorough history and examination are indeed helpful initial assessment tools when investigating any symptoms that come to attention. These items can provide an essential list of probable diagnoses, including alarming diseases that usually present with red flags.² In our case, other than the nonspecific history, the finding of mild splenomegaly did provide us with an important clue that an underlying hematological disease needed to be ruled out. His splenomegaly could have been missed if we had not elicited for Traube's space dullness during the abdominal examination.

A *full blood* count is not only essential for an initial investigation of a chronic skin presentation, but it is also useful as an adjunctive supporting tool for patients presenting with chronic symptoms with any degree of splenomegaly. In our case, the patient presented with nonspecific thigh pain, which was unusual as it had been occurring in the same area for up to a year. The presence of purpura, in fact, added further to the need for performing a full blood count to rule out any bleeding disorder, specifically low platelets. Surprisingly, an extremely high level of platelets was detected.

Essential thrombocythemia is characterized by the following criteria: 1) persistent thrombocytosis greater than 450,000/ μ L from a full blood count, 2) megakaryocytic hyperplasia, 3) splenomegaly, and 4) a thrombotic or hemorrhagic event. Our case presented with all of these related features.^{4,7,8} His positive JAK2 mutation indicates a poor prognosis for his disease, for which early treatment is needed. He benefited from low-dose aspirin and hydroxyurea and was symptom-free during follow-up, with his purpura resolved. Hydroxyurea is generally

considered to be the first-line drug for cytoreductive therapy in essential thrombocythemia.

Conclusion

This case has indeed proven that a focused and proper history taking, a directed and appropriate physical examination with a high index of suspicion, as well

as a selective and simple supportive investigation commonly practiced in a primary care setting play an important role in identifying uncommon presentations of uncommon medical conditions, which, in this case, led to a timely intervention. Chronic palpable purpura may signify hematological malignancies rather than vasculitis, especially in males and those aged 40-years-old and above.

How does this paper make a difference to general practice?

- Though platelet disorders usually present with flat, red-purplish purpura, they can also present with palpable, raised skin lesions, which reflect chronicity, especially in hematological malignancy. Therefore, primary care providers need to differentiate palpable purpura from chronic urticaria, which may also present with similar skin lesions, although they are usually generalized.
- This case report shows that detailed history taking and a complete, thorough examination can identify the possible diagnosis, even without an investigation, at the primary care level. Traube's space dullness needs to be elicited in any abdominal examination whenever the spleen is not palpable in order to not miss mild splenomegaly, which provides an important clue towards an underlying suspected hematological disease.
- This case report proved that a simple full blood count can provide an impressive amount of information for primary care practitioners, even without a peripheral blood film, in chronic skin lesions.
- Skin lesions requires a proper examination, including inspection of the surrounding area to look for alarming signs. Differential diagnosis can be further divided into blanchable or non-blanchable skin erythema.
- This case report showed that pain is one of the alarming symptoms in any skin disorder. Further characterization of the pain needs to be conducted by the primary care provider to rule out other, non-related diseases.

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Purple urine bag syndrome: A startling phenomenon of purple urine in a urine drainage bag. A primary care approach and literature review

Wong YWE, Abdullah N

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Authors:

Eva Wong Yi Wah

(Corresponding author)

MBBS (MMMC)

Department of Primary Care Medicine, University of Malaya Medical Centre (UMMC) Malaysia.

Email: drevawong@live.com

Nurdiana Abdullah

MBBS (Mal), MMed (FamMed) (Mal)

Department of Primary Care Medicine, University of Malaya Medical Centre (UMMC) Malaysia.

Abstract

Purple urine bag syndrome (PUBs) is a rare and startling phenomenon of purple discolouration in the urine or urinary catheter and bag. It is reported in chronically debilitated elderly patients, mostly in women on long-term urinary catheters. Its prevalence is strikingly more common in nursing home residents. Several factors contribute to the formation of indigo (blue) and indirubin (red) pigments from a breakdown of dietary tryptophan, which stains the urine purple. These factors include constipation, dysmotility of the bowel, bowel bacterial overgrowth, dehydration, and urinary tract infection. The presence of purple urine may cause undue alarm to both the patient and the doctor. Thus, we present this case report on an 86-year-old woman, a nursing home resident on a long-term urinary catheter, who presented to the primary care clinic. Her urine cleared after antibiotic therapy, replacement of her urinary catheter, and supportive management, which included hydration and nutrition. In addition to these measures, reducing the time between urinary catheter changes was recommended to prevent recurrence of this condition.

