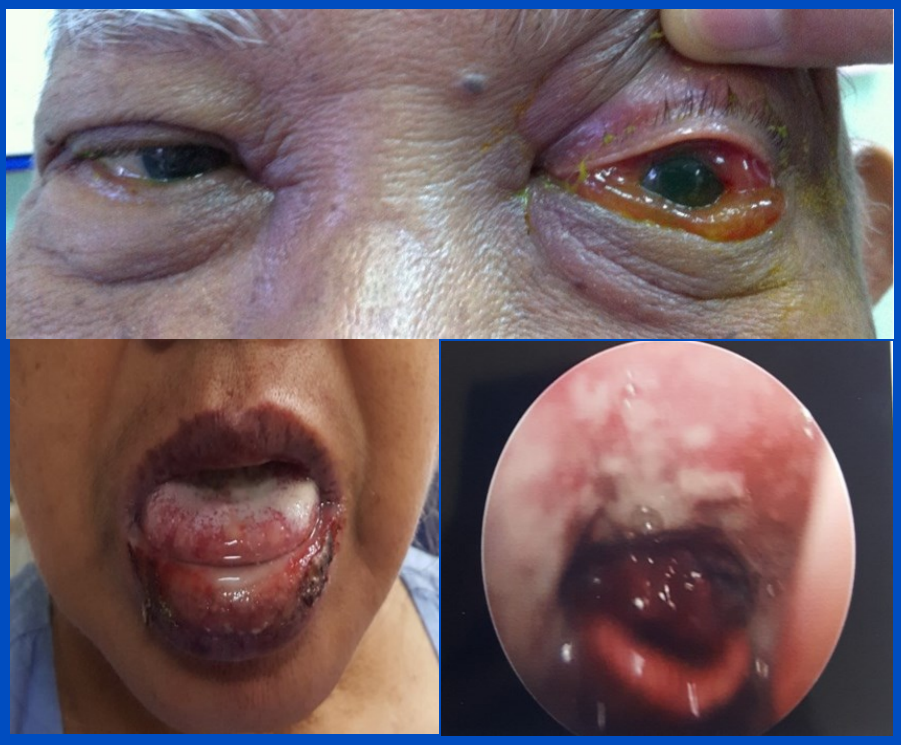
Brunei International Medical Journal

OFFICIAL PUBLICATION OF
THE MINISTRY OF HEALTH,
BRUNEI DARUSSALAM

Volume 13, Issue 3

15 June 2017 (20 Ramadhan 1438H)



ISSN 1560 5876 Print
ISSN 2079 3146 Online

Online version of the journal is available at www.bimjonline.com

Brunei International Medical Journal (BIMJ)
Official Publication of the Ministry of Health, Brunei Darussalam

ISSN 1560-5876 Print
ISSN 2079-3146 Online

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Prevalence of Impaired Glucose Tolerance and Diabetes among patients with Impaired Fasting Blood Sugar in Seria Health Centre.

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ABSTRACT

Introduction: Fasting Plasma Glucose test is the mostly used screening test for Diabetes Mellitus in Brunei Darussalam. Oral Glucose Tolerance Test is recommended to determine exact glucose tolerance status if Fasting Plasma Glucose is impaired between 6.1 mmol/L and 6.9 mmol/L. It was assumed that there would be some undiagnosed Diabetes Mellitus and Impaired Glucose Tolerance among those with impaired Fasting Plasma Glucose but local data about their exact glucose tolerance status were not available. **Materials and Methods:** Oral Glucose Tolerance Test results of 59 patients with impaired Fasting Plasma Glucose in Seria Health Centre during three-year period (1st Nov 2012 - 31st Oct 2015) were reviewed to determine the proportion of undiagnosed Diabetes Mellitus, Impaired Glucose Tolerance, pure Impaired Fasting Glucose and to find the factors associated with different degree of glucose tolerance. **Results:** The finding revealed that 47.5 % (n=28) of sample were undiagnosed Diabetic, 22 % (n=13) with Impaired Glucose Tolerance, 6.8% (n=4) with pure Impaired Fasting Glucose and 23.7 % (n=14) were normoglycaemic. Among the undiagnosed diabetic patients (n=28), 2-hour Plasma Glucose test could detect 92.7 % (n=26) of them but Fasting Plasma Glucose test could detect only 42.9% (n=12) of them as Diabetics. More than half of these patients, 57.1% (n=16) would be misdiagnosed if Fasting Plasma Glucose test alone was repeated on their follow up. The sociodemographic factors and presence of risk factors for Diabetes showed no significant association with different degree of glucose tolerance. **Conclusion:** The study indicates that patients with impaired Fasting Plasma Glucose should be further tested with Oral Glucose Tolerance Test on follow up visits since repeating Fasting Plasma Glucose test alone could fail to detect Impaired Glucose Tolerance and 57% of Diabetes.

Keywords: Diabetes Mellitus, Oral Glucose Tolerance Test, Impaired Fasting Glucose, Impaired Glucose Tolerance.

INTRODUCTION

Diabetes Mellitus (DM) is the third leading cause of death in Brunei Darussalam for decades.[1;2] Prevalence of DM in Brunei was 12.4% and it was estimated that 44% of adult diabetes cases in the community were undiagnosed.[3]

It is important to diagnose DM in early stage and treat them aggressively and effectively because the longer a person lives with undiagnosed and untreated diabetes, the

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worse the health outcomes are.[4] Brunei Darussalam's BruMap-NCD targets to halt the rise in diabetes and Health Screening Services for Non-communicable Diseases (NCD) in Primary Health Centres were started in 2013.[5]

Diabetes can be diagnosed by measuring Fasting Plasma Glucose (FPG), 2-hour Oral Glucose Tolerance Test (OGTT) or glycated haemoglobin (HbA1c).[6;7] FPG is routinely used to screen for DM at Primary Health Centres in Brunei Darussalam. Those with FPG 7.0 mmol/ L and above are diagnosed with Diabetes.[4;7;8] FPG 6.0 mmol/L or less is considered normoglycaemia and FPG level between 6.1 mmol/L and 6.9 mmol/ L is considered as Impaired Fasting Glucose state (IFG).[7-12] Any abnormal FPG result needs further confirmation by one of the 3 tests mentioned previously.[13]

Two hour Plasma Glucose (2hPG) level 11.1 mmol/ L is diagnostic level for Diabetes while 2hPG between 7.8 mmol/L and 11.0 mmol/L is diagnosed as Impaired Glucose Tolerance (IGT) and 2hPG less than 7.8 mmol/L is considered normal.[7-12]

It is assumed that there would be some undiagnosed DM and IGT among those with impaired FPG level between 6.1 mmol/L and 6.9 mmol/ L, whose diagnosis could be confirmed by OGTT tests. OGTT test is recommended in Clinical Practice Guidelines of Brunei Darussalam to determine the exact glucose tolerance status if a person has impaired FPG.[7] However, data on the proportion of patients with IFG who subsequently undergo OGTT at Primary Health Centres, who are later diagnosed with DM, is not available. Hence it is commonly observed that despite recommendation to conduct OGTT in local Clinical Practice Guidelines, many patients with IFG are still tested with repeat FPG inappropriately.

This study's primary objective is to evaluate the proportion of patients with pure IFG, IGT and undiagnosed DM among patients with initial impaired FPG. Secondary objective is to investigate the associations of sociodemographic factors and presence of risk factors for DM of the patients with different degree of glucose tolerance.

MATERIALS AND METHODS

This was a retrospective cross-sectional study of patients attending Seria Health Centre during a three-year period from 1st November 2012 to 31st October 2015. Seria Health Centre is in the District of Belait, which provide an outpatient service to the town of Seria and the surrounding area, with a recorded annual outpatient attendance of 20,678 in 2012. [2] Clinical data of patients with OGTT test performed during the study period were extracted from the phlebotomy registry and their blood results and clinical details were extracted from their medical records. Patients aged over 18 years with initial FPG between 6.1-6.9 mmol/L were included in the study. Pregnant mothers, previously diagnosed DM and patients who were follow up in other health facilities were excluded.

Those who met inclusion criteria were selected for the study and their medical records were reviewed. The data was collected by using the data collection form for each patient and transferred to a Microsoft Excel spreadsheet for analysis.

OGTT test procedures in Seria HC

Patients who need to check OGTT were referred to phlebotomist in Seria Health Centre for instructions and appointment. Patients were explained the procedure, instructed to take usual diet on prior days but to fast for 8 hours before appointment. The first blood sample was taken as baseline FPG. Patients were instructed to ingest 75 G of glucose provided in drinking water after taking first blood

Table 1: Socio-demographic and risk factors in relation with different degrees of Glucose Tolerance.

