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*"Intelligence without ambition is a bird without wings."*

**Salvador Dali (1904 – 1989)**
Spanish artist and surrealist

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ANNALS
ACADEMY OF MEDICINE SINGAPORE

## Free Papers

**Images in Medicine**

Editorial

# The Threat of Multiresistant Nosocomial Fungi

Louis YA Chai,[1,2,3] *MRCP(UK), PhD*, Paul A Tambyah,[1,2] *MD*

In 2014, the World Health Organization (WHO) raised concern about the worldwide threat of antimicrobial resistance to public health.[1] Many bacteria which cause common infections are now resistant to a broad range of antimicrobials. The WHO recently released a list of antibiotic-resistant "priority-pathogens" warranting urgency for research and control.[2] Featured in this list of 12 pathogens were carbapenem-resistant *Acinetobacter baumannii, Pseudomonas aeruginosa*, and third-generation cephalosporin-resistant *Enterobacteriaceae*. These pathogens are also common in local hospitals.[3] However, noticeably absent from the WHO list were fungal pathogens.

Candidaemia is the fourth most common cause of nosocomial bloodstream infection (BSI) worldwide.[4] *Candida* causing nosocomial outbreaks have been well described especially because of biofilm formation on devices and in intensive care units.[5,6] Amongst the *Candida* species causing nosocomial BSI are many non-albicans *Candida* with a higher frequency of resistance to azoles and echinocandins.[7,8] However, the threat of a pan-drug-resistant nosocomial *Candida* joining the ranks of multi-resistant bacteria was not apparent until the recent emergence of *Candida auris*.

*Candida auris* was first described in Japan in 2009[9] and since then, has been progressively reported worldwide, including the United States, Europe, Africa, North Asia, South Asia and nearby Malaysia.[10] Amongst the cases reported—invariably linked to healthcare institutions—have been reports of drug-resistant *C. auris* outbreaks[11,12] aided by environmental contamination by the yeast. In this issue of the Annals, Tan and her colleague report the first 3 cases of *C. auris* in Singapore.[13] The first case was in 2012, the second and third were in 2016. The temporal sequence of presentation (with the first case 4 years apart from the other 2) highlights a number of challenges; first with diagnosis. *Candida auris* can be misidentified with automated and conventional microbiological phenotypic and biochemical techniques employed in many microbiology laboratories including ours in Singapore, such as the Vitek 2 system and API 20C (both Biomerieux, Marcy-l'Étoile, France), BD Phoenix yeast identification system (BD, Franklin Lakes, NJ, USA) and MicroScan (Beckman Coulter, Brea, CA, USA) yielding instead the related but less resistant *C. haemulonii* or other rarer yeasts such as *Rhodotorula*. Tan and her colleague did not report if there had been difficulties with initial identification in their cases although their index of suspicion for *C. auris* was raised early prompting molecular confirmation and appropriate treatment modification. Microbiology facilities in Singapore and elsewhere who use automated systems may consider reviewing previous *C. haemulonii* cases as it has been reported that incidence of misidentification of *C. auris* as *C. haemulonii* might be as high as 88%.[14] This is not just academic but it has significant infection control implications.

The 3 cases illustrated here highlight many of the important characteristics of *C. auris* infection. There are significant differences between the 4 geographical clades of *C. auris* as elucidated by genetic analyses[15] and it may well be the *C. auris* is actually *C. auris* "species complex" similar to *C. glabrata*. Such variation is reflected in the antifungal resistance profile of the *C. auris* cases described here. Most previously reported strains have high fluconazole minimum inhibitory concentration (MIC), reduced susceptibility to other triazoles, amphotericin and variable MIC to echinocandins.[16] For the individual patient, treatment choice should be guided by in vitro MIC determination to determine the most effective antifungal agent, although at present, echinocandins appear to be the most effective with resistance rates of less than 10% compared with about 30% for amphotericin and 80% for azoles. However, consensus breakpoints for *C. auris* have yet to be established so it is not clear how well these in vitro results correlate with clinical success.

All 3 patients described here shared some notable traits. They were transferred from overseas hospitals to Singapore for continuing care and had received extensive

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prior treatment including broad-spectrum antimicrobials for their primary condition. It was probably not coincidental that all 3 patients were screened positive for drug-resistant carbapenemases of NDM-1 and OXA-232. All our hospitals now actively perform carbapenemase-producing carbapenem-resistant *Enterobacteriaceae* (CP-CRE) screening for patients with identified epidemiological risks.[17] The epidemiological risks for *C. auris* carriage and infection are similar to that of the CREs. As Tan and her colleague point out, heightened and possibly targeted concurrent screening for *C. auris* in patients with CP-CRE may need to be conducted to avoid large scale outbreaks such as those that have happened in other countries. As with all active surveillance programmes, the cost-effectiveness of such measures will need to be clearly demonstrated. Thanks to the vigilance of Tan and her colleague leading to the prompt implementation of appropriate infection control measures related to CP-CRE, there were no local transmissions reported arising from the 3 cases. Nonetheless, this report, in tandem with the others already described worldwide, places *C. auris* on the world stage of multidrug-resistant organisms (MDROs) necessitating a comprehensive approach including microbiology, molecular and clinical epidemiology, pharmacology, infectious diseases and a strong public health commitment to appropriate action to prevent this emerging multiresistant fungal pathogen from taking root and causing serious morbidity and mortality in our vulnerable patients in intensive care units, haematology-oncology units, surgical and transplant wards.

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REFERENCES

1. World Health Organization. Antimicrobial Resistance. Global Report on Surveillance: Global Report on Surveillance 2014. Available at: http://www.who.int/drugresistance/documents/surveillancereport/en/. Accessed on 17 February 2018.
2. World Health Organization. WHO publishes list of bacteria for which new antibiotics are urgently needed. 2017. Available at: http://www.who.int/mediacentre/news/releases/2017/bacteria-antibiotics-needed/en/. Accessed on 17 February 2018.
3. Cai Y, Venkatachalam I, Tee NW, Tan TY, Kurup A, Wong SY, et al. Prevalence of healthcare-associated infections and antimicrobial use among adult inpatients in Singapore acute-care hospitals: results from the first National Point Prevalence Survey. Clin Infect Dis 2017;64:S61-7.
4. Wisplinghoff H, Bischoff T, Tallent SM, Seifert H, Wenzel RP, Edmond MB. Nosocomial bloodstream infections in US hospitals: analysis of 24,179 cases from a prospective nationwide surveillance study. Clin Infect Dis 2004;39:309-17.
5. Tumbarello M, Posteraro B, Trecarichi EM, Fiori B, Rossi M, Porta R, et al. Biofilm production by Candida species and inadequate antifungal therapy as predictors of mortality for patients with candidemia. J Clin Microbiol 2007;45:1843-50.
6. Chai LY, Denning DW, Warn P. Candida tropicalis in human disease. Crit Rev Microbiol 2010;36:282-98.
7. Pfaller MA, Moet GJ, Messer SA, Jones RN, Castanheira M. Candida bloodstream infections: comparison of species distributions and antifungal resistance patterns in community-onset and nosocomial isolates in the SENTRY Antimicrobial Surveillance Program, 2008-2009. Antimicrob Agents Chemother 2011;55:561-6.
8. Farmakiotis D, Kontoyiannis DP. Epidemiology of antifungal resistance in human pathogenic yeasts: current viewpoint and practical recommendations for management. Int J Antimicrob Agents 2017;50:318-24.
9. Satoh K, Makimura K, Hasumi Y, Nishiyama Y, Uchida K, Yamaguchi H. Candida auris sp. nov., a novel ascomycetous yeast isolated from the external ear canal of an inpatient in a Japanese hospital. Microbiol Immunol 2009;53:41-4.
10. Chowdhary A, Sharma C, Meis JF. Candida auris: a rapidly emerging cause of hospital-acquired multidrug-resistant fungal infections globally. PLoS Pathog 2017;13:e1006290.
11. Schelenz S, Hagen F, Rhodes JL, Abdolrasouli A, Chowdhary A, Hall A, et al. First hospital outbreak of the globally emerging Candida auris in a European hospital. Antimicrob Resist Infect Control 2016;5:35.
12. Biswal M, Rudramurthy SM, Jain N, Shamanth AS, Sharma D, Jain K, et al. Controlling a possible outbreak of Candida auris infection: lessons learnt from multiple interventions. J Hosp Infect 2017;97:363-70.
13. Tan YE, Tan AL. Arrival of Candida auris fungus in Singapore: report of the first 3 cases. Ann Acad Med Singapore 2018;47:260-2.
14. Kathuria S, Singh PK, Sharma C,Prakash A, Masih A, Kumar A, et al. Multidrug-resistant Candida auris misidentified as Candida haemulonii: characterization by matrix-assisted laser desorption ionization-time of flight mass spectrometry and DNA sequencing and its antifungal susceptibility profile variability by Vitek 2, CLSI broth microdilution, and etest method. J Clin Microbiol 2015;53:1823-30.
15. Chatterjee S, Alampalli SV, Nageshan RK, Chettiar ST, Joshi S, Tatu US. Draft genome of a commonly misdiagnosed multidrug resistant pathogen Candida auris. BMC Genomics 2015;16:686.
16. Lockhart SR, Etienne KA, Vallabhaneni S, Farooqi J, Chowdhary A, Govender MP, et al. Simultaneous emergence of multidrug-resistant Candida auris on 3 continents confirmed by whole-genome sequencing and epidemiological analyses. Clin Infect Dis 2017;64:134-40.
17. Singapore MOH. Guidelines for control and prevention of multi-drug resistant organisms (MDROS) in healthcare facilities, 2013. Available at: https://www.moh.gov.sg/content/dam/moh_web/Publications/Guidelines/Infection%20Control%20guidelines/GUIDELINES%20FOR%20CONTROL%20AND%20PREVENTION%20OF%20MULTI-DRUG%20RESISTANT%20ORGANISMS%20%28MDROS%29%20IN%20HEALTHCARE%20FACILITIES%20-%20Nov%202013.pdf. Accessed on 17 February 2018.