Introduction

Purple urine bag syndrome (PUBs) is an interestingly startling and rare phenomenon of purple discolouration of the urine, catheter, and urine bag which was first reported by Barlow and Dickson in 1978.¹ In Malaysia, PUBs have been reported in patients presenting to secondary care settings.^{2,3} This purple hue may be alarming to the patient, family and even to the medical practitioner. For most patients, this condition may be managed in the primary care setting. It is associated with chronically debilitated, elderly patients who are on long term catheters. Several factors contribute to the formation of indigo (blue) and red indirubin(red) pigments from the breakdown of dietary tryptophan. These factors include constipation, dysmotility of the bowel, bowel bacterial overgrowth, dehydration and urinary tract infection. Its pathogenesis is outlined in **Table 1**. Alkaline urine is another feature of this condition, along with a concurrent urinary tract infection. While a urinary tract infection is a common condition seen in primary care, PUBs is rarely encountered, resulting in alarm in many of the physicians who encounter the

condition. Thus, this case report highlights the condition and primary care approach to managing this rather benign condition.

Case Report

An 86-year-old woman, who is a nursing home resident, was brought in to the primary care clinic in December 2016 by her sister with complaints of purple discolouration of urine, catheter, and urinary bag for two months. The patient's sister had been informed by the nursing home caregiver regarding the patient's foul-smelling, purple urine a few weeks earlier; however, she delayed in bringing the patient to the clinic due to her poor health.

The patient had been on a long-term silicon urinary catheter since May 2015. In May 2015, she was admitted for uterine prolapse and developed acute urinary retention secondary to a urinary tract infection. She was subsequently discharged to a nursing home with a urinary catheter, which was changed every 6 weeks.

During the first clinic visit, she was asymptomatic of urinary tract infection, with

no history of pain at the tip of the urethra, hematuria, or fever. However, her sister reported the history of foul-smelling urine as indicated to her by the nursing home caregiver. Her last urinary catheter change had been 5 weeks ago. She was well-hydrated and drank approximately 500 ml of water every 2 hours and did not have history of altered bowel habits. Her diet included 5 meals in a day, which consisted of biscuits, rice, chicken, and fish. She was semi-dependent in her daily activities and ambulated with a walking frame. Other geriatric assessment revealed progressive memory loss for the past 1 year.

On examination, she was afebrile with a temperature of 36.6 degrees Celsius. Her blood pressure was 130/100 mmHg, and her pulse rate was 74/minute. She was well hydrated with good pulse volume and capillary refill time of less than 2 seconds. Her mini mental scale examination (MMSE) was 11/30. She was orientated to people but not to time and place. However, she was alert and cooperative. Her abdomen and other systemic examinations were unremarkable.

Her laboratory investigation revealed urinalysis results of PH 8, leucocyte 3+, protein 2+, nitrite negative, ketone negative, haemoglobin 5+ and specific gravity 1.01. No baseline full blood count or other blood investigations were taken in view of the patient not being septic. However, urine was sent to the lab for culture and sensitivity.

The patient was treated empirically for urinary tract infection with oral cefuroxime 500mg twice a day for 1 week. It was arranged to have her silicon urinary catheter changed on the same day, and instructions were given to reduce the time between changes of the silicon urinary catheter to 4 weeks, thereafter. Her sister was advised to keep her well-hydrated, and maintain good nutrition.