Socio-demographic factors	Degree of Glucose Tolerance				
	Normal N=14 (23.7%)	**IFG N=4 (6.8%)**	**IGT N=13 (22.0%)**	**DM N=28 (47.5%)**	**Total N=59 (100%)**
Age					
< 40 years	1 (7.1)	0 (0)	2(15.4)	2 (7.1)	5 (8.5)
40-59 years	7 (50.0)	3 (75.0)	4 (30.8)	12(42.9)	26 (44.0)
60 years and above	6 (42.9)	1 (25.0)	7 (53.8)	14 (50.0)	28 (47.5)
Gender					
Male	5 (35.7)	2 (50)	2 (15.4)	12(42.9)	21 (35.6)
Female	9 (64.3)	2 (50)	11(84.6)	16(57.1)	38 (64.4)
Co-morbidities/Risk Factors					
Family history of DM	2 (14.3)	2 (50)	1 (7.7)	4 (14.3)	9 (15.3)
Obese with sedentary life style (BMI > 25)	11(78.6)	4 (100)	10(76.9)	21 (75)	46 (78)
Hypertension	11(78.6)	3 (75)	11 (84.6)	25 (89.3)	50 (84.7)
Previous gestational diabetes mellitus	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
Polycystic ovary syndrome with BMI> 30	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
Triglyceride level >2.82 mmol/L	4 (28.6)	0 (0)	1 (7.7)	5 (17.9)	10 (16.9)
Status of body weight					
Normal	2 (14.3)	0 (0)	1 (7.7)	3 (10.7)	6 (10.2)
Over weight	7 (50)	1 (25)	9 (69.2)	16(57.1)	33 (55.9)
Obese	5 (35.7)	3 (75)	3 (23.1)	9 (32.1)	20 (33.9)
Cumulative Risk Factors					
0-1 Risk Factor	3 (21.4)	1 (25)	4 (30.7)	7 (24.9)	15 (25.5)
2 Risk factors	8 (57.1)	1 (25)	6 (46.2)	15(53.6)	30 (50.8)
>3 Risk Factors	3 (21.5)	2 (50)	3 (23.1)	6 (21.5)	14 (23.7)

sample. A second sample was taken as 2hPG, 2 hours after ingestion of the glucose solution. Specimen were sent to Raja Isteri Pengiran Anak Saleha (RIPAS) hospital Laboratory for analysis using glucose oxidase method. WHO's definition criteria which was adopt by Brunei Clinical Practice Guidelines was used to diagnose different level of glucose tolerance (Annex 1).[7;8]

Statistical Analysis

The proportions of different degree of glucose tolerance were analysed by frequency distribution tables. The associations between their demographic factors, presence of risk factors for diabetes and different level of Glucose tolerance were further analysed by Chi-square test and Logistic Regression analysis, using IBM SPSS version 22 statistical package. The risk factors of diabetes described in Clinical Practice Guidelines of Brunei Darussalam were used for this analysis (Annex 2).[7]

RESULTS

A total of 59 patients met sampling criteria for study. Our results showed that for patients with initial impaired FPG, a subsequent OGTT according to the recommendation made by guidelines revealed that 47.5% (n=28) of them were confirmed to have undiagnosed DM, 22% (n=13) were categorised as IGT, 6.8 % (n=4) were diagnosed as pure IFG and 23.7 % (n=14) were normoglycaemic. The distribution of sociodemographic factors and risk factors of the patients in relation to different degree of glucose tolerance are demonstrated in Table 1.

Table 2: Sensitivity, Specificity, Positive Predictive Value (PPV) and Negative Predictive Value (NPV) of FPG and 2hPG tests.

Validity	DM by FPG	DM by 2hPG
Sensitivity	42.86 %	92.86 %
Specificity	100 %	100 %
PPV	100 %	100 %
NPV	65.96 %	93.94 %

Table 3: Association between patient factors and different degree of glucose tolerance.

Risk Factors	OR	95% Confidence Interval	*p value*
< 40 yrs*			0.79
40-59 yrs	1.11	0.13-9.43	0.93
60 yrs and above	1.84	0.17-9.51	0.61
Male*			
Female	0.55	0.16-1.96	0.35
Malay*			0.41
Chinese	0.40	0.10-1.69	0.22
Others	0.83	0.16-4.19	0.82
No Family History of Diabetes*			
Family History of Diabetes	1.83	0.19-18.04	0.61
No Hypertension*			
Hypertension	2.78	0.31-24.52	0.36
Triglyceride level <2.82 mmol/L*			
Triglyceride level >2.82 mmol/L	1.25	0.16-9.94	0.83
Normal *			0.91
Over weight	1.63	0.14-19.13	0.70
Obese	1.37	0.11-16.76	0.81
Patients with 0-1 Risk Factors*			0.73
Patients with 2 Risk Factors	0.51	0.07-4.01	0.52
Patients with 3-4 Risk Factors	0.29	0.01-6.31	0.43

* Reference group

Of the 28 patients with undiagnosed diabetes based on OGTT, the 2hPG fraction of OGTT test could detect 92.7 % (n=26) of the undiagnosed diabetic patients but FPG test could only detect 42.9% (n=12). The validity of two fractions of OGTT test for Diabetes Mellitus are illustrated in Table 2. 2hPG showed higher sensitivity (92.9% vs 42.9%) and negative predictive value (93.9% vs 66%) compared to FPG.

The association of sociodemographic factors and presence of risk factors for DM of the patients with different degree of glucose tolerance were further analysed by multiple logistic regression analysis (Table 3). None of the patient factors showed significant association with different degree of glucose tolerance. The outcome of OGTT test among IFG patients was further grouped into two; diabetes and non-diabetes according to WHO diagnostic criteria (Annex 1) and was tested for any association with the presence of risk factors in the patients. No statistically significant association was found with Chi square analysis for diabetes and presence of multiple risk factors (Table 4).

DISCUSSION

The findings highlighted that almost half of sample population with FPG 6.1 - 6.9 mmol/L were undiagnosed diabetes based on OGTT testing. Repeating FPG test alone at their follow up clinic visits, which is currently being performed by some clinics, could miss their diagnosis and early intervention and treatment would not have been started. Our study showed that FPG testing has a low sensitivity compared to OGTT and this has been reported by other study to be between 40% and 65%.[13] FPG test also failed to diagnose IGT which were present in 22% of our study population.

Our results add further support to the Clinical Practice Guidelines of Brunei Darussalam to recommend an OGTT to determine the exact glucose tolerance status if a patient

Table 4: Association of multiple risk factors with final diagnosis in patients with IFG.

Cumulative Risk Factors	Final Diagnosis			Chi sq value	df	*p value*
	No DM N=31(%)	DM N=28(%)	Total N=59 (%)			
0-1 Risk Factor	8 (25.8)	7 (25)	15 (25.4)	0.20	2	*0.905*
2 Risk Factors	15 (48.4)	15 (53.6)	30 (50.8)			
3-4 Risk Factors	8 (25.8)	6 (21.4)	14 (23.7)			

is noted to have impaired FPG.[7] Thus all patients with FPG 6.1 - 6.9mmol/L should be tested with OGTT to determine their exact glucose tolerance level to ensure not to miss the diagnosis of diabetes in early stage since those with IGT which is also highly associated with increased risk of cardiovascular disease, including heart disease, stroke and peripheral vascular disease.[13]

Recently, many studies have proved that HbA1c test also can be used as screening and diagnostic test for diabetes. However, HbA1c may be affected by a variety of genetic, haematological and illness-related factors.[11] Diagnostic cut off level of HbA1c also varies in different centres. American Diabetes Association and WHO set the diagnostic level of HbA1c at 6.5% but Clinical Practice Guidelines in Brunei accepted the diagnostic level at 7%.[7;11;14] It is important to consider that a value of less than 6.5% does not exclude diabetes diagnosed using glucose tests if HbA1c test is used as confirmatory test to diagnose DM.[11] As a result, replacing OGTT test with HbA1c as confirmatory test is still controvesial. Combination of FPG and OGTT test is still considered as gold standard in defining prediabetes and DM.[15;16]

Limitations

This study was conducted as a pilot survey in a single Healthcare in the Belait district, which accounts for the small sample size, a major limitation to the study design. This may have resulted in a non-significant finding on multiple logistic regression analysis of the associated risk factors. However, our results is valid in that performing a repeat FPG alone is not clinically appropriate since more than half of the test sample will miss out on a diagnosis of diabetes if present. The further follow up study to the patients with IFG and IGT may be beneficial to understand the progression towards diabetes and to explore modifiable risk factors among these patients.

CONCLUSION

Based on an OGTT, nearly half (47.5%) of patients attending Seria Health Centre, whose initial FPG showed an IFG picture with glucose levels between 6.1 mmol/L and 6.9 mmol/L were confirmed as undiagnosed DM. If only a repeat FPG was carried out as a confirmatory test, instead of an OGTT, more than half (57.1%) of these patients with undiagnosed DM would be misdiagnosed as not diabetic. The study highlighted that all patients with IFG should be further tested with OGTT as recommended by the Clinical Practice Guidelines in Brunei Darussalam, to detect undiagnosed DM and IGT. Further study at multiple health centres with larger sample size may be required to validate these findings and explore the associated risk factors for different level of glucose tolerance.

Financial Disclosure and conflicts of interests
This study did not use any financial support from any agency. There was no conflict of interests but the study was to support the recommendation in the Clinical Practice Guidelines for Diabetes Mellitus by Ministry of Health, Brunei Darussalam.

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Annex 1. Definition and diagnosis of Diabetes Mellitus and intermediate hyperglycaemia by WHO. [8]

Test	Impaired Fasting Glucose (IFG)	Impaired Glucose Tolerance (IGT)	Diabetes Mellitus (DM)
Fasting Plasma Glucose (FPG)	6.1 -6.9 mmol/L	6.1 -6.9 mmol/L	7.0 mmol/L or more
2 –h Plasma Glucose (2hPG)	Less than 7.8 mmol/L	7.8 to 11.0 mmol/L	11.1 mmol/L or more

Annex 2. Risk factors for Diabetes[7]

- Family history of diabetes in first degree relatives
- Obese with sedentary life style (BMI $\geq$ 25)
- Ischemic heart disease, cerebrovascular disease, peripheral vascular disease
- Hypertension
- Previous gestational diabetes mellitus
- Polycystic ovary syndrome with BMI$\geq$ 30
- Triglyceride level >2.82 mmol/L

Development and psychometric validation of Malay version of Parental Report on Auditory Training (MyPRAT) questionnaire for clinical use.

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ABSTRACT

Introduction: For promoting optimum speech and language development, children with sensorineural hearing loss are required to use hearing amplification devices and undergo a specific auditory training program. The aim of the study was to develop and validate a new questionnaire for documenting the progress of the auditory training among Malay hearing impaired children. **Materials and Methods:** In the first phase of this validation study, Malay version of Parental Report on Auditory Training (MyPRAT) questionnaire was developed accordingly. In the second phase, the validity and reliability of MyPRAT were determined. Specifically, its content validity (n=9), face validity (n=33) and construct validity (n=11) were tested. For reliability analysis, its internal consistency was determined by means of item-total correlation, Cronbach's alpha and split-half reliability. **Results:** As reported by clinical experts, content validity index (CVI) values of MyPRAT were high (0.78-1.00) indicating excellent content validity. The face validity of MyPRAT was adequate as the majority of respondents (>80%) rated the format, content and language use of MyPRAT as "good". Items in Part A of MyPRAT were highly correlated with Meaningful Auditory Integration Scale (MAIS) scores (r=0.86, p<0.001) indicating good construct validity of MyPRAT. The internal consistency of MyPRAT questionnaire was good as revealed by item total correlations (0.43-0.97), Cronbach's alpha (0.90-0.92) and split-half reliability (0.96-0.98).**Conclusion:** The newly developed MyPRAT questionnaire has been proven to be valid and reliable for its intended clinical applications. Nevertheless, further research is welcome to support the outcomes obtained from the present study.