Original Article

# Quality of Life across Mental Disorders in Psychiatric Outpatients

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## Abstract

**Introduction: Literature has shown that individuals with various psychiatric disorders experience a lower quality of life (QoL). However, few have examined QoL across disorders. The current study explored differences in QoL and symptom severity across 4 psychiatric diagnostic groups: anxiety disorders (including obsessive compulsive disorder [OCD]), depressive disorders, schizophrenia, and pathological gambling. Materials and Methods: Data analysed was from a previous study that examined the prevalence of hoarding symptoms among outpatients (n = 500) in a tertiary psychiatric hospital in Singapore. Measures utilised included the Beck Anxiety Inventory (BAI), Beck Depression Inventory-II (BDI-II) and Quality of Life Enjoyment and Satisfaction Questionnaire-Short Form (Q-LES-Q-SF). Sociodemographic information and details on type and number of comorbidities were also collected. Results: The depressive disorder group had the highest level of depressive and anxiety symptoms and the lowest QoL whereas; the schizophrenia group had the lowest level of depressive symptoms and the highest QoL. Age and employment status were the only sociodemographic correlates which were significantly associated with QoL. After controlling for sociodemographic factors, only the type of mental disorder was found to have a significant effect in explaining BAI, BDI-II and Q-LES-Q-SF. Conclusion: Findings offer insight in terms of the burden associated with the various disorders.**

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**Key words: Anxiety, Comorbid, Depression, Symptom severity**

## Introduction

Quality of life (QoL) can be defined as an "individual's perception of their position in life...in relation to their goals, expectations, standards and concerns".[1] Assessing the QoL of an individual is invaluable as it looks beyond the "direct manifestations of an illness" to examine its effects on the individual's daily life and life satisfaction.[2-3] Furthermore, it also acts as a useful measure in assessing the efficacy of mental health interventions.[3-8]

QoL has been shown to be considerably impaired among individuals with various mental illnesses[9-11] including schizophrenia spectrum disorders,[2,6,12] depressive disorders,[13-16] anxiety disorders,[17-18] and pathological gambling;[19-20] with a large majority of these studies conducted in clinical populations. Mastoff et al[11] for instance, found Dutch outpatients diagnosed with an Axis I or Axis II disorder to score worse on all domains of the World Health Organization Quality of Life-Bref (WHOQOL-Bref) compared to the general population whereas, a recent meta-analysis found patients with anxiety disorders to have lower QoL than non-clinical controls.[18]

While the aforementioned studies have shown QoL to be compromised among individuals with specific mental illnesses (e.g., anxiety disorders only),[18] few have

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compared QoL across disorders. Of the few that did, Pirkola et al[21] found the least severe scores on several health-related measures to be associated with pure alcohol use disorder, followed by pure anxiety and depressive disorders, comorbid alcohol use disorder, and comorbid anxiety and depressive disorders. Comparing scores on the EuroQol 5 dimensions questionnaire (EQ-5D) across disorders in the Singapore population, Subramaniam et al[22] found major depressive disorder (MDD) to have the greatest impact on QoL, followed by obsessive compulsive disorder (OCD) and bipolar disorder (BP), after controlling for sociodemographic factors, physical and psychiatric comorbidity. Roberts et al[23] on the other hand, found mental health conditions such as depression, mixed anxiety and depressive disorders, and long-term depression to have the highest decrements in health state utility as measured by SF-6D and EQ-5D indices.

Several factors have been examined in relation to QoL including sociodemographic correlates, psychiatric symptoms, and comorbidity. With regard to sociodemographic factors, unemployment, low socioeconomic status, poor social support, and lower educational attainment have been consistently associated with a poorer QoL.[4,24-25]

Psychopathology—especially anxiety and depressive symptoms—has been associated with lower QoL. Huppert et al[26] found higher scores of anxiety and depression on the Brief Psychiatric Rating Scale (BPRS) to be associated with a lower QoL among schizophrenia patients. In particular, depressive symptoms had a significant negative impact on various indices of subjective QoL including global score, financial and social contacts domains. In contrast, anxiety symptoms had a significant negative impact on the daily activities, family, and health domains of QoL. Similarly, a meta-analysis examining the relationship between positive, negative, and general psychopathology symptoms (e.g., depression and anxiety) and QoL in schizophrenia, found general psychopathology symptoms to consistently emerge as the strongest determinant of poor QoL.[27] A majority of these studies, however, have been conducted among those with schizophrenia and thus, provide limited insight into how these symptoms impact QoL in other disorders.

Psychiatric comorbidity has also been linked to lower QoL.[10,21,26] The European Study of the Epidemiology of Mental Disorders (ESEMeD) study found disability and loss of QoL among non-institutionalised individuals to increase with number of mental disorders.[24] This finding was replicated by Mastoff et al[11] who found a gradual decrease in QoL scores among Dutch psychiatric outpatients as the number of disorders increased, with the highest QoL reported by the general population and the lowest by psychiatric outpatients with comorbidities. Watsons et al,[10] on the other hand, found the addition of 1 comorbid condition to significantly decrease QoL in social anxiety disorder, panic disorder, and BP, and 2 or more comorbidities to decrease QoL in unipolar mood disorder, eating disorder, and generalised anxiety disorder. The presence of a comorbid depressive and anxiety condition had a significant negative impact on QoL across all diagnostic groups.

Overall, the majority of the extant literature has examined QoL in relation to a particular disorder rather than comparing it across disorders. While this provides some understanding of the burden associated with individual disorders and their impact on individuals' QoL, it precludes comparisons across disorders. The current study sought to address this limitation by comparing QoL across disorders and to explore its association with sociodemographic correlates, anxiety and depressive symptoms, and comorbidity in a multiethnic psychiatric outpatient population in Singapore.

## Materials and Methods

### *Sample*

Data for the current study was obtained from a larger survey examining the prevalence of hoarding symptoms among outpatients (n = 500) recruited between May 2014 and April 2015 from the Institute of Mental Health (IMH), a tertiary psychiatric hospital in Singapore, and its satellite clinics. Participants were eligible for the study if they were at least 21 years old, had a primary DSM-IV (Diagnostic and Statistical Manual of Mental Disorders, 4th Edition) diagnosis of any anxiety disorders (including OCD), depressive disorders, schizophrenia, or pathological gambling, were conversant in English, and capable of providing informed consent. Patients who were cognitively incapable were not included. Primary diagnosis was established clinically by psychiatrists based on DSM-IV criteria and was obtained from patient records. Ethics approval was obtained from the institutional ethics committee (National Healthcare Group, the Domain Specific Review Board). All participants provided informed consent prior to study participation.