She came back to the clinic for follow-up 2 weeks later, and her sister reported that her urine colour had normalized from the point of her last urinary catheter change. Her urine culture and sensitivity report came back as mixed growth. She remained well and did not have symptoms of urinary tract infection or recurrent purple discolouration of urine. She was referred to a geriatrics memory clinic for her deterioration in cognitive function. With the patient's and her sister's consent, a telephone call was made to her caregiver at the

nursing home to explain her general condition and necessary supportive measures of adequate hydration, good nutrition, and avoiding constipation. The duration of use of each catheter, shortened to 4 weeks, was explained to her caregiver as well.

Discussion

The incidence of PUBs and its association with urinary tract infection in elderly and chronically catheterized patients is evident in a study done at a community hospital in Taipei on 157 patients with urinary catheters, 13 of whom exhibited PUBs. Of the 13 affected patients, 11 were women, and 2 were men.⁴ This points to its association largely with elderly females. The study also concluded that a majority of patients with PUBs lived in nursing homes as compared to those with urinary tract infections without PUBs with prevalence rates of 67.2% and 43.1%, respectively. Interestingly, 12 out of the 13 patients with PUBs reported that their urine was alkaline with a PH of equal to greater than 7. This study also indicated that being bedridden, having Alzheimer's disease, and having dementia were risk factors for PUBs likely, due to the poor self-care and hygiene.⁴

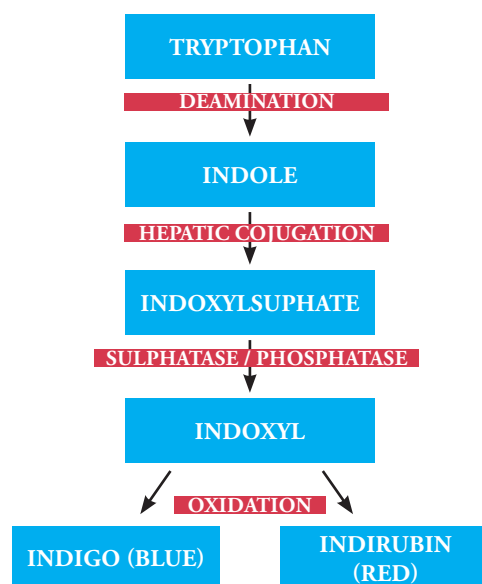
The major risk factors associated with the conversion of dietary tryptophan into the end products of indigo (blue) and indirubin (red) pigment are having a tryptophan diet, chronic constipation, a chronic indwelling catheter, a high bacterial load in urine, alkaline urine, and renal failure.⁵ The biochemical pathway to the breakdown of tryptophan into the indigo and indirubin pigments is outlined in **Figure 1**.

The rarity of PUBs could be questioned as there are under reported cases, and physicians, in general, have little exposure to and experience in managing it. Another case study on 10 elderly patients with PUBs in two nursing homes in Taiwan reported that 19 out of the 74 residents in these two nursing homes had a Foley catheterization. Out of those who were catheterized, the prevalence of PUBs was 42.1%. Of the residents with PUBs, 10 had been catheterized for at least 12 months. A significant number, i.e., 8 out of 10 of these residents, reported a positive urine culture, which points towards its association with urinary tract infection.⁶

The outline for management of PUBs is directed at treating the urinary infection, good urologic sanitation and control of constipation.⁵ Thus,

in this case report, the patient was treated empirically with cefuroxime for urinary tract infection and her urinary catheter changed. In addition, the time each silicon catheter was used was shortened to prevent further recurrence of this condition. Other supportive measures, such as proper nutrition, adequate hydration, and sanitation were advised to further support in prevention of a recurrence.

Figure 1: Biochemical pathway of conversion of dietary tryptophan into indigo and indirubin pigments



Adapted from: Khan F et al⁵

Figure 2: Purple discoloration of the urine, urine bag and tubing.



Disclaimers

There are no disclaimers or conflicts of interests.

Consent

Informed consent has been obtained from the patient and family.

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TEST YOUR KNOWLEDGE

No thumbs up for the boy!