Keywords: Hearing loss, Language therapy, auditory, questionnaire, Reproducibility of results

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INTRODUCTION

Having an intact hearing ability is vital in communication. If the hearing system is compromised, the quality of life can be tremendously affected. Hearing loss, in fact, is common in children and adults. [1-3] If untreated, it

can lead to various adverse consequences including speech delay, language impairment, poor academic achievement and poor psychosocial development. [1, 4, 5]

Hearing impairment can be divided into three types, namely conductive hearing loss, sensorineural hearing loss and mixed hearing loss. While the conductive hearing losses are mostly treatable medically and surgically, the sensorineural hearing loss is permanent and the use of hearing amplification devices such as hearing aids or cochlear implants is required. [6]

For promoting optimum speech and language development, children with congenital sensorineural hearing loss must be treated as early as possible. [7] After being fitted with the appropriate amplification devices, they need to undergo a specific auditory training program. Speech language pathologists are the main clinical professionals who provide an intensive speech therapy program for hearing impaired children. Following the dedicated auditory training program, improvements in hearing and speech skills should be noted.

Having validated questionnaires is useful to document the progress of the intervention. Many clinical questionnaires are available but are not without limitations. As an effort to cover relevant aspects of audition and speech, some of them can be long and complicated to be completed by the parents. [8, 9] In fact, not many validated questionnaires are available in Malay language. Meaningful Auditory Integration Scale (MAIS) and Meaningful Use of Speech Scale (MUSS) are examples of questionnaires that have been validated in Malay version. [10] They have been frequently used in hearing intervention studies. [11-13]

Based on the aforementioned issues, there is a need to have a simpler questionnaire to determine the treatment effect of the auditory training. This questionnaire should be short and easy to be filled in by the parents of hearing-impaired children. It should cover specific improvements of auditory skills and parents' satisfaction on the overall therapy program. The present study, hence, was carried out to develop and validate a new questionnaire, known as Parental Report on Auditory Training (PRAT) using specific psychometric validation techniques. Specifically, the Malay version of PRAT (MyPRAT) was studied and tested for its validity and reliability.

MATERIALS AND METHODS

All procedures performed in the present study were approved by Human Ethics Committee of Universiti Sains Malaysia (USM), which is in accordancewith the Helsinki Declaration of 1975 and its later amendments. This validation study had two consecutive phases. The first phase was about developing MyPRAT content and the validation of MyPRAT was carried out in the second phase. In the first phase, five clinical experts (1 otorhinolaryngologist, 2 audiologists, 2 speech language pathologists) aged 36-56 years (3 males and 2 females) and one male post-graduate student (aged 54 years old) were involved in this task. The appropriate items for the questionnaire were initially constructed in English version based on the literatures, available clinical questionnaires and clinical experiences of the experts. To ensure cultural appropriateness, relevant cultural factors were considered when choosing the items. After several meetings and discussions, the items of PRAT were finalized. It consists of two sections: Part A and Part B (Appendices 1A and 1B, respectively). Both sections have five closed-ended questions and one open-ended question. For the closed-ended questions, a 5-point response scale (1-5) is used (1 indicates "strongly disagree", 2 indicates "disagree", 3 indicates "unsure", 4 indicates "agree" and 5

indicates "strongly agree"). The Part A of PRAT questionnaire consists of items covering specific improvements of auditory and related skills. The report on the overall satisfaction of the auditory training is provided in the Part B of PRAT.

The English version of PRAT questionnaire was then translated into Malay version by language experts from School of Languages, Literacies and Translation, USM. The Malay version of PRAT (MyPRAT) questionnaire had been developed and was ready for subsequent validation tasks (Appendices 2A and 2B).

In the second phase of study, the validity and reliability of the newly developed MyPRAT questionnaire were determined. Specifically, the content validity, face validity and construct validity of MyPRAT were tested. The internal reliability (consistency) of MyPRAT questionnaire was determined by calculating its item-total correlation, Cronbach's alpha and split-half reliability.

In the content validity task, nine clinical experts were invited to give their expert opinions on MyPRAT questionnaire. In this task, content validity index (CVI) was measured to determine the content validity of MyPRAT questionnaire in a more objective manner. [14] The clinical experts were instructed to state their opinion on the relevancy of each close-ended item of MyPRAT by choosing one of the following options: 1 for "not relevant", 2 for "somewhat relevant", 3 for "relevant" or 4 for "highly relevant".

To ensure that MyPRAT can be conveniently administered among Malaysian population, the face validity of MyPRAT was determined in 33 subjects with diverse backgrounds. The sample size was calculated based on the known central limit theorem (i.e. at least 30 subjects are required to produce data with normal distribution) and 10% drop-out rate. Herein, they were instructed to provide comments on MyPRAT questionnaire in terms of its format, content and language use. Specifically, they were asked to rate MyPRAT questionnaire as "good", "unsure" or "poor". All of them were selected randomly among students and staff members of USM.

In the next task, by using convenience sampling, eleven Malay hearing impaired children (aged 3 to 9 years) who have been undergoing conventional auditory training programs (for at least 3 months) in Hospital Universiti Sains Malaysia were selected. Their respective parents were instructed to fill in MyPRAT questionnaire for providing comments on the effectiveness of the auditory training. Prior to this, a short briefing was given to them on how to answer the questionnaire. They were advised to give honest answer for each question. For determining the construct validity of MyPRAT, the parents were also required to fill in the Malay version of MAIS questionnaire. [10] The score for each item as well as the total score were recorded for each subject for both questionnaires.

Data analysis

Descriptive and inferential statistical analyses were carried out as applicable. For the content validity task, both item-level CVI (I-CVI) and scale-level CVI (S-CVI) were calculated based on the method proposed by Lynn. [14] Specifically, for each of MyPRAT items, the I-CVI was calculated by dividing the number of experts who rated 3 or 4 (on the 4-point relevance scale) by the total number of experts. The S-CVI was determined by averaging all 10 I-CVI values of MyPRAT (Part A and Part B). The data for face validity task were analyzed descriptively.

Since the data were found to be normally distributed (as shown by Kolmogorov Smirnov test, $p>0.05$), parametric analyses could be carried out. For determining the construct validity of MyPRAT questionnaire, Pear-

son product-moment analysis was used to determine the correlation between MyPRAT and MAIS questionnaire. For determining the internal consistency of MyPRAT questionnaire, Cronbach's alpha and Guttman split-half reliability were measured. The Pearson correlation analysis was also used to determine the item-total correlations of MyPRAT questionnaire. The resultant *p* values of less than 0.05 were considered statistically significant. All data analyses were carried out using the SPSS software version 20 (SPSS Inc, Chicago, IL).

RESULTS

After being developed and translated, the MyPRAT questionnaire underwent several validity and reliability tasks. Recall that in the content validity task, nine experts were involved (mean age of 40.4 ± 8.2 years) and the majority of them were males (67%). Two of them were otorhinolaryngologists, three were audiologists and four were speech language pathologists.

In this task, the I-CVI values for MyPRAT items were found to be high and ranged from 0.78 to 1.00. The lowest I-CVI (0.78) was found for Q2 and Q4 in Part B. The S-CVI (or S-CVI/Ave) that provides a general measure of content validity of MyPRAT questionnaire was found to be excellent (0.91).

In the face validity task, 33 participants (mean age of 32.6 ± 11.8 years) were recruited. The majority of them were females (66.7%). In terms of occupation, 30.3% of them were university students, followed by cleaners (18.2%), housewives (15.2%), unemployed individuals (15.2%), cafe workers (12.1%) and teachers (9.0%). Malay participants are the majority (63.6%), followed by Chinese (24.2%) and Indian (12.2%) respondents. Figures 1 to 3 reveal the outcomes of the face validity task.

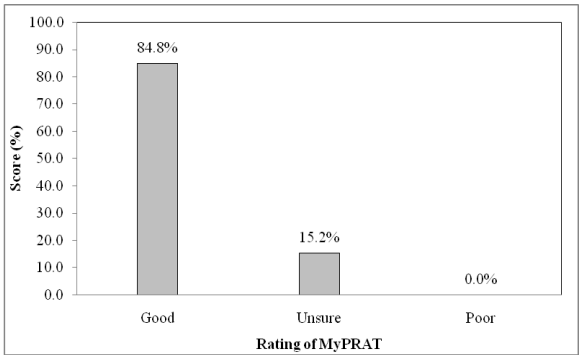

Figure 1: Respondents' rating of MyPRAT in terms of its format (in percentage).

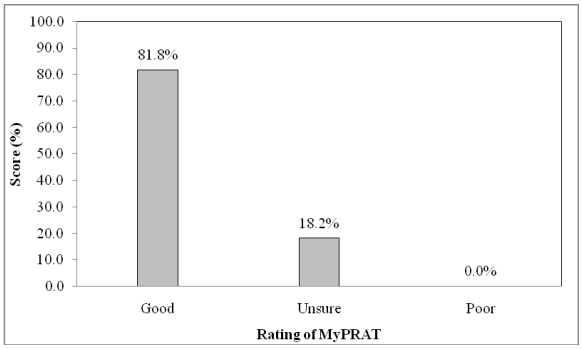

Figure 2: Respondents' rating of MyPRAT in terms of its content (in percentage).