### *Measures*

#### Anxiety Symptoms

The Beck Anxiety Inventory (BAI)[28] is a 21-item self-report measure that examines distress associated with anxiety symptoms. Items are rated on a scale of 0 (not bothered at all) to 3 (severely bothered). The BAI has shown high internal consistency, test-retest reliability as well as good concurrent and discriminant validity.[28]

#### Depressive Symptoms

The Beck Depression Inventory-II (BDI-II)[29] is a 21-item self-report measure assessing depressive symptoms. Items are rated from 0 to 3, with higher scores indicating

greater severity. The scale has demonstrated high internal reliability and convergent validity.[30]

Quality of Life

The Quality of Life Enjoyment and Satisfaction Questionnaire-Short Form (Q-LES-Q-SF)[31] is a 16-item scale that assesses enjoyment and satisfaction across various life domains such as physical health, social relationships, and economic status over the past week.[32] Each item is rated on a scale of 1(not at all or never) to 5 (frequently or all the time), with higher scores indicating a higher subjective QoL. A total score is obtained by summing the first 14 items. The last 2 items (i.e., medication and overall life satisfaction) are not included in the total score.[31]

*Statistical Analysis*

All statistical analyses were performed using SPSS version 21.0. BAI and BDI-II scores were obtained by adding up the 21 items in each scale. Q-LES-Q-SF raw total score was transformed into a percentage maximum possible score.[32]

One-way ANOVA was used to examine the differences of BAI, BDI-II and Q-LES-Q-SF across diagnostic groups (anxiety disorders, depressive disorders, schizophrenia, pathological gambling). Bonferroni correction was applied in the posthoc comparisons to reduce the risk of Type I error.

To examine the unique variance of each independent variable (IV), associations between sociodemographic variables, diagnostic groups, type and number of mental-health comorbidities with BAI, BDI-II, Q-LES-Q-SF were examined using multiple linear regressions. Sociodemographic variables including age, gender, ethnicity, education level, marital status, employment status were used to predict BAI, BDI-II and Q-LES-Q-SF, using "enter" method (first block of regression analysis). Subsequently, diagnostic groups were entered as an independent variable in the second block of regression analysis. Type of mental-health comorbidity and number of mental-health comorbidities were entered 1 at a time into the third block of regression analysis. "Enter" method refers to the selection method where all predictors listed/mentioned in the text are included in the regression analyses[33] whereas, block regression analyses is a term used in SPSS to refer to hierarchical regression.[34] In hierarchical regression, IVs are entered in a prespecified manner by the researcher, which is driven by theoretical considerations and is referred to as hierarchical because different number of set of predictors are entered for comparison.[34]

## Results

*Sample Distribution*

Majority of the participants were of Chinese ethnicity, employed, had received at least secondary level education, were never married, and were staying with their immediate family (Table 1). Anxiety disorders, depressive disorders and schizophrenia each constituted approximately 30% of the entire sample, whereas pathological gamblers composed 10% of the sample. The anxiety disorder group had the highest percentage of comorbidity; 15.3% had a secondary anxiety disorder, and 12.9% had a comorbid depressive disorder. The pathological gambling group had the highest percentage of comorbid depressive disorder (18.9%) (Table 2).

Table 1. Sociodemographic Distribution of Sample across Diagnostic Groups

| | All Sample (n = 500) | | Anxiety Disorders (n = 144, 28.8%) | | Depressive Disorders (n = 153, 30.6%) | | Schizophrenia (n = 150, 30%) | | Pathological Gambling (n = 53, 10.6%) | |
|---|---|---|---|---|---|---|---|---|---|---|
| | n | % | n | % | n | % | n | % | n | % |
| Age | | | | | | | | | | |
| Mean | 35.3 | | 33.1 | | 34.8 | | 37.5 | | 36.7 | |
| SD | 10.1 | | 9.66 | | 10.4 | | 9.6 | | 10.4 | |
| Age group | | | | | | | | | | |
| 21 – 30 | 183 | 36.6 | 64 | 44.4 | 62 | 40.5 | 40 | 26.7 | 17 | 32.1 |
| 31– 40 | 177 | 35.4 | 51 | 35.4 | 45 | 29.4 | 63 | 42.0 | 18 | 34.0 |
| 41– 50 | 95 | 19.0 | 21 | 14.6 | 35 | 22.9 | 27 | 18.0 | 12 | 22.6 |
| Older than 50 | 45 | 9.0 | 8 | 5.6 | 11 | 7.2 | 20 | 13.3 | 6 | 11.3 |
| Gender | | | | | | | | | | |
| Male | 282 | 56.4 | 88 | 61.1 | 62 | 40.5 | 81 | 54.0 | 51 | 96.2 |
| Female | 218 | 43.6 | 56 | 38.9 | 91 | 59.5 | 69 | 46.0 | 2 | 3.8 |

*Housing and Development Board (HDB) flats are a type of public housing managed by the HDB, a statutory board of the Singapore government. The majority of Singapore residents stay in HDB flats, which range in size from 1 to 5 rooms.

†Nursing homes are a type of housing where stay-in-care is provided to psychiatric patients with milder clinical symptoms.

Table 1. Sociodemographic Distribution of Sample across Diagnostic Groups (Cont'd)

| | All Sample (n = 500) | | Anxiety Disorders (n = 144, 28.8%) | | Depressive Disorders (n = 153, 30.6%) | | Schizophrenia (n = 150, 30%) | | Pathological Gambling (n = 53, 10.6%) | |
|---|---|---|---|---|---|---|---|---|---|---|
| | n | % | n | % | n | % | n | % | n | % |
| Ethnicity group | | | | | | | | | | |
| Chinese | 351 | 70.2 | 106 | 73.6 | 102 | 66.7 | 98 | 65.3 | 45 | 84.9 |
| Malay | 50 | 10.0 | 15 | 10.4 | 17 | 11.1 | 18 | 12.0 | 0 | 0 |
| Indian | 67 | 13.4 | 15 | 10.4 | 17 | 11.1 | 29 | 19.3 | 6 | 11.3 |
| Others | 32 | 6.4 | 8 | 5.6 | 17 | 11.1 | 5 | 3.3 | 2 | 3.8 |
| Education level | | | | | | | | | | |
| No formal/primary | 23 | 4.6 | 3 | 2.1 | 9 | 5.9 | 11 | 7.3 | 0 | 0 |
| Secondary/O-level | 147 | 29.4 | 23 | 16.0 | 39 | 25.5 | 65 | 43.3 | 20 | 37.7 |
| A-level | 40 | 8.0 | 11 | 7.6 | 11 | 7.2 | 17 | 11.3 | 1 | 1.9 |
| Polytechnic/diploma | 196 | 39.2 | 79 | 54.9 | 56 | 36.6 | 39 | 26.0 | 22 | 41.5 |
| University | 94 | 18.8 | 28 | 19.4 | 38 | 24.8 | 18 | 12.0 | 10 | 18.9 |
| Marital status | | | | | | | | | | |
| Never married | 309 | 61.9 | 93 | 64.6 | 78 | 51.0 | 116 | 77.3 | 22 | 42.3 |
| Currently married | 132 | 26.5 | 42 | 29.2 | 41 | 26.8 | 24 | 16.0 | 25 | 48.1 |
| Divorced/separated | 51 | 10.2 | 9 | 6.3 | 29 | 19.0 | 8 | 5.3 | 5 | 9.6 |
| Widowed | 7 | 1.4 | 0 | 0 | 5 | 3.3 | 2 | 1.3 | 0 | 0 |
| Employment status | | | | | | | | | | |
| Employed | 281 | 56.8 | 80 | 56.3 | 77 | 50.7 | 79 | 53.4 | 45 | 84.9 |
| Economically inactive | 83 | 16.8 | 34 | 23.9 | 32 | 21.1 | 13 | 8.8 | 4 | 7.5 |
| Unemployed | 131 | 26.5 | 28 | 19.7 | 43 | 28.3 | 56 | 37.8 | 4 | 7.5 |
| Living arrangement | | | | | | | | | | |
| Staying alone | 43 | 8.7 | 5 | 3.5 | 17 | 11.1 | 15 | 10.1 | 6 | 11.3 |
| Roommate(s) | 37 | 7.4 | 8 | 5.6 | 7 | 4.6 | 21 | 14.2 | 1 | 1.9 |
| Spouse/non-married partner | 43 | 8.7 | 13 | 9.1 | 15 | 9.8 | 5 | 3.4 | 10 | 18.9 |
| Extended family | 26 | 5.2 | 8 | 5.6 | 8 | 5.2 | 8 | 5.4 | 2 | 3.8 |
| Immediate family | 344 | 69.2 | 107 | 74.8 | 105 | 68.6 | 99 | 66.9 | 33 | 62.3 |
| Resident type | | | | | | | | | | |
| Bungalow/terrace | 15 | 3.0 | 3 | 2.1 | 7 | 4.6 | 3 | 2.0 | 2 | 3.8 |
| Private condo/flat | 35 | 7.1 | 12 | 8.5 | 15 | 9.9 | 4 | 2.7 | 4 | 7.7 |
| HDB* | 433 | 87.7 | 127 | 89.4 | 129 | 85.4 | 131 | 87.9 | 46 | 88.5 |
| Nursing home† | 11 | 2.2 | 0 | 0 | 0 | 0 | 11 | 7.4 | 0 | 0 |

*Housing and Development Board (HDB) flats are a type of public housing managed by the HDB, a statutory board of the Singapore government. The majority of Singapore residents stay in HDB flats, which range in size from 1 to 5 rooms.