Muhamad Effendi F, Sikkandar MF

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Authors:

Ferdhany Muhamad Effendi

(Corresponding author)
MD(UKM), DrOrth&Tr (UKM)
Department of Orthopaedics
Faculty of Medicine Universiti
Teknologi MARA, Sg. Buloh Campus
Jalan Hospital, 47000, Sg Buloh
Selangor, Malaysia.
Email: ferdhany@yahoo.com

Mohd Faizal Sikkandar

MBBS (IIUM), DrOrth&Tr (UKM)
Faculty Of Medicine
Universiti Teknologi MARA
Malaysia.

Case summary

A 7-year-old boy presented with both of his thumbs flexed (Figure 1), the inability to perform the 'thumbs-up' gesture, and difficulties in opposing thumbs and fingers in activities such as holding a pencil during writing, pincer movements, and picking up small objects. His mother only observed the deformity for one month after the boy complained of difficulty in writing during class. He had no prior history of trauma to the thumbs or pain and swelling in other joints. There were no other birth anomalies noticed by his parents. Upon examination, the boy had flexion deformities of the interphalangeal joint (IPJ) on both of the thumbs. Passive range of motion of the IPJ was not possible and both were fixed at 60° of flexion. Power of both thumbs could not be assessed as there was no motion of the joint. The range of motion of the metacarpophalangeal joints (MCPJ) of both thumbs and all other finger joints was normal. A 0.5cm x 0.5cm subcutaneous nodule was palpable at the volar crease of the MCPJ bilaterally. The nodule was tender on palpation; however, no overlying skin changes were evident.



Figure 1. Clinical picture showing bilateral thumb IPJ flexion deformity.

Questions

1. What is the most likely diagnosis?
2. What are the differential diagnoses?
3. What is the natural history of the condition?
4. What are the treatment options?

Answers:

1. The most likely diagnosis is bilateral congenital trigger thumb. As there is no history of trauma to the thumbs, it is most likely that the deformity has existed since

birth but went unnoticed by the parents until one month prior to presentation. As is usually the case, the child only sought treatment after a functional impairment became noticeable, i.e., difficulty in writing. Congenital trigger thumb occurs in 3.3 cases per 1000 live births and is caused by a disturbance in normal flexor pollicis longus (FPL) tendon gliding due to a size mismatch between the tendon and A1 pulley. This mismatch occurs when there is fibrous tissue formation on the FPL tendon of the thumb within the A1 pulley.¹ The condition is characterized clinically by “triggering” or an inability

to fully extend the IPJ of the thumb. The definitive etiology is unknown, but studies suggest dysfunctional myofibroblast may be responsible for the condition. Congenital trigger thumb is rare,² and some authors suggest the term congenital is a misnomer as it does not necessarily manifest at birth.³

2. The differential diagnoses of flexion deformity of the thumb in a child include congenital clasp thumb and thumb contracture secondary to trauma. These can be readily excluded by a history and physical examination. Congenital clasp thumb, also known as the 'thumb-in-palm' deformity, is a flexion deformity due to the contracture of the MCPJ, as opposed to a flexion deformity at the IPJ of the thumb. Furthermore, congenital clasped thumb is commonly associated with systemic conditions, such as cerebral palsy and arthrogryposis, whereas congenital trigger thumb occurs typically in isolation, without any other conditions or syndromes. No further investigation is required as the condition can be diagnosed clinically. Radiograph of the hand is useful in cases

with suspected metacarpal or phalanx fractures.

3. Spontaneous resolution can be expected in up to 63% of cases but may take up to 4 years in duration.⁴ In a retrospective review of 31 trigger thumbs in 23 children with a mean age of 7.46 years, surgical release of the A1 pulley was successfully achieved in all patients, and there were no recurrences or complications noted at the average follow-up period of 2 years and 3 months. The author also concluded that a satisfactory result can be expected after surgical release of the A1 pulley to facilitate FPL tendon gliding in trigger thumb, even in delayed diagnosis or late treatment.⁵
4. Passive range of motion exercises performed by the parents may help to hasten the spontaneous recovery of the trigger thumb. However, in cases which cause a disturbance in functional daily activities, have bilateral involvement, and are seen in children more than 4 years old, early referral for surgical release is advised.

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