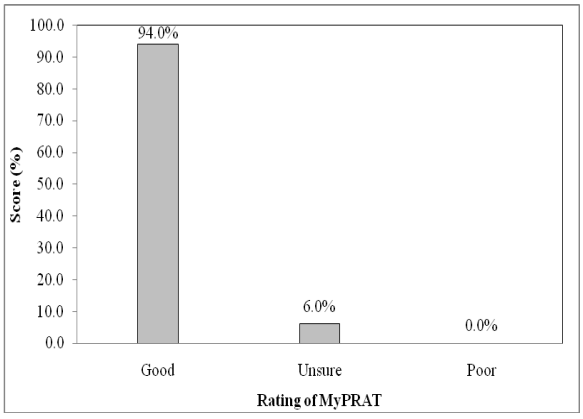

Figure 3: Respondents' rating of MyPRAT in terms of its language use (in percentage).

As revealed in Figure 1, most of the respondents rated the format of MyPRAT questionnaire as "good" (84.8%). The rest of participants were unsure of the suitability of MyPRAT format (15.2%). Similarly, as illustrated in Figure 2, the majority of participants rated the content of MyPRAT as "good" (81.8%), while 18.2% of them rated the MyPRAT content as "unsure". In terms of language use of MyPRAT questionnaire, nearly all participants (94.0%) rated MyPRAT as

"good" (Figure 3). Only 6.0% of respondents were unsure of the language use of MyPRAT. For all three aspects, none of respondents rated MyPRAT questionnaire as "poor".

Table 1 shows the mean, standard deviation and range of total scores for MyPRAT and MAIS questionnaires. A strong correlation was found between the scores in Part A of MyPRAT questionnaire and the scores in MAIS questionnaire (r=0.86, p<0.001). In contrast, the scores in Part B of MyPRAT questionnaire were not correlated with the MAIS scores (r=0.55, p=0.079).

Table 1: Mean, standard deviation (SD) and range of scores for MyPRAT and MAIS questionnaires.

	MyPRAT		MAIS
	Part A	**Part B**	
Mean (SD)	16.5 (4.4)	17.2 (4.0)	18.2 (3.2)
Range	8 - 22	10 - 21	14 - 24

To determine the reliability of MyPRAT, its internal consistency was measured. As shown in Table 2, for Part A, its item-total correlation ranged between 0.43 and 0.97. For Part B of MyPRAT, the item-total correlations were from 0.72 to 0.91 (Table 2). The Cronbach's alpha values for both parts of MyPRAT were found to be high (0.90 for Part A and 0.92 for Part B). These findings are further supported by the high values of Guttman split-half reliability coefficients (0.98 for Part A and 0.96 for Part B) indicating good test reliability of MyPRAT questionnaire.

DISCUSSION

A newly developed instrument must be proven valid and reliable prior to its application. Validity is simply defined as the ability of the instrument to measure what it is purporting to measure. [15] On the other hand, reliability is defined as the ability of the instrument to measure repeatedly the same results and be internally consistent. [15] Recall that the present study was conducted to develop and validate an alternative questionnaire that is simpler to be administered among parents. To determine the effectiveness of intervention method, parental report and judgment can be useful. Herein, the parental reports have been shown to be valid and reliable in regard to children's communicative abilities. [16, 17] Moreover, in evaluating speech skills, a strong correlation was found between parental judgments of their children's skills and the results of speech language pathologist. [18]

The items of MyPRAT questionnaire were chosen based on specific requirements. For simplicity, it is comprised of only 12 questions divided into two parts. For each closed-ended

Table 2: Internal consistency analyses of MyPRAT items.

Item of MyPRAT		**Item-total correlation**	**Cronbach's alpha**	**Cronbach's alpha if item is deleted**	**Split-half reliability**
Part A	Q1	0.95	0.90	0.87	0.98
	Q2	0.97		0.85	
	Q3	0.95		0.87	
	Q4	0.97		0.85	
	Q5	0.43		0.98	
Part B	Q1	0.72	0.92	0.96	0.96
	Q2	0.89		0.90	
	Q3	0.91		0.88	
	Q4	0.91		0.88	
	Q5	0.91		0.88	

item, the 5-point Likert scale rating was used. Among the options, 5-point and 7-point Likert scales are commonly used in the questionnaires. [19] Questionnaires that utilize lower response categories (less than 5-point) might be less accurate than the ones with higher response options. Conversely, questionnaires with higher response categories (7-point and more) might cause confusions to respondents and the response time can be prolonged. [20] Therefore, the 5-point response category utilized in MyPRAT questionnaire was considered optimum.

In order to validate MyPRAT questionnaire, several validity and reliability tasks were carried out. In the content validity task, content validity index (CVI) was measured to determine the clinical experts' opinion on MyPRAT questionnaire. As suggested by Lynn, [14] in order to achieve acceptable content validity, the I-CVI should be more than or equal to 0.70. In the content validity task where 6 to 10 experts are involved, the content validity of a particular questionnaire can be considered excellent if the I-CVI and S-CVI are at least 0.78 and 0.90, respectively. [21] Recall that in the present study, nine clinical experts were involved. As revealed, I-CVI values for MyPRAT items were high (ranged from 0.78 to 1.00) and none of the item was below 0.78. Furthermore, the S-CVI for MyPRAT was also high (0.91). Based on the high I-CVI and S-CVI values, the MyPRAT questionnaire can be said to have excellent content validity.

Since MyPRAT questionnaire is self-administrated, its format, content and language must be appropriate and understandable to people with various backgrounds, cultures and educational levels. To serve this, the face validity of MyPRAT questionnaire was determined. As revealed, the majority of respondents (> 80%) rated the format, content and language of MyPRAT to be good. Furthermore, all respondents never rated MyPRAT items as "poor". This shows that the MyPRAT questionnaire has good face validity.

The MyPRAT questionnaire was also found to have good construct validity (particularly for items in Part A) as its scores were highly correlated with the scores in MAIS questionnaire. Since the auditory skills and behaviors are adequately covered by both questionnaires, the high correlation between them was sensible. When the scores in Part B of MyPRAT were compared with the MAIS scores, no significant correlation was found between them. This finding was also expected as the items in Part B of MyPRAT questionnaire measure different aspects of auditory training (that are not covered by MAIS questionnaire). In this regard, it seems advantageous to have MyPRAT questionnaire as specific auditory improvements (Part A) and the overall satisfaction on the auditory training (Part B) can be conveniently documented.

In the present study, the reliability of MyPRAT questionnaire was determined by measuring its internal consistency. As shown, the lowest item-total correlation (0.43) was found for Q5 in Part A. This value, nevertheless, is higher than the minimum recommended value. That is, for an item to be considered appropriate and internally reliable, its item-total correlation must be more than 0.20. [22] The good reliability of MyPRAT is further supported by Cronbach's alpha and split-half reliability outcomes. In general, to achieve acceptable internal consistency, the Cronbach's alpha value should be more than 0.70. [23] In the current study, the Cronbach's alpha values were high (>0.90) implying that the items of myPRAT questionnaire are internally consistent and reliable.

The present study is not without limitations. Since the study sample was small, factor analysis of MyPRAT questionnaire could not be conducted to further support its construct validity. This is subject to further large-

large-scale research. Furthermore, only quantitative data were analyzed in the present study. To further explore the usefulness of MyPRAT questionnaire, its open-ended questions should also be analyzed accordingly.

CONCLUSION

In conclusion, an effort has been made to develop and validate an alternative questionnaire to document the progress of auditory training among Malay hearing impaired children. After undergoing a series of validity and reliability tasks, the MyPRAT questionnaire has been proven to be valid and reliable for its intended applications. Nevertheless, future studies are welcome to further support findings obtained from the present study.

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Appendix 1A: MyPRAT Questionnaire (Part A-English)

Parental Report on Auditory Training (PRAT)

1-*Strongly Disagree* 2-*Disagree* 3-*Unsure* 4-*Agree* 5-*Strongly Agree*

Part A

1. My child is more responsive to environmental sounds (e.g. sounds of telephone, animal sounds etc.) after undergoing the auditory training program

1	2	3	4	5

2. My child is more responsive to speech sounds after undergoing the auditory training program

1	2	3	4	5

3. My child uses hearing a lot to communicate after undergoing the auditory training program

1	2	3	4	5

4. My child's listening skills become better after undergoing the auditory training program

1	2	3	4	5

5. My child's other skills (e.g. concentration, social etc.) become better after undergoing the auditory training program

1	2	3	4	5

6. Five improvements of skills that are observed (if any):

_____

_____

_____

_____

_____

Appendix 1B: MyPRAT Questionnaire (Part B-English)

Part B

1. I am satisfied with my child's progress after undergoing the auditory training program

1	2	3	4	5

2. I am satisfied with the service given by the clinician/student who performs the auditory training

1	2	3	4	5

3. This auditory training should be conducted on every hearing impaired child

1	2	3	4	5

4. I would recommend this auditory training to others

1	2	3	4	5

5. Overall, I am satisfied with this auditory training program

1	2	3	4	5

6. State your specific opinions on this auditory training.

_____

_____

_____

_____

_____

Appendix 2A: MyPRAT Questionnaire (Part A-Malay)

Malay version of Parental Report on Auditory Training (MyPRAT)

1-*Sangat Tidak Bersetuju* 2-*Tidak Bersetuju* 3-*Tidak Pasti* 4-*Bersetuju* 5-*Sangat Bersetuju*

Part A

1. Anak saya lebih responsif kepada bunyi persekitaran (bunyi telefon, bunyi binatang dsb.) selepas mengikuti program latihan auditori

1	2	3	4	5

2. Anak saya lebih responsif kepada bunyi pertuturan selepas mengikuti program latihan auditori

1	2	3	4	5

3. Anak saya lebih banyak menggunakan pendengaran untuk berkomunikasi selepas mengikuti program latihan auditori

1	2	3	4	5

4. Kemahiran mendengar anak saya menjadi lebih baik selepas mengikuti program latihan auditori

1	2	3	4	5

5. Kemahiran lain anak saya (penumpuan, sosial dsb.) menjadi lebih baik selepas mengikuti program latihan auditori

1	2	3	4	5

6. Lima peningkatan kemahiran yang diperhatikan (jika ada):

_____

_____

_____

_____

_____

Appendix 2B: MyPRAT Questionnaire (Part B-Malay)