†Nursing homes are a type of housing where stay-in-care is provided to psychiatric patients with milder clinical symptoms.

*One-way ANOVA*

BAI (F [3,379] =10.94, $P$ <0.001), BDI-II (F [3,441] = 20.1, $P$ <0.001) mean scores and Q-LESQ-SF percentage maximum score (F [3, 430] = 9.45, $P$ <0.001) significantly differed across diagnostic groups.

Table 3 shows posthoc comparisons with Bonferroni correction across diagnostic groups. Depressive disorder group had the highest BAI rating; this was significantly higher than the schizophrenia ($P$ <0.001) and pathological gambling groups ($P$ <0.001), but was not significantly different from the anxiety disorder group ($P$ = 1.00). In addition, the depressive disorder group had the highest BDI-II ratings, and the lowest Q-LES-Q-SF score compared to the other 3 groups.

Pathological gambling group reported considerably higher level of depressive symptoms than the schizophrenia group (but comparable to the anxiety disorder group). This may partly be due to the high percentage of comorbid depressive disorders in the pathological gambling group. Despite the higher level of depressive symptoms endorsed, the pathological gambling group did not endorse low QoL.

Table 2. Types and Number of Comorbid Mental Disorders across Diagnostic Groups

| | Type of Comorbidity | | | | | | | | Number of Comorbidities | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | Anxiety Disorder | | Depressive Disorder | | Personality Disorder | | Adjustment Disorder | | 1 Comorbidity | | 2 or More Comorbidities | |
| | n | (%) | n | (%) | n | (%) | n | (%) | n | (%) | n | (%) |
| Anxiety disorders | 22 | 15.3 | 39 | 16.1 | 2 | 1.4 | 1 | 0.7 | 52 | 36.1 | 8 | 5.6 |
| Depressive disorders | 13 | 12.9 | 0 | 0 | 10 | 6.5 | 1 | 0.7 | 26 | 32.1 | 1 | 3.7 |
| Schizophrenia | 5 | 12.6 | 7 | 4.7 | 1 | 0.7 | 0 | 0 | 10 | 6.7 | 2 | 1.3 |
| Pathological gambling | 2 | 4.5 | 10 | 18.9 | 0 | 0 | 5 | 9.4 | 17 | 11.1 | 1 | 1.3 |

Table 3. Posthoc Comparisons with Bonferroni Correction on Beck Anxiety Inventory, Beck Depression Inventory-II, Q-LES-Q-SF across Diagnostic Groups

| | | BAI | | | BDI-II | | | Q-LES-Q-SF | | |
|---|---|---|---|---|---|---|---|---|---|---|
| | | Δ Mean | SE | *P* Value | Δ Mean | SE | *P* Value | Δ Mean | SE | *P* Value |
| Anxiety disorders | Depressive disorders | -1.18 | 1.54 | 1 | -8.19* | 1.60 | <0.001 | 7.98* | 2.21 | 0.002 |
| | Schizophrenia | 5.74* | 1.54 | <0.001 | 3.74 | 1.62 | 0.13 | -2.84 | 2.21 | 1 |
| | Pathological gambling | 7.25* | 2.09 | 0.004 | -2.47 | 2.17 | 1.00 | -1.96 | 2.90 | 1 |
| Depressive disorders | Schizophrenia | 6.92* | 1.52 | <0.001 | 11.93* | 1.58 | <0.001 | -10.81* | 2.18 | <0.001 |
| | Pathological gambling | 8.43* | 2.08 | <0.001 | 5.72* | 2.14 | 0.046 | -9.94* | 2.88 | 0.004 |
| Schizophrenia | Pathological gambling | 1.51 | 2.08 | 1 | -6.21* | 2.15 | 0.02 | 0.87 | 2.88 | 1 |

BAI: Beck Anxiety Inventory; BDI-II: Beck Depression Inventory-II; SE: Standard error; Q-LES-Q-SF: Quality of Life Enjoyment and Satisfaction Questionnaire-Short Form

*$P$ value <0.001.

Overall, the depressive disorder group showed the worst symptomology (highest ratings in BAI, BDI-II) and lowest QoL, whereas the schizophrenia group showed the least symptomology and highest QoL.

*Multiple Linear Regressions*

Unique variances of sociodemographic variables, diagnostic groups, comorbidity types, and number of comorbid conditions are presented in Table 4. All 3 regression analyses—with sociodemographic variables predicting BAI, BDI-II, Q-LES-Q-SF—showed significant R-square value. However, only age and employment status were significantly associated with subjective QoL. Those who were aged 41-50 years ($\beta = 6.72$, $P = 0.012$) reported higher subjective QoL compared to those aged 21-30 years; whereas those who were unemployed ($\beta = -13.70$, $P < 0.01$) reported lower QoL compared to those who were employed.

Adjusting for sociodemographic variables, diagnostic groups were entered in the second block. All 3 regression analyses showed significant R-square value improvement, indicating that diagnostic groups had a significant role in explaining BAI, BDI-II, and Q-LES-Q-SF.

The effect of diagnostic groups on BAI, BDI-II, Q-LES-Q-SF were similar to those found in one-way ANOVA—the schizophrenia group had significantly lower BAI, BDI-II scores, and higher Q-LES-Q-SF scores, whereas the depressive disorder group had significantly higher BDI-II scores and lower Q-LES-Q-SF scores, as compared to the anxiety disorder group.

In the third block, types of comorbidity were first entered. R-square improvements were not significant at $P > 0.05$ in all 3 regression analyses. Subsequently, types of comorbidity were removed and the number of comorbid conditions was entered. Except for BAI, the number of comorbidities did not add significant R-square improvement to the other 2 regression analyses.

## Discussion

Age and employment status emerged as the only sociodemographic correlates which were significantly associated with QoL in the current sample. Those who were younger and unemployed reported a lower subjective QoL. This was in line with Adewuya and Makanjuola[7] and Priebe et al[25] who found unemployment to be associated with lower QoL among schizophrenia patients. One reason for this is that employment not only provides financial remuneration but also represents a "normalising experience" for individuals to integrate into society which in turn, contributes to their self-worth and QoL.

In contrast to Subramaniam et al[22] who found increasing age to be associated with lower QoL in the general population, the current study among psychiatric outpatients found otherwise. Relative to the general population whereby younger age is associated with better well-being

Table 4. Multiple Linear Regressions on BAI, BDI-II and Q-LES-Q-SF

| | BAI | | BDI-II | | Q-LES-Q-SF | |
|---|---|---|---|---|---|---|
| | **β (SE)** | ***P* Value** | **β (SE)** | ***P* Value** | **β (SE)** | ***P* Value** |
| **1st block** | | | | | | |
| Age group | | | | | | |
| 21 – 30 | ref | | ref | | ref | |
| 31 – 40 | -4.03 (1.61) | 0.01 | -4.08 (1.69) | 0.02 | 1.66 (2.22) | 0.46 |
| 41 – 50 | -6.74 (1.90) | <0.001 | -6.69 (2.03) | <0.001 | 6.72 (2.67) | 0.012 |
| Older than 50 | -7.95 (2.45) | <0.001 | -7.47 (2.81) | 0.008 | 6.91 (3.74) | 0.07 |
| Gender | | | | | | |
| Male | ref | | ref | | ref | |
| Female | 1.38 (1.20) | 0.25 | -0.62 (1.29) | 0.63 | 3.07 (1.70) | 0.07 |
| Ethnicity group | | | | | | |
| Chinese | ref | | ref | | ref | |
| Malay | -3.38 (2.08) | 0.10 | -4.42 (2.20) | 0.045 | 2.84 (2.86) | 0.32 |
| Indian | 0.13 (1.80) | 0.94 | 0.55 (1.98) | 0.78 | -1.58 (2.63) | 0.55 |
| Others | 1.87 (2.50) | 0.46 | 1.10 (2.61) | 0.67 | 1.38 (3.49) | 0.69 |
| Education level | | | | | | |
| No formal/primary | ref | | ref | | ref | |
| Secondary/O-level | -5.78 (3.19) | 0.07 | -4.80 (3.13) | 0.13 | 2.18 (4.38) | 0.62 |
| A-level | -6.58 (3.73) | 0.09 | -9.52 (3.72) | 0.01 | 3.50 (5.07) | 0.49 |
| Polytechnic/diploma | -6.13 (3.23) | 0.06 | -7.58 (3.18) | 0.02 | 5.86 (4.41) | 0.18 |
| University | -9.18 (3.35) | 0.006 | -8.34 (3.33) | 0.01 | 3.71 (4.63) | 0.42 |
| Marital status | | | | | | |
| Never married | ref | | ref | | ref | |
| Currently married | 1.75 (1.55) | 0.26 | 2.60 (1.66) | 0.12 | -1.78 (2.21) | 0.42 |
| Divorced/separated | 5.04 (2.14) | 0.02 | 7.36 (2.33) | 0.002 | -5.19 (3.01) | 0.09 |
| Widowed | 7.19 (5.48) | 0.19 | 0.17 (6.2) | 0.98 | -1.96 (10.12) | 0.85 |
| Employment status | | | | | | |
| Employed | ref | | ref | | ref | |
| Economically inactive | -1.13 (1.78) | 0.53 | 2.62 (1.93) | 0.18 | -1.33 (2.56) | 0.61 |
| Unemployed | 6.08 (1.44) | <0.001 | 6.62 (1.54) | <0.001 | -13.70 (2.10) | <0.001 |
| R-square | 0.102 | | 0.111 | | 0.136 | |
| *P* value (for R-square) | <0.001 | | <0.001 | | <0.001 | |
| **2nd block** | | | | | | |
| Diagnostic groups | | | | | | |
| Anxiety disorders | ref | | ref | | ref | |
| Depressive disorders | -0.15 (1.57) | 0.93 | 7.47 (1.59) | <0.001 | -7.86 (2.14) | <0.001 |
| Schizophrenia | -7.70 (1.63) | <0.001 | -5.60 (1.69) | <0.001 | 6.49 (2.25) | 0.004 |
| Pathological gambling | -7.15 (2.15) | <0.001 | 2.39 (2.21) | 0.28 | 2.08 (2.91) | 0.48 |
| R-square | 0.164 | | 0.226 | | 0.216 | |
| ΔR-square | 0.062 | | 0.115 | | 0.079 | |
| *P* value (for ΔR) | <0.001 | | <0.001 | | <0.001 | |
| **3rd block** | | | | | | |
| Comorbidity types | | | | | | |
| Comorbid anxiety disorders | -1.32 (2.10) | 0.53 | -2.83 (2.19) | 0.20 | 4.72 (2.94) | 0.11 |
| Comorbid depressive disorders | 1.53 (1.97) | 0.44 | 3.58 (2.02) | 0.08 | -2.55 (2.68) | 0.34 |

BAI: Beck Anxiety Inventory; BDI-II: Beck Depression Inventory-II; SE: Standard error; Q-LES-Q-SF: Quality of Life Enjoyment and Satisfaction Questionnaire-Short Form

Table 4. Multiple Linear Regressions on BAI, BDI-II and Q-LES-Q-SF (Cont'd)

| | BAI | | BDI-II | | Q-LES-Q-SF | |
|---|---|---|---|---|---|---|
| | β (SE) | *P* Value | β (SE) | *P* Value | β (SE) | *P* Value |
| **3rd block** | | | | | | |
| Comorbidity types | | | | | | |
| Comorbid personality disorder | 4.83 (3.65) | 0.19 | 6.46 (3.62) | 0.08 | -1.71 (5.17) | 0.74 |
| Comorbid adjustment disorder | -4.36 (4.97) | 0.38 | -3.06 (4.93) | 0.54 | 5.98 (6.54) | 0.36 |
| R-square | 0.171 | | 0.241 | | 0.224 | |
| ΔR-square | 0.007 | | 0.015 | | 0.008 | |
| *P* value (for ΔR) | 0.46 | | 0.077 | | 0.362 | |
| Number of comorbidities | | | | | | |
| No comorbidity | ref | | | | | |
| 1 other comorbidity | -0.99 (1.47) | 0.50 | 0.62 (1.51) | 0.68 | -0.196 (2.02) | 0.92 |
| 2 and more comorbidities | 9.64 (3.75) | 0.01 | 4.75 (3.91) | 0.23 | 0.96 (6.03) | 0.87 |
| R-square | 0.178 | | 0.229 | | 0.216 | |
| ΔR-square | 0.014 | | 0.003 | | 0.000 | |
| *P* value (for ΔR) | 0.023 | | 0.463 | | 0.981 | |

BAI: Beck Anxiety Inventory; BDI-II: Beck Depression Inventory-II; SE: Standard error; Q-LES-Q-SF: Quality of Life Enjoyment and Satisfaction Questionnaire-Short Form

and functioning, the early onset of illness might confer substantial burden on younger adults as they may not have sufficient resources or adaptive mechanisms to cope with their illness compared to older individuals, resulting in a lower subjective QoL.[7,35]

Individuals in the depressive disorder group reported the highest anxiety symptoms followed by the anxiety disorder, schizophrenia, and the pathological gambling groups. Depressive symptoms were the highest in the depressive disorder group, followed by pathological gambling, anxiety disorder, and the schizophrenia group. With respect to QoL, the schizophrenia group reported the highest QoL, followed by the pathological gambling, anxiety disorders, and depressive disorders group. The latter finding paralleled those of Goppoldova et al,[36] who in examining subjective QoL across individuals with psychosis, mood, and anxiety disorders noted QoL to be the best among those with psychosis and worst among those with mood disorders. Likewise, Mack et al[37] found those with mood (and somatoform) disorders to have the highest disability levels and strongest loss of QoL compared to externalising disorders (e.g. alcohol use disorder) in a German population.

The tendency for schizophrenia patients to report a higher QoL has been linked to illness-specific mechanisms such as poor insight, minimisation, and denial of own situations, which may result in a distorted appraisal of their illness.[36,38] In line with this, Goppoldova et al[36] found a discrepancy in illness severity ratings, whereby patients with psychosis rated their illness as significantly less severe compared to their psychiatrists' ratings. However, Adewuya and Makanjuola[7] found schizophrenia patients in a Nigerian population to rate their QoL as lower than that reported in previous studies; this anomalous result was attributed to the lack of mental health services in their population. Conversely, the low subjective QoL among those with depressive disorders has been associated with symptoms such as pessimism, decreased motivation and energy levels, which may have caused individuals to perceive their QoL to be worse than it is.[36]

Interestingly, results of the current study indicating lowest QoL among those with mood disorders—particularly depressive disorders and anxiety disorders—has been replicated in samples across other countries. For instance, Roberts et al[23] found depression, mixed anxiety and depressive disorders and long-term depression to be associated with the highest decrements in QoL among the general population in England whereas, Alonso et al[24] found dysthymia, MDD, post-traumatic stress disorder (PTSD), panic disorder, and social phobia to have the strongest impact on QoL after adjusting for gender, age, and mental and/or physical comorbidity. Thus, it is possible that despite cross-cultural differences, there might be some consistency in the QoL decrements in particular disorders.

Though the link between QoL and symptom severity was not directly examined in the current study, the depressive group with the highest anxiety and depressive symptoms also reported the lowest QoL, whereas the schizophrenia group with relatively lower anxiety and depressive symptoms reported the highest QoL. These results were consistent with past studies,[26-27] which found more symptoms of

depression and anxiety to be associated with lower subjective QoL. Tomida et al,[12] for instance, found higher depression and anxiety symptoms on the Positive and Negative Syndrome Scale (PANSS) to have a negative impact on the psychosocial and motivation/energy domains of QoL among Japanese schizophrenia patients. Similarly, Adewuya and Makanjuola[7] found anxiety/depressive symptoms (on the BPRS) to be the most important correlate of poor subjective QoL in Nigerian patients with schizophrenia. Interpretation of results should, however, be made with caution as relative to our study which used distinct measures (BAI, BDI-II) to assess depressive and anxiety symptoms across disorders; the aforementioned studies were conducted predominantly among patients with schizophrenia and used scales specific to the population.