Part B

1. Saya berpuashati dengan perkembangan anak saya selepas menjalani latihan auditori

1	2	3	4	5

2. Saya berpuashati dengan perkhidmatan yang diberikan oleh ahli klinikal/pelajar yang menjalankan latihan auditori ini

1	2	3	4	5

3. Latihan auditori ini bagus dilakukan pada setiap kanak-kanak bermasalah pendengaran

1	2	3	4	5

4. Saya akan mencadangkan latihan auditori ini kepada orang lain

1	2	3	4	5

5. Secara keseluruhan, saya berpuashati dengan program latihan auditori ini

1	2	3	4	5

6. Nyatakan pendapat spesifik anda terhadap latihan auditori ini:

_____

_____

_____

_____

_____

Jeyasakthy SANIASIAYA, Irfan MOHAMAD, Khairul Bariah JOHAN @ RAHMAT, Sakinah MOHAMAD, Norhafiza MAT LAZIM

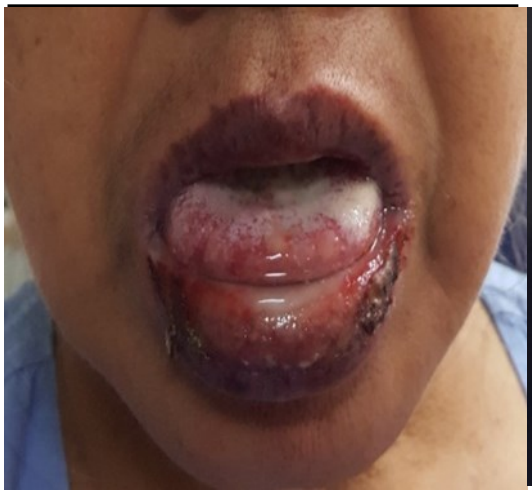

Figure 1

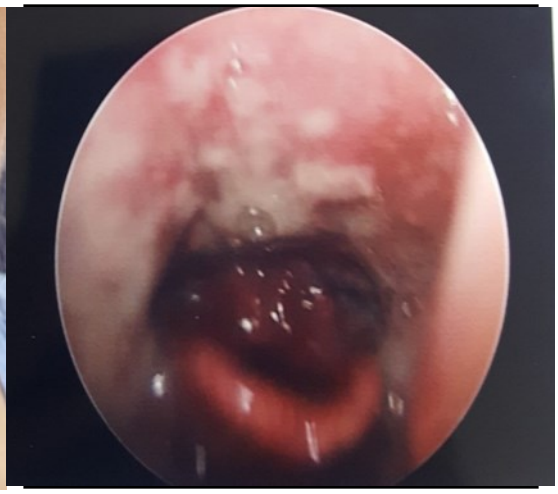

Figure 2

A 64-year-old Malay female with underlying hypertension and ischemic heart disease presented with a brief history of sorethroat, fever and odynophagia for the past 2 days. She was only able to tolerate liquids and soft diet. This was then followed by a high-grade fever with no chills or rigor. She had no shortness of breath, noisy breathing or hoarseness. There was no neck swelling, joint pain or stiffness or any rashes. On examination, patient was comfortable, not septic looking. Her lips were swollen, sloughy and tender. Her tongue was coated and sloughy (Figure 1). Oral cavity examination revealed slough over buccal mucosa, floor of mouth and tongue. Bilateral tonsils were coated with slough. The mucosa overlying the oral cavity was friable and bled upon contact. Endoscopy revealed inflamed and edematous laryngeal mucosa with slough (Figure 2).

What is the diagnosis?

***Answer**: refer to page 109*

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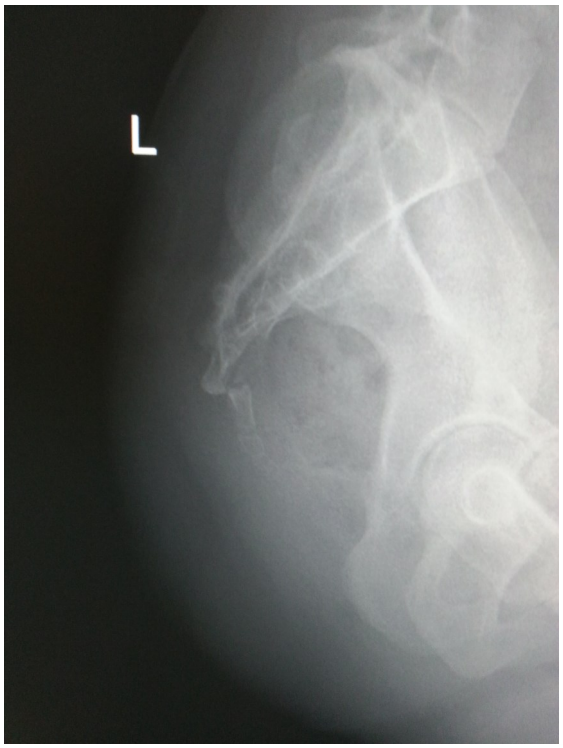

Figure 1

A 39-year-old lady presented to accident and emergency department with pain in her buttock and anal region following an accidental fall. She landed on her buttock in a sitting position while skating three days before. She started experiencing pain in her nether region after the fall and took some simple analgesics for the pain. But the pain intensity increased while driving and sitting which led her to seek medical advice. A sacral xray was taken (Figure 1).

What is diagnosis?

***Answer**: refer to page 110*

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Burkholderia Cepacia Orbital Cellulitis Causing Blindness: A Case Report.

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ABSTRACT

Burkholderia cepacia is an aerobic gram-negative bacillus with multidrug resistance found in various moist environments. It has been reported in keratitis and endophthalmitis. We described a case of *Burkholderia cepacia* orbital cellulitis, which believed to be the first reported case. A 71-year-old gentleman with underlying poorly controlled Type 2 diabetes mellitus and hypertension, presented with left eye sudden blindness and complete ptosis for one day. On examination, left eye was non-perceptive to light with positive relative afferent pupillary defect, mild proptosis, chemosis, complete ptosis and total ophthalmoplegia. Eye swab culture revealed *Burkholderia cepacia*. Culture for fungal growth was negative. Despite treatment with intravenous cloxacillin, ceftriaxone and metronidazole, and later vancomycin, the nerve dysfunction and visual loss were irreversible. Bacterial orbital cellulitis rarely presents with blindness. This case represents the virulent nature of *Burkholderia cepacia*.

Keywords: Burkholderia cepacia, blindness, orbital cellulitis, ophthalmoplegia, virulence

INTRODUCTION

Orbital cellulitis is an acute infection of the soft tissue around the eye. It is caused by bacteria or fungus with potentially serious complications including blindness, meningitis, cavernous sinus thrombosis, and intracranial abscess formation.[1-3] The most common causative bacteria are *Streptococcus* species, *Staphylococcus aureus,* and *Haemophilus influenza*, whereas *Pseudomonas, Klebsiella, Enterococcus* and *Eikenella* are less common organisms.[3, 4] We described the first reported case of orbital cellulitis caused by *Burkholderia cepacia* and its virulent nature that leads to blindness.

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CASE REPORT

A 71-year-old gentleman with underlying poorly controlled Type 2 diabetes mellitus and hypertension with no previous eye complaints, presented with left eye blindness and complete ptosis. It was preceded with left eye progressive blurred vision and eyelid swelling for 2 days. He denied diplopia, ocular trauma nor insect bite on the eyelid and did not have

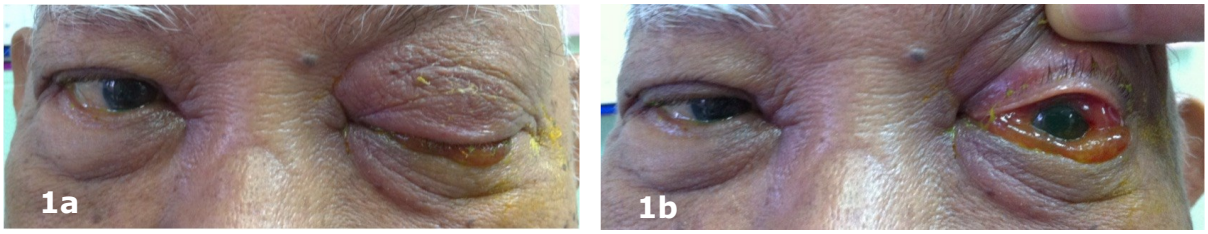

Figure 1. (a) Left eye complete ptosis with (b) mild proptosis and extensive chemosis.

any fever. On examination, there was no perception to light in the left eye with positive relative afferent pupillary defect. Other examination revealed mild proptosis with 2 mm difference, mild lid erythema and edema, chemosis, complete ptosis and total ophthalmoplegia [Figure 1(a) and (b)]. Ocular examination was unremarkable except cataract and mild non-proliferative diabetic retinopathy. Eye swab culture was taken and this grew *Burkholderia cepacia*. Blood culture for bacterial and fungal growth was negative. Computed tomography of orbit and paranasal sinuses did not show evidence of subperiosteal abscess or sinusitis [Figure 2(a) and (b)]. Endoscopic examination of nasal passages by otorhinolaryngology team did not reveal sinusitis, or necrotic tissue that was suggestive of fungal infection. The patient received intravenous cloxacillin, ceftriaxone and metronidazole for 1 week. However in view of poor response, cloxacillin was changed to vancomycin on Day 3 of treatment for more empirical coverage. Subsequently the chemosis and proptosis resolved following antibiotic treatment. However, patient did not recover vision in his left eye, with complete ptosis and total ophthalmoplegia at 1 year of follow up.