Despite the high prevalence of depressive symptoms among pathological gamblers, these individuals reported higher QoL compared to the anxiety and depressive group. It is possible that pathological gamblers in our study were relatively well functioning given that the majority were employed; thus, accounting for their better QoL. Also, it is likely that other factors besides psychopathology may have a more pivotal role in influencing QoL in this group.[35] The current result, however, was consistent with previous findings, which found the EQ-5D index of pathological gamblers to be significantly lower than that of non-gamblers and non-problem gamblers in Singapore but higher than those with MDD, BP, generalised anxiety disorder (GAD), OCD and alcohol dependence.[20,22]

After controlling for sociodemographic factors, only diagnostic group had a significant effect in explaining BAI, BDI-II, and Q-LES-Q-SF. Type of and number of comorbid conditions did not add significantly in accounting for BDI-II and Q-LES-Q-SF. This was in contrast with past studies, which have shown increasing comorbidity to be associated with substantial reductions in the mental health component of QoL.[37] One reason for this might be the low number of outpatients in our study who had a comorbid condition, which could have reduced the likelihood of detecting a significant effect. It is also worth noting that our results indicate no unique contribution of comorbid conditions to the regression models, after accounting for primary diagnoses. In other words, the putative effect of secondary diagnoses on psychopathology and QoL may be better explained by patients' primary symptoms. Few studies have associated certain disorders—especially depressive disorders—with substantial burden in and of itself, such that comorbid conditions have a negligible effect on QoL.[10] Similarly, Trompenaars et al[16] found comorbidity with mood-related disorders to have an impact on QoL only if the comorbid condition was a personality disorder; comorbidity with Axis I disorders did not have an additional impact on QoL.

*Limitations*

Results from this study, however, should be considered in view of certain limitations. Individuals in the current study were not diagnosed using a structured diagnostic interview. However, given that primary diagnosis was established clinically by psychiatrists based on DSM-IV criteria and was obtained from patient records, the diagnosis obtained is believed to be accurate. QoL in the current study was assessed as an overall composite score. While the overall score is useful in comparing QoL across disorders, it might not be an accurate representation of the impact disorders have on various domains of QoL. For instance, Beard et al[17] found different anxiety disorders to be associated with different domains of health-related quality of life (HR-QoL). PTSD and comorbid OCD were found to predict worse self-reported physical functioning, whereas social phobia, GAD, and comorbid MDD were found to predict worse self-reported mental functioning. Moreover, given that the Q-LESQ-SF assessed QoL over the past 1 week, this might not have been accurate in capturing the impact of a disorder on the QoL of individuals.

While the study examined the effects of anxiety and depressive symptoms, number and type of comorbidity as well as sociodemographic factors in relation to QoL across disorders, it is plausible that other factors not examined in the current study (e.g., social support, chronic physical conditions) might have had a more significant role in influencing QoL. Chong et al,[39] for instance, found HRQoL to be worse in those with both a mental and medical disorder compared to those with either a mental or medical disorder in the Singapore adult population. Lastly, causal interpretations regarding disorders and their effect on QoL cannot be made given the cross-sectional nature of the study.

## Conclusion

The study provides insight into the impact mental illnesses have on QoL. Although the specific domains with regard to QoL were not examined, it provides a comparison of overall QoL across the disorders, such that those with schizophrenia reporting the highest QoL and those with depressive disorders the lowest. In particular, the consistent finding of lower QoL among those with depressive and anxiety disorders across various countries is interesting. However, the lack of significance with regard to the impact of comorbidity on overall QoL was surprising given results from past studies suggesting otherwise. Hence, while current study results offer useful information in terms of the burden and impairment associated with the various disorders, examining the impact across different QoL domains would further allow healthcare professionals to make informed decisions in terms of targeting specific domains to improve QoL among care recipients.

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REFERENCES

1. WHOQOL Group. The World Health Organization Quality of Life Assessment (WHOQOL): position paper from the World Health Organization. Soc Sci Med 1995; 10:1403-9.
2. Xiang YT, Weng YZ, Leung CM, Tang WK, Ungvari GS. Quality of life of Chinese schizophrenia outpatients in Hong Kong: relationship to sociodemographic factors and symptomatology. Aust N Z J Psychiatry 2007;41:442-9.
3. Schmitz N, Kruse J, Kugler J. The association between physical exercises and health-related quality of life in subjects with mental disorders: results from a cross-sectional survey. Prev Med 2004;39:1200-7.
4. Cichocki Ł, Cechnicki A, Franczyk-Glita J, Błądziński P, Kalisz A, Wroński K. Quality of life in a 20-year follow-up study of people suffering from schizophrenia. Compr Psychiatry 2015;56:133-40.
5. Adelufosi AO, Ogunwale A, Abayomi O, Mosanya JT. Socio-demographic and clinical correlates of subjective quality of life among Nigerian outpatients with schizophrenia. Psychiatry Res 2013;209:320-5.
6. Dan A, Kumar S, Avasthi A, Grover S. A comparative study on quality of life of patients of schizophrenia with and without depression. Psychiatry Res 2011;189:185-9.
7. Adewuya AO, Makanjuola ROA. Subjective quality of life of Nigerian schizophrenia patients: sociodemographic and clinical correlates. Acta Psychiatr Scand 2009;120:160-4.
8. Vatne S, Bjørkly S. Empirical evidence for using subjective quality of life as an outcome variable in clinical studies: a meta-analysis of correlates and predictors in persons with a major mental disorder living in the community. Clin Psychol Rev 2008;28:869-89.
9. Barnes AL, Murphy ME, Fowler CA, Rempfer MV. Health-related quality of life and overall life satisfaction in people with serious mental illness. Schizophr Res Treatment 2012;2012:245103.
10. Watson HJ, Swan A, Nathan PR. Psychiatric diagnosis and quality of life: the additional burden of psychiatric comorbidity. Compr Psychiatry 2011;52: 265-72.
11. Masthoff ED, Trompenaars FJ, Van Heck GL, Hodiamont PP, De Vries J. Quality of life and psychopathology: investigations into their relationship. Aust N Z J Psychiatry 2006;40:333-40.
12. Tomida K, Takahashi N, Saito S, Maeno N, Iwamoto K, Yoshida K, et al. Relationship of psychopathological symptoms and cognitive function to subjective quality of life in patients with chronic schizophrenia. Psychiatry Clin Neurosci 2010;64:62-9.
13. Fried EI, Nesse RM. The impact of individual depressive symptoms on impairment of psychosocial functioning. PloS One 2014;9:e90311.
14. Årdal G, Lund A, Hammar Å. Health-related quality of life in recurrent major depressive disorder-A 10-year follow-up study. Nord J Psychiatry 2013;67:339-43.
15. Hope ML, Page AC, Hooke GR. The value of adding the Quality of Life Enjoyment and Satisfaction Questionnaire to outcome assessments of psychiatric inpatients with mood and affective disorders. Qual Life Res 2009;18:647-55.
16. Trompenaars FJ, Masthoff ED, Van Heck GL, Hodiamont PP, De Vries J. Relationship between mood related disorders and quality of life in a population of Dutch adult psychiatric outpatients. Depress Anxiety 2006;23: 353-63.
17. Beard C, Weisberg RB, Keller MB. Health-related quality of life across the anxiety disorders: findings from a sample of primary care patients. J Anxiety Disord 2010;24: 559-64.
18. Olatunji BO, Cisler JM, Tolin DF. Quality of life in the anxiety disorders: a meta-analytic review. Clin Psychol Rev 2007;27:572-81.
19. Subramaniam M, Abdin E, Shijia Q, Winslow M. Quality of life in pathological gamblers in a multiethnic Asian setting. Ann Acad Med Singapore 2011;40:264-8.
20. Subramaniam M, Abdin E, Vaingankar JA, Wong KE, Chong SA. Comorbid physical and mental illnesses among pathological gamblers: results from a population based study in Singapore. Psychiatry Res 2015;227:198-205.
21. Pirkola S, Saarni S, Suvisaari J, Elovainio M, Partonen T, Aalto AM, et al. General health and quality-of-life measures in active, recent, and comorbid mental disorders: a population-based health 2000 study. Compr Psychiatry 2009;50:108-14.
22. Subramaniam M, Abdin E, Vaingankar JA, Nan L, Heng D, McCrone P, et al. Impact of psychiatric disorders and chronic physical conditions on health-related quality of life: Singapore Mental Health Study. J Affect Disord 2013;147:325-30.
23. Roberts J, Lenton P, Keetharuth AD, Brazier J. Quality of life impact of mental health conditions in England: results from the adult psychiatric morbidity surveys. Health Qual Life Outcomes 2014;12:6.
24. Alonso J, Angermeyer MC, Bernert S, Bruffaerts R, Brugha TS, Bryson H, et al. Disability and quality of life impact of mental disorders in Europe: results from the European Study of the Epidemiology of Mental Disorders (ESEMeD) project. Acta Psychiatr Scand 2004;109:38-46.
25. Priebe S, Reininghaus U, McCabe R, Burns T, Eklund M, Hansson L, et al. Factors influencing subjective quality of life in patients with schizophrenia and other mental disorders: a pooled analysis. Schizophr Res 2010;121:251-8.
26. Huppert JD, Weiss KA, Lim R, Pratt S, Smith TE. Quality of life in schizophrenia: contributions of anxiety and depression. Schizophr Res 2001;51:171-80.
27. Eack SM, Newhill CE. Psychiatric symptoms and quality of life in schizophrenia: a meta-analysis. Schizophr Bull 2007;33:1225-37.
28. Beck AT, Epstein N, Brown G, Steer RA. An inventory for measuring clinical anxiety: Psychometric properties. J Consult Clin Psychol 1988;56:893-97.
29. Beck AT, Steer RA, Brown GK. Manual for the Beck Depression Inventory-II. 2nd ed. San Antonio, TX: Psychological Corporation; 1996.
30. Dozois DJA, Dobson KS, Ahnberg JL. A psychometric evaluation of the Beck Depression Inventory–II. Psychol Assess 1998;10:83-9.
31. Lee YT, Liu SI, Huang HC, Sun FJ, Huang CR, Yeung A. Validity and reliability of the Chinese version of the short form of Quality of Life Enjoyment and Satisfaction Questionnaire (Q-LES-Q-SF). Qual Life Res 2014;23:907-16.
32. Endicott J, Nee J, Harrison W, Blumenthal R. Quality of life enjoyment and satisfaction questionnaire. Psychopharmacol Bull 1993;29:321-6.
33. Landau S, Brian SE. A Handbook of Statistical Analyses Using SPSS. CRC Press LLC; 2004.
34. Gaur AS, Gaur SS. (2006). Statistical Methods for Practice and Research: A Guide to Data Analysis Using SPSS. Sage; 2006.

35. Ruggeri M, Gater R, Bisoffi G, Barbui C, Tansella M. Determinants of subjective quality of life in patients attending community-based mental health services. The South-Verona Outcome Project 5. Acta Psychiatr Scand 2002;105:131-40.
36. Goppoldova E, Dragomirecka E, Motlova L, Hajek T. Subjective quality of life in psychiatric patients: diagnosis and illness-specific profiles. Can J Psychiatry 2008;53:587-93.
37. Mack S, Jacobi F, Beesdo-Baum K, Gerschler A, Strehle J, Höfler M, et al. Functional disability and quality of life decrements in mental disorders: results from the Mental Health Module of the German Health Interview and Examination Survey for Adults (DEGS1-MH). Eur Psychiatry 2015;30:793-800.
38. Hasson-Ohayon I, Kravetz S, Roe D, David AS, Weiser M. Insight into psychosis and quality of life. Compr Psychiatry 2006;47:265-9.
39. Chong SA, Abdin E, Nan L, Vaingankar JA, Subramaniam M. Prevalence and impact of mental and physical comorbidity in the adult Singapore population. Ann Acad Med Singapore 2012;41:105-14.

Original Article

# The Prevalence and Severity of Myopia among Suburban Schoolchildren in Taiwan

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## Abstract

**Introduction: We aimed to determine the prevalence and severity of myopia in suburban schoolchildren. The refractive error, best corrected visual acuity (BCVA) and other ocular indices of 6069 schoolchildren (aged 6 to 15 years) from elementary and junior high schools in Chiayi County, Taiwan were examined in 2013-2015. Materials and Methods: Spherical equivalent (SE) was stratified into 4 categories: emmetropia, mild myopia, moderate myopia, and high myopia for underlying analysis. Chi-squared ($\chi^2$) tests were used to determine significant associations between myopia and BCVA and age levels. To compare statistical significance among different age levels, *P* values of Bonferroni tests were calculated. Receiver operating characteristic (ROC) curves and correlation coefficient were calculated to assess the correlation between myopia and each ocular index. Results: The youngest subject diagnosed with myopia was a 7-year-old. Myopia had significant associations with both BCVA and age levels (95% confidence intervals [CI] = 2.553, 2.713 and -0.284, -0.248, respectively), under *P* <0.05. Among the calculated ROC values, BCVA had the highest area of 0.676 with myopia. This further confirmed that BCVA was highly correlated with myopia in schoolchildren. Other ocular indices like intraocular pressure (IOP), pupil distance, ocular alignments, or ocular height had ROC curves below 0.5 to myopia. Conclusion: This study concluded that the onset of myopia started earlier and progressively worsened with years of investigation among the suburban schoolchildren. Myopia had significant associations with BCVA and age levels. To effectively reduce the prevalence and severity of myopia, it is time to take actions on eye care education for suburban schoolchildren.**


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**Key words: Mean refractive index, Ocular condition, Visual acuity**

## Introduction

The prevalence and severity of myopia has been studied in 5 large-scale, population-based, and cross-sectional surveys of schoolchildren aged 7 to 18 years old.[1,2,3] Researchers found that the increase in prevalence of myopia among schoolchildren was caused by the onset at an early age, and then the severity was alleviated progressively with age. In Asia, the prevalence of myopia is still high, especially among the Chinese[3-5] and the Japanese.[6,7] In 1944, Motegi et al did a survey on ocular refraction in Taiwan and revealed that over 80% of the studied population were emmetropic.[8-11] In 1982, Chung et al studied 227 aboriginal students, aged 6 to 13 years old and residents in mountainous areas of Pingtung County, Taiwan, and found 59.3% with hypermetropia, 38.3% with emmetropia, and 2.4% with myopia.[12] In a study conducted by Chen et al in the mountainous areas of Hwalian County in 1984, 366 elementary schoolchildren were examined, of whom 295 (80.6%) were aboriginal.[13] They found that 9.73% of non-aboriginal students and 3.06% of aboriginal students had myopia.

On 15 May 2014, Taipei Times reported that myopia had become a serious health problem for elementary school students, especially for more than 35% of second grade students in Taipei. A myopia prevention programme

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organised by the Taipei City government said that 35.63% of second grade students had myopia and their parents were unaware of it. Furthermore, 3.18% of the second grade students suffered from 300 degrees or above of myopia. Taipei Veterans General Hospital reported that children with myopia in early childhood presented the most prevalent medical condition in the nation. Children with myopia at a younger age may develop myopia to 600 degrees or higher by the time they are in high school or reach adulthood.[14] Myopic children were highly recommended to avoid spending long periods of time in reading at a short distance and to reduce excessive use of computers and electronic devices. They are encouraged to participate in more outdoor activities. If they have to use electronic devices, they need to take at least 10 minutes break for every 30 minutes of usage.[14] On 12 March 2015, Kastner reported in The Diplomat that as Taiwanese children were pushed by academic institutions and parents to study for viciously long hours, 18% of first graders, 52% of sixth graders and 80% of university students on the island were myopic in early 2014.[15] He also reported that the average degree of the eye's degeneration was much higher than that of schoolchildren residing in countries of the Western hemisphere. Kung, former deputy director of the Taiwanese government's Health Promotion Centre, said that most Taiwanese parents have full-time jobs that prompt their children to spend not only weekday evenings at cram schools but also during the weekends.[14]

Looking at the changing trends of myopia over the past 2 decades in Taiwan, the survey at various elementary and junior high schools in Chiayi County, Taiwan on ocular refraction levels among schoolchildren is investigated in this study. To facilitate appropriate comparisons of the relative prevalence of myopia, we compared our study with nationwide myopia prevalence surveys previously conducted in Taiwan by Lin et al in the years 1983, 1986, 1999, 1995 and 2000.[2,16-19]

## Materials and Methods

From September 2013 to May 2015, 6069 participants aged 6 to 15 years old were enrolled from numerous elementary and junior high schools in Chiayi County, Taiwan. Written informed consent was obtained from all parents or guardians. The Institutional Review Board of the Chang Gung Foundation (IRB-102-4827B) had approved this study. The research was conducted according to the principles of the Declaration of Helsinki. A detailed personal history, general paediatric health examination, ophthalmological assessment, and lifestyle questionnaire were conducted for all participants. Hospital and school authorities scheduled dates for the examinations. All data were collected from temporary setup clinical environments in each school where various examinations for different ocular indices were conducted by Dr Lai, co-author of this paper, her assistants and some clinical staff from the Chang Gung Memorial Hospital.