DISCUSSION

Orbital cellulitis is most commonly caused by adjacent sinusitis, accounting for more than 90% of all cases.[1] It can be caused by direct extension of infection from the globe, eyelids, or periocular tissues. Bacterial orbital cellulitis usually presents with marked proptosis, ophthalmoplegia and decreased vision.[3] It rarely presents with complete loss of vision as is our case. Severe visual impairment and rapid deterioration are mostly seen in orbital cellulitis caused by mucormycosis; however such clinical picture has been reported in bacterial infection caused by necrotizing strains of *Streptococcus pyogenes* and methicillin-resistant *Staphylococcus aureus.*[5, 6]

In our patient, eye swab culture was

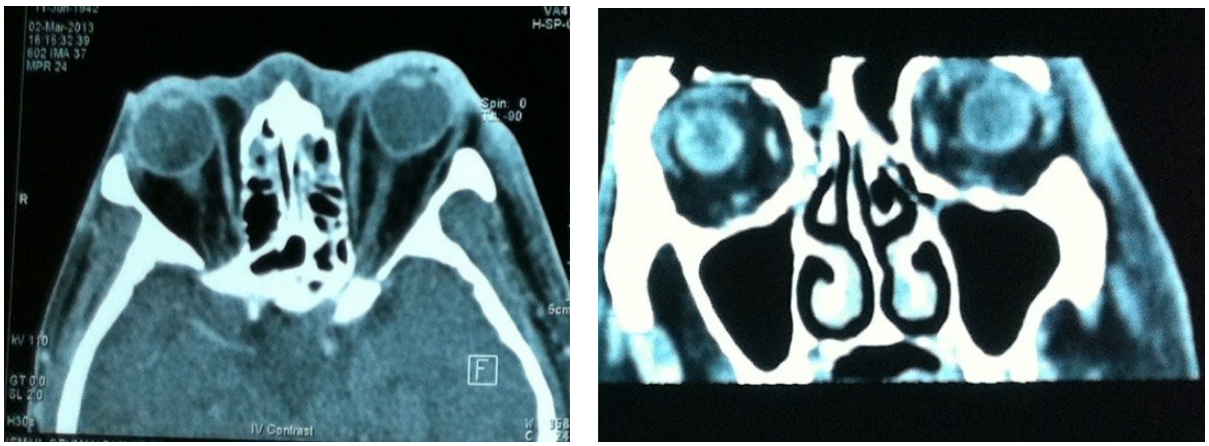

Figure 2. Contrasted computed tomography of orbit and paranasal sinuses revealed (a) minimal left eye proptosis (b) but did not show evidence of subperiosteal abscess or sinusitis.

the only positive culture which grew *Burkholderia cepacia. Burkholderia cepacia* (previously known as *Pseudomonas cepacia*) is a gram-negative, oxidase-positive, non-fermentative bacillus.[7] It can be found in soil, water, and infected plants, animals, and humans.[8] It has significant agricultural uses for promoting crop growth. In Malaysia, *Burkholderia cepacia* can be found in oil palm roots.[9] Our patient lives in a residential area near an oil palm estate and it is possible that he may have acquired the infection from there.

Patients may acquire *Burkholderia cepacia* from the environment or through patient-to-patient transmission.[10] It has become a significant opportunistic pathogen in immunosuppressed patients, causing the fatal "Cepacia Syndrome", especially in patients with cystic fibrosis. However, it is seldom found outside the lungs or in immunocompetent hosts. Ocular infections caused by *Burkholderia cepacia* are rare. To date, cases due to this gram-negative organism were reported in keratitis and endophthalmitis.[7, 11-13] Sachdeva *et al* reported that *Burkholderia cepacia* endophthalmitis accounts for 1.8% of culture positive endophthalmitis cases.[12] It can present as post-traumatic, acute-onset and delayed-onset post-operative endophthalmitis; and is associated with poor visual outcomes.[12]

Burkholderia cepacia is a highly virulent multidrug resistant organism.[14] It possesses antibiotic efflux pumps to remove antibiotic from the cell and forms biofilms to decrease contact to antibiotic. It also acquires beta-lactamases and altered penicillin-binding proteins. Because of multiple virulent factors, it has developed resistance to a number of antibiotics such as aminoglycosides, first- and second-generation cephalosporins, anti-pseudomonal penicillins, polymyxins, chloramphenicol, trimethoprim and fluoroquinolones.[10] Despite the multidrug resistance towards common ophthalmic medication, cases of successful treatment were reported but rare.[15, 16] A patient with *Burkholderia cepacia* post-operative endophthalmitis with initial visual acuity of hand movement was able to achieve 6/6 vision after vitrectomy and five intravitreal antibiotic injection including ceftazidime and amikacin.[15] Another patient with *Burkholderia cepacia* keratitis following laser-assisted in situ keratomileusis (LASIK) was successfully treated with topical imipenem-cilastatin and polymyxin B/ trimethoprim ophthalmic solution.[16]

In addition, *Burkholderia cepacia* can survive in aqueous environments such as a variety of solutions, medications, intravenous fluids, and even disinfectants and antiseptics such as benzalkonium chloride and chlorhexidine.[17] It is also unaffected by many preservatives including Betadine. Two studies reported that acute post-operative endophthalmitis following uneventful cataract surgery are due to *Burkholderia cepacia* from contaminated anaesthetic eye drops and contaminated trypan blue dye.[13, 18] In view of this, *Burkholderia cepacia* contamination test must be conducted on pharmaceutical products to ensure the absence of *Burkholderia cepacia*.

Fungal infection of the orbits such as Mucomycosis generally presents with more severe visual impairment and rapid progression.[19] Severe symptoms such as eyelid edema, proptosis, visual loss, pain and orbital apex syndrome involving cranial nerves II, III, IV, V1, and VI, and orbital sympathetics have been reported in Mucomycosis. It may lead to nasal and palatal necrosis, hence biopsy obtained from necrotic tissue is essential for timely diagnosis. Fungal orbital cellulitis has a high mortality rate in patients who are immunocompromised.[20] Thus, in patients with orbital cellulitis that associated with rapid clinical deterioration and visual loss, one should not neglect the possibility of fungal infection.

Work up including imaging and co-management with otorhinolaryngology team are essential for prompt diagnosis. In cases suspicious of fungal infection, a more aggressive approach to look for necrotic tissues at nasal passages and palate is crucial for the diagnosis of mucormycosis. In our case, the patient sustained blindness following virulent *Burkholderia cepacia* infection, which we postulated that he acquired infection from his residential environment. Combined with his poor sugar control, possibly led to an immunosuppressed state that promoted rapid and severe orbital infection. The mechanism of visual loss in the presented eye remained unclear. The severe infection may have caused ischemic necrosis, bacterial invasion, compression and stretching of the retrobulbar optic nerve.[2]

CONCLUSION

In conclusion, bacterial orbital cellulitis that presents with rapidly decreased vision is rare. High level of suspicion for fungal causes must be maintained especially in immunosuppressed patients. In spite of poor visual outcome, aggressive treatment in orbital cellulitis is needed to prevent intracranial extension that is life threatening. This case demonstrated the virulent nature of *Burkholderia cepacia*.

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Thyroid Abscess with Extensive Retropharyngeal Extension successfully treated with open Gravitational Drainage

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ABSTRACT

Thyroid abscess is a very rare condition comprising 0.1-7% of thyroid-related surgical cases. The common causative organisms are staphylococcus and streptococcus species. Thyroid abscess can be treated with antibiotics and surgical intervention. We reported a case of thyroid abscess with a large retropharyngeal extension in a 59 year-an old gentleman who was successfully treated with antibiotics, neck exploration, left hemithyroidectomy and gravitational drainage.

Keywords: Abscess, Acute suppurative thyroiditis, Mediastinum, Retropharyngeal Abscess, Thyroidectomy

INTRODUCTION

Thyroid infection or abscess is a rare medical condition, partly because of the high concentration of iodinated colloid compounds in the gland and it vascularity. Congenital third or fourth branchial arches anomalies are the commonest cause of thyroid abscess in children.[1] Other causes include trauma with neck injuries, recent thyroid surgery, immune-compromised patients or patients with pre-existing thyroid pathology and bacterial infection, either from haematogenous or lymphatic spread and the commonest causative organisms are staphylococcus and streptococcus.[1,2] We reported a case of thyroid abscess with a large retropharyngeal extension in a 59 year-an old gentleman who was successfully treated with antibiotics, neck exploration, left hemithyroidectomy and gravitational drainage.

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CASE REPORT

A 59 year-old gentleman presented with painful left sided neck swelling associated with fever for one week, dysphagia and muffled voice. There was no sign of respiratory distress. Patient has adult onset type 2 diabetes mellitus, which was well controlled with treatment. There were no symptoms of hyperthyroidism or hypothyroidism.

On examination, body temperature was 37.8°C. Neck examination revealed a tender left sided neck swelling measuring 4x3cm at the level of thyroid gland. Indirect laryngoscopy showed fullness of the left lateral and posterior pharyngeal wall obliterating the left pyriform fossa. The overlying mucosa

and epiglottis were normal and both vocal cords were mobile.

Total white blood count was raised at $21x10^9$/L, with a predominantly neutrophilic picture. Blood sugar level was raised at 19.6mmol/L**.** Serum free thyroxine level was high at 55.9 pmol/L. Blood cultures were taken but was negative for bacterial growth after 48 hours. An initial lateral neck x-ray revealed widening of the pre-vertebral space extending inferiorly from the fourth cervical vertebra to thorax.

Computed tomography of neck and thorax revealed multiple hypodense lesions within the left thyroid gland, which was in continuity with a large retropharyngeal collection at its superomedial aspect, which extended to retro-esophageal space and posterior mediastinum up to the level of left main bronchus and anterior to descending aorta. There was no evidence of any foreign body in the thyroid gland or any features of multinodular goiter.

Direct laryngoscopy with neck exploration were performed. Intraoperatively, the left thyroid gland was inflamed and friable, resulting in a spontaneous rupture of the abscess at the posterior surface during dissection of the gland. Extension of the abscess posteriorly was traced to a defect into the retropharyngeal space and down along retro-esophageal space. Left hemithyroidectomy was performed to facilitate drainage of the abscess from retropharyngeal space. Patient was then positioned in 30° Trendelenburg position for gravitational drainage of retropharyngeal and posterior mediastinum abscess. Corrugated drain was inserted at the left thyroid bed and in the retropharyngeal area.

Post operatively, patient was kept intubated and nursed in 30° Trendelenburg position with two-hourly chest percussion to assist drainage of posterior mediastinum abscess. Intravenous ceftriaxone 2g daily and metronidazole 500mg tds were continued and patient was extubated two days later once pus drainage has reduced and the wound showed improvement. Flexible nasopharyngolaryngoscopy revealed resolution of the bulge previously seen at the left lateral and posterior pharyngeal wall. There was no vocal cord palsy.

Pus culture grew Streptococcus species which was sensitive to ceftriaxone. Histopathological examination of the thyroid abscess wall showed large area of necrosis filled with necrotic materials and neutrophils. There was no evidence of malignancy seen.
His subsequent recovery was uneventful and was discharge after one month of hospitalization. His last follow up was six months postoperative and he was doing well.

DISCUSSION

Thyroid abscess accounts for only 0.1-0.7% of surgically treated thyroid pathologies.[3] The rarity of thyroid abscess are due to the innate protective properties which are its thick capsule, iodine-rich environment, rich blood supply, anatomically separated from other structure in the neck by fascial planes and generation of hydrogen peroxide as a requirement for the synthesis of thyroid hormone.[4] The commonest cause of thyroid abscess in children are congenital anomalies of the hypopharyngeal region leading to pyriform sinus fistula formation.[1,5] They usually present with history of recurrent inflammatory events and barium contrast study shows evidence of fistulous tract.[5] In adults, thyroid abscess can result from direct trauma from foreign bodies, oropharyngeal infection, infection from neighbouring structures and pre-existing thyroid pathologies.[6] A few cases of thyroid malignancy presented with thyroid abscess have also been also reported.[7-9]

Hematogenous and lymphatic spread

of infection from a remote area can also cause thyroid abscess formation especially in patients with systemic disorder and compromised immunity.[1,2] Infections within the gland with abscess formation which subsequently breached its capsule and overlying fascia can result in local extension of the infection into the retropharyngeal space in the neck, as with our case.[1] The commonest pathogens in thyroid abscess are *Staphylococcus aureus* and *Stretococcus pneumoniae*. Besides that, *Escherichia coli, Bacteroides, Salmonella, Acinetobacter and Klebsiella species. Mycobacteria* and fungi have been well documented.[10]

Frequently thyroid abscess presented with preceding history of upper respiratory tract infection. Clinical presentation of thyroid abscess may include fever, dysphagia, painful neck swelling, skin eythema, hoarseness or muffled voice, and if airway is compromised, patient can present with shortness of breath or stridor. Symptomatic thyrotoxicosis may occur due to increase release of thyroid hormone in the blood stream from increase vascularity from the infection. Thyroid abscess must be quickly diagnosed and managed or it can potentially result in septicaemia, vocal cord paralysis, retropharyngeal and mediastinum abscess.[2] If left untreated, particularly with anaerobic infection may spread and cause thrombophlebitis of the internal jugular vein, a condition called Lemierre's syndrome (post-anginal septicaemia).[11] Infectious mononucleosis have also been reported in adolescents presenting with thyroid abscess.[11] Thyroid malignancy also has to be ruled out in view of reported cases of thyroid malignancy presenting as thyroid abscesses.[7,8]

Management of thyroid abscess includes administration of broad spectrum antibiotics and immediate surgical intervention. Empirical broad-spectrum antibiotic therapy should be initiated early and this can be changed once sensitivity profile is available. Image guided serial aspiration or incision and drainage for managing unruptured thyroid abscesses have been reported to be fairly effective but in some cases, thyroidectomy may be required, particularly in recurrent thyroid abscesses associated with pyriform sinus, pre-existing thyroid disease and suspicion of thyroid malignancy.[1,5,6, 12,13] Partial thyroidectomy has also been reported to prevent inflammatory neuritis of recurrent laryngeal nerve.[13]

Abscess from head and neck region can spread inferiorly to mediastinum through the retropharyngeal space causing of mediastinitis. It is a life threatening condition with 20 -40% of mortality rate.[14] Treatment of mediastinal abscess includes broad spectrum antibiotics and adequate drainage. A combination of trans-cervical and trans-thoracic mediastinal drainage can be considered in patients with mediastinal extension. Some reported that trans-cervical mediastinal drainage alone was sufficient in cases of localized infection limited to superior mediastinum and a combined approach is recommended in patients with extensive mediastinal infection beyond the level of carina.[15] Trans-thoracic approach provides adequate exposure of all mediastinal compartments to achieve optimum drainage but is a more invasive procedure than trans-cervical mediastinal drainage and with risk of pleural contamination. Median sternotomy is an alternative approach for draining anterior mediastinal abscess but the disadvantages are inadequate exposure of visceral compartment and risk of osteomyelitis.[15]

Left hemithyroidectomy was performed in our case and the abscess was drained from the left thyroid bed, which was in continuity with the retropharyngeal space and patient was put in Trendelenburg position to facilitate gravitational drainage of the posterior mediastinal abscess. Posterior mediastinal abscess was adequately drained via two-hourly gravitational drainage with chest percussion. The advantage of this method is

that it is less invasive than the trans-thoracic approach. A few physiological changes may occur as a setback which are the orthostatic effect of the cardiovascular system with raised central venous pressure with facial and body congestion, splinting of diaphragm and also risk of aspiration as gastric juice, saliva and mucous will be collected in the nasopharynx and oropharynx. However, measures have been taken to monitor the condition of the patient with central venous pressure monitoring, optimizing ventilator setting and placement of Ryle's tube to prevent aspiration.

CONCLUSION

Thyroid abscess is a rare disorder, which if not treated early can extend to posteriorly into the retropharyngeal space and downward into the mediastinum. Successful management of thyroid abscess with extensive retropharyngeal and retrosternal involvement includes a combination of antibiotic therapy, radiological or surgical neck exploration and drainage with post-operative gravitational drainage as in this case can avoid a more invasive thoracotomy or median sternotomy. Partial thyroidectomy may be required particularly if the gland is completely damaged or if malignancy is suspected.

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A Rare Case of Wernicke's Encephalopathy and Dry Beri-beri Complicating Hyperemesis Gravidarum.

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ABSTRACT

Hyperemesis gravidarum occurs in approximately 0.3-2.0% of pregnancies. We present a rare case of Wernicke's encephalopathy and dry beriberi as a complication of hyperemesis gravidarum. A 23-year-old female, at 19 weeks gestation, presented with persistent vomiting since early pregnancy and feeling generally weak. Transabdominal ultrasound on presentation confirmed a non-viable foetus which was surgically removed. Throughout admission, she was noted to have confusion lasting a few days, horizontal nystagmus and progressive weakness with peripheral neuropathy of bilateral lower limbs. Her CT brain and lumbar puncture was normal. Nerve conduction studies was done, and coupled with her neurological findings, conclusion of thiamine deficiency was made. She was treated with thiamine and with rehabilitation she has currently made significant improvement. Thiamine deficiency manifesting with features suggestive of an overlap between Wernicke's encephalopathy and dry beriberi in patients with hyperemesis gravidarum is rare.

Key words: Wernicke encephalopathy, Beriberi, thiamine deficiency, hyperemesis gravidarum

INTRODUCTION

Hyperemesis gravidarum is a complex condition with a multifactorial aetiology characterized by severe intractable nausea and vomiting.[1] Hyperemesis gravidarum occurs in approximately 0.3-2.0% of pregnancies.[1] Wernicke's encephalopathy is a well known sequelae of thiamine deficiency which can occur in hyperemesis gravidarum.[2] It is characterised by the classic triad of encephalopathy, ophthalmoplegia and ataxia. In dry beriberi there is usually symmetric, non-specific polyneuropathy with myelin degeneration and disruption of motor, sensory and reflex arc which occurs with thiamine deficiency. We report a rare case of Wernicke's encephalopathy and dry beriberi as a complication of hyperemesis gravidarum. This patient was treated with thiamine, and with rehabilitation she has had significant improvement of her neurological symptoms.

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CASE REPORT

A 23-year-old female, at 19 weeks gestation, presented with persistent vomiting up to 10

times a day since early pregnancy and generalised weakness. She had poor appetite and reduced oral intake for over a month prior to presentation. She experienced significant weight loss of at least 5 kilograms. There were no other significant symptoms. She had been attending the emergency department and her local clinic a few times, and was treated for urinary tract infection once and had been given intravenous hydration. Premorbidly, she had a complete miscarriage 2 years previously. She did not take any traditional or over the counter medications. She did not consume alcohol.

On examination, there was evidence of dehydration with dry mucous membranes. Uterus was palpable corresponding to 18 weeks of gestation. Initial haematological investigations showed increased urea (16.7 mmol/L) and creatinine (180 µmol/L); low sodium (129 mmol/L), potassium (2.0 mmol/L) and magnesium (0.53 mmol/L) ; abnormal liver function tests (ALP: 113 U/L, AST:217 U/L, ALT: 367 U/L); and metabolic alkalosis on venous blood gas. Urine dipstick showed ketone:4+, urobilinogen: 4+, bilirubin: 1+, leukocytes: 3+ and nitrate: negative. Thyroid function test was normal. B12 and folate levels were normal as well. Transabdominal ultrasonography showed single non viable foetus, in which foetal heart activity was not seen.

She was admitted for intravenous hydration, with magnesium and potassium replacement. A course of amoxicillin-clavulanate was commenced. Suction and curettage was done for removal of products of conception. Despite these treatments, and also an improvement in her vomiting, her weakness persisted. She was unable to walk and also had reduced sensation of lower limbs bilaterally which has progressed for a few days since admission. She also had intermittent confusion which lasted a few days. On neurological examination, her Glasgow Coma Scale was full. Examination of lower limbs showed normal tone, power ⅗ at the hip, ⅖ at the knees and ⅕ of both dorsi and plantar flexion. Reflexes were absent throughout both lower limbs, and absent sensation of all modalities in a stocking distribution up to level of thighs. She was unable to stand. Upper limbs examination showed normal tone, power of ⅘, with absent reflexes and normal sensation. There was presence of horizontal nystagmus, and past pointing bilaterally.

At that time, potassium level remained low at 3.0 mmol/L. Other renal profile and liver function tests had normalised. Magnesium had also normalised after replacement. Creatinine kinase was normal. Her potassium was immediately replaced, however her neurological symptoms persisted despite normalisation.

She had a computed tomography of the brain which was normal. Lumbar puncture showed normal protein, glucose, no organism on gram stain, and no evidence of malignancy or infection. Histopathology results from suction and currettage confirmed products of conception, no malignancy and no hydropic changes were noted. Nerve conduction study (NCS) showed evidence of predominantly sensory with mild motor axonal polyneuropathy involving both upper and lower limbs. There was no evidence suggestive of demyelination and F waves were normal. A provisional diagnosis of thiamine deficiency was made in the context of recurrent vomiting throughout pregnancy, poor oral intake, memory impairment with mild horizontal nystagmus and NCS findings. Thiamine level in whole blood was sent with expectant results in 4 weeks.

A 5 day course of parenteral multivitamin replacement was immediately commenced, followed by oral thiamine supplementation. There were no further episodes of confusion after replacement. Subsequently

her test result revealed a low thiamine level (52nmol/L (66-200nmol/L)). A final diagnosis of Wernicke's encephalopathy and dry beriberi secondary to hyperemesis gravidarum was made.

Rehabilitation was initiated with involvement of the physiotherapist and occupational therapist teams. After 4 weeks of rehabilitation she was able to stand, with gradual return of reflexes and sensation. She was transferred to a specialist rehabilitation unit for continuation of rehab.

DISCUSSION

The above case describes a pregnant patient with thiamine deficiency manifesting with features suggestive of an overlap between Wernicke's encephalopathy and dry beriberi. Although it is a recognised complication of hyperemesis gravidarum, it is rare to present with both central and peripheral neurological symptomatology. Improvements in health systems and care delivery in Malaysia, with a great emphasis on maternal and child wellness, such overt manifestations of thiamine deficiency is rarely seen in pregnant mothers in routine day to day practice.

Thiamine (vitamin B1) is a micronutrient that is easily available in the diet through foods such as rice, grains and lean meat.[3] Widespread consumption of refined foods such as polished rice, white sugar and white flour could predispose to reduced dietary availability of thiamine as they contain very little amounts.[3] Once thiamine is absorbed from the gut it undergoes phosphorylation to produce thiamine pyrophosphate (TPP) which is a functionally active coenzyme of the vitamin.[3] Among the major functions of TPP is to regulate oxidative decarboxylation of alpha-ketoacids to produce adenosine triphosphate (ATP),acts as a cofactor in the pentose phosphate pathway and in a manner that has not yet been fully determined maintains neural membranes and normal nerve conduction (mainly peripheral nerves).[3]

Thiamine deficiency has been well known to cause multi-system manifestations including to the nervous system, cardiac system, gastrointestinal system and vision.[4] Symptoms such as palpitations and persistent vomiting such as exhibited by our patient are known to have occurred.[4] Time taken to deplete the body's store of thiamine is thought to be approximately 3 weeks.[5]

Wernicke's encephalopathy is a well known sequelae of thiamine deficiency, most commonly seen in patients with chronic alcohol abuse. Prevalence in non-alcoholic patients varies from 0.04% to 0.13%, the most frequent settings being malignant disease (18.1%), post gastrointestinal surgery (16.8%), and hyperemesis gravidarum (12.2%).[6,7] It is characterised by the classic triad of encephalopathy, ophthalmoplegia and ataxia. Our patient had exhibited two of these. If left untreated, Wernicke's encephalopathy in the pregnant patient could progress to permanent neurological deficits, cognitive impairment and Korsakoff syndrome which can be fatal in up to 10-20% of cases; whereas in the foetus only about half of affected pregnancies will result in the birth of a normal baby, as it may lead to miscarriage, preterm birth, and also intrauterine growth retardation.[6,7]

Carbohydrate loading in a patient with thiamine deficiency may precipitate Wernicke's encephalopathy, hence it is highly recommended that in patients with suspected thiamine depletion, levels should first be taken and parenteral replacement instituted prior to commencing normal feeding or intravenous glucose.[2] There may also be a genetic predisposition as there is evidence of an abnormal form of transketolase that binds thiamine less avidly in patients who develop WE compared to that of controls.[8]

Our patient showed further neurological findings which were not consistent with Wernicke's encephalopathy, including reduced deep tendon reflexes, paraesthesia of extremities and progressive weakness of limbs. These peripheral neurological manifestations are all features of dry (neuritic) beriberi.[4] In dry beriberi there is usually symmetric, non-specific polyneuropathy with myelin degeneration and disruption of motor, sensory and reflex arcs.[3] It has a tendency to affect the legs before extending to the arms with sensory loss being accompanied by muscular weakness and hypo- or areflexia.[3]

It is likely that our patient had a combination of factors that had led to her thiamine depleted state. Pregnancy is a high consumptive state which has been known to lead to thiamine deficiency.[4] Pernicious vomiting in her 1st trimester also has led her into a thiamine deficient state. Even though she received parenteral hydration, inadequate thiamine replacement may have resulted in her unable to replenish her thiamine stores. It is possible that this deficiency had further continued further into her 2nd trimester contributing to her persistent state of vomiting.

A variability of clinical features may be present in patients with thiamine deficiency. The delayed development and complexity of her neurological signs is a common pitfall in getting a timely clinical diagnosis, and late thiamine replacement may have even contributed to her miscarriage. [6]

CONCLUSION

Thiamine deficiency manifesting with features suggestive of an overlap between Wernicke's encephalopathy and dry beriberi is rare. A high index of suspicion needs to be retained when pregnant patients present with prolonged vomiting and poor oral intake coupled with both central and peripheral neurological symptomatology. By missing such symptomatology further complications from beri-beri and Wernicke's encephalopathy can occur and if unheeded can ultimately lead to fetal and even maternal death.

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(*Refer to page 94*)

Answer: Drug induced oro-laryngeal ulceration

Further history from patient revealed that two weeks prior to the symptoms, she was prescribed with oral Indapamide for her hypertension. Indapamide was immediately withheld with close monitoring of her blood pressure and was started on intravenous Amoxicillin/Clavulanate acid along with Thymol gargle and oral topical gel. After one-week her symptoms along with her oral and laryngeal ulceration resolved.

Adverse drug reaction (ADR) may occur immediately after consumption of any drug or delayed to a few weeks or years later, albeit the standard dose and form of application[1]. ADR following oral medication are not typical, thus it's often overlooked.[1] Oral ADR may masquerade other oral lesions including of viral aetiology. In our patient, possibility of viral origin of oro-laryngeal ulceration cannot be ruled out. Reported forms of systemic adverse reactions among others are hyposalivation, burning mouth syndrome, oral ulceration, erythema multiform, lichenoid reaction, gingival hyperplasia and angioedema.[2] The most common oral ADR are secondary to sulfamethoxazole and trimethoprim antibiotics and non-steroidal anti-inflammatory analgesics (NSAIDS).

Indapamide, a sulphonamide diuretics prescribed mostly for hypertension has been reported to caused ADR with onset of symptoms as early as 2 days or in our case, delayed by up to 14 days and symptoms can range from pruritus, urticaria, to more severe reaction such as angioedema, erythema multiforme, Steven-Johnson syndrome and toxic epidermal necrolysis.[3-5]

Most diagnosis of oral ADR are made after detailed medical history and clinical findings. In the previous years, radioallergosorbent test, basophil degranulation test and blastic transformation test were performed, but due to high false-positive and false-negative results, these tests are no longer commonly used. The only objective test to confirm diagnosis is a 're-challenge' which requires patient's to re-consume the offending drug causing the reaction after being discontinued which often is carried out in hospital setting owing to the devastating possibility of anaphylactic reaction.[1] 'Re-challenge' was not carried out in our patient, weighing the huge risk of developing anaphylaxis reaction in addition to her age. Management mainly involves instant discontinuation of the offending drug along with systemic or topical steroids.[1]

In conclusion, it is prudent for all physicians to inform their patients regarding adverse drug reactions especially, when prescribing a new drug and to seek urgent treatment in case of any reactions. Patients who suffered from any drug reaction should be alerted and be provided with a drug-alert card which should be presented to any physicians in the future.

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(***Refer to page 95***)

Answer: Anterior Dislocation of the coccyx

This is an anterior dislocation of the coccyx **(Figure 1)**. The patient was admitted to the department of Orthopaedics. Under spinal anaesthesia, reduction of the coccyx per-rectum was attempted but failed. Patient was discharged with analgesics and advised avoid putting pressure on her coccyx for three weeks and regularly followed up in orthopaedic clinic. After six months of the incident, the patient had no further pain or tenderness in the coccyx region. The patient resumed all her activities normally without any discomfort.

Acute anterior dislocation of coccyx is extremely rare. In current literature, this type of dislocation occurs sporadically following some form of accidental fall or trauma to the sacral region and treatment are usually either closed or open reduction of the fracture or conservatively with analgesia. [1,2,3] The result of both types of treatment are reported to be satisfactory.

Kim et al. reported a closed reduction of the dislocation using a joy stick technique new technique have shown promising results. Fang et al. reported the 56 cases of fracture dislocation of coccyx with the application of both open reduction and internal fixation (ORIF) and closed reduction methods with similarly good results.[3]

Coccygeal instability and coccydynia are also common complications after dislocation or fracture dislocation of the coccyx.[4] Surgical resection for such complications of coccygeal fracture is still controversial, with intractable post-traumatic coccydynia being an indication to surgery and results after the surgical resection are not very encouraging.[4]

Our patient agreed for a trial of closed manipulation under anaesthesia, failing which she refused for further surgical intervention and opted for conservatively treatment with analgesia and rest. The later is just as effective although recovery time may be prolonged.

CONCLUSION

Coccyxeal dislocation is an extremely rare and can be treated conservatively with excellent result.

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