In this study, spherical equivalent (SE) was stratified into 4 categories: emmetropia (SE = 0D), mild myopia (-3D <SE <0D), moderate myopia (-6D <SE = -3D), and high myopia (SE = -6D).[20] We measured best corrected visual acuity (BCVA) in decimal values by using the instrument Topcon kr-800/rm800 (Topcon Corporation, Japan), and IOP by using Tonopachy NT-530P (Nidek, Gamagori, Japan). We conducted various examinations on students regarding their right and left eye vision, pupil distance (PD), medications usage, glasses condition, height, and weight. Intraocular pressure (IOP) values ranged from 2 mmHg to 55 mmHg for the right eyes and 1 mmHg to 40 mmHg for the left eyes. PD values ranged from 11 cm to 99 cm. The values of visual acuity ranged from -0.3 to 1.3 (LogMAR) for both eyes.

### *Data Analysis*

All data were analysed using IBM SPSS version 21.0 (IBM, Armonk, New York). Chi-squared ($\chi^2$) test and linear regression models were used to calculate statistically significant differences among data. The Bonferroni multiple comparisons in analysis of variance (ANOVA) were used to cross compare different age categories. Bonferroni was used to reduce the chance of obtaining false-positive results. Receiver operating characteristic (ROC) analysis was applied to determine the sensitivity and specificity of different ocular indices to myopia.

## Results

Table 1 shows the age distribution of students from 5 separate surveys[1] in 1983-2000 and our study in 2013-2015. The 5 surveys were conducted by the Department of Epidemiology, National Taiwan University while our study in 2013-2015 was conducted by the Department of Ophthalmology, Chang Gung Memorial Hospital, Chiayi County. Table 1 also shows the distribution of mean refractive index (D) corresponding to each age group from those 5 surveys and from our study. The past surveys indicated that mean refractive index drifted toward myopia at the age of 11 in 1983 and progressively started at a younger age of 9 in 1995 and 8 in 2000. Our study in 2013-2015 showed that the mean refractive index started at the early age of 7 and progressively increased year after year. This study revealed that the initial age of myopia started earlier than the previous study. This confirmed the prevalence and severity of myopia among suburban schoolchildren.

Table 2 shows the mean refractive index studied by Lin et al in 2004 for schoolchildren aged 7 to 18 years old with respect to the 10 development levels of urbanisation.[1] For

Table 1. Distribution of Age and Mean Refractive Index (D) from 5 Surveys and Our Study

| Age (Years) | 1983 | 1986 | 1990 | 1995 | 2000 | 2013 – 2015 |
|---|---|---|---|---|---|---|
| 6 | - | | - | - | - | 79 (1.30%)<br>0.19 (± 0.95) |
| 7 | 260 (6.30%)<br>0.52 (± 0.98) | 737 (7.02%)<br>0.66 (± 1.01) | 774 (8.93%)<br>0.52 (± 0.97) | 996 (8.91%)<br>0.52 (± 1.01) | 924 (8.24%)<br>0.17 (± 1.00) | 621 (10.23%)<br>-0.22 (± 1.04) |
| 8 | 265 (6.42%)<br>0.45 (± 1.03) | 774 (7.37%)<br>0.50 (± 1.10) | 792 (9.14%)<br>0.38 (± 1.04) | 920(8.23%)<br>0.18 (± 1.31) | 915 (8.41%)<br>-0.15 (± 1.40) | 730 (12.03%)<br>-0.62 (± 1.50) |
| 9 | 263 (6.38%)<br>0.08 (± 1.11) | 752 (7.16%)<br>0.33 (± 1.23) | 713 (8.23%)<br>0.04 (± 1.25) | 910 (8.14%)<br>-0.15 (± 1.38) | 890 (8.18%)<br>-0.59 (± 1.37) | 737 (12.14%)<br>-0.92 (± 1.42) |
| 10 | 268 (6.50%)<br>-0.07 (± 1.57) | 767 (7.30%)<br>0.06 (± 1.56) | 785 (9.06%)<br>-0.08 (± 1.54) | 1023 (9.15%)<br>-0.37 (± 1.74) | 945 (8.69%)<br>-0.77 (± 1.81) | 870 (14.34%)<br>-1.11 (± 1.53) |
| 11 | 263 (6.38%)<br>-0.27 (± 1.72) | 751 (7.15%)<br>-0.15 (± 1.70) | 765 (8.83%)<br>-0.33 (± 1.68) | 1017 (9.10%)<br>-0.72 (± 1.81) | 944 (8.68%)<br>-1.20 (± 1.93) | 979 (16.13%)<br>-1.39 (± 1.78) |
| 12 | 266 (6.45%)<br>-0.48 (± 1.83) | 750 (7.14%)<br>-0.30 (± 1.81) | 613 (7.07%)<br>-0.58 (± 1.83) | 1082 (9.68%)<br>-1.04 (± 1.95) | 920 (8.46%)<br>-1.45 (± 2.21) | 887 (14.62%)<br>-1.77 (± 1.86) |
| 13 | 265 (6.42%)<br>-0.68 (± 1.90) | 813 (7.74%)<br>-0.75 (± 1.93) | 648 (7.48%)<br>-0.94 (± 1.96) | 1016 (9.09%)<br>-1.45 (± 2.20) | 969 (8.91%)<br>-2.11 (± 2.35) | 369 (6.08%)<br>-1.89 (± 1.80) |
| 14 | 264 (6.40%)<br>-1.25 (± 1.98) | 788 (7.50%)<br>-1.29 (± 2.21) | 677 (7.81%)<br>-1.53 (± 2.18) | 1000 (8.95%)<br>-1.73 (± 2.31) | 960 (8.83%)<br>-2.44 (± 2.64) | 403 (6.64%)<br>-2.12 (± 2.01) |
| 15 | 257 (6.23%)<br>-1.49 (± 2.20) | 775 (7.38%)<br>-1.50 (± 2.36) | 648 (7.48%)<br>-1.84 (± 2.35) | 1001 (8.96%)<br>-2.27 (± 2.55) | 937 (8.61%)<br>-2.89 (± 2.70) | 394 (6.49%)<br>-2.31 (± 2.03) |
| 16 | 576 (13.96%)<br>-2.11 (± 2.35) | 1285 (12.24%)<br>-2.16 (± 2.55) | 760 (8.77%)<br>-2.25 (± 2.56) | 816 (7.30%)<br>-2.94 (± 2.64) | 816 (7.30%)<br>-2.94 (± 2.64) | - |
| 17 | 604 (14.64%)<br>-2.22 (± 2.39) | 1255 (11.95%)<br>-2.40 (± 2.57) | 826 (9.53%)<br>-2.64 (± 2.66) | 745 (6.67%)<br>-3.07 (± 2.70) | 745 (6.67%)<br>-3.07 (± 2.70) | - |
| 18 | 574 (13.92%)<br>-2.55 (± 2.55) | 1053 (10.03%)<br>-2.68 (± 2.62) | 666 (7.69%)<br>-2.93 (± 2.71) | 649 (5.81%)<br>-3.32 (± 2.75) | 649 (5.81%)<br>-3.32 (± 2.75) | - |
| Total | 4125 | 10,500 | 8667 | 11,175 | 10,878 | 6069 |

Table 2. Mean Refractive Index (D) of Schoolchildren in Different Areas in 1995 and 2000, and in Chiayi in 2013-2015 (Right Eyes Only)

| | Boys | | | | Girls | | | |
|---|---|---|---|---|---|---|---|---|
| | Elementary School | | Junior High School | | Elementary School | | Junior High School | |
| | 1995 | 2000 | 1995 | 2000 | 1995 | 2000 | 1995 | 2000 |
| Taipei | -0.58 | -0.88 | -2.04 | -2.48 | -0.87 | -1.03 | -2.70 | -3.12 |
| Kaohsiung | -0.60 | -0.66 | -2.26 | -2.92 | -0.53 | -0.92 | -2.43 | -2.81 |
| Provincial cities | -0.14 | -0.76 | -1.82 | -2.83 | -0.39 | -0.85 | -2.60 | -3.23 |
| Developing area | -0.02 | -0.52 | -1.14 | -2.44 | -0.04 | -0.62 | -1.53 | -2.53 |
| Industrial area | -0.40 | -0.64 | -1.72 | -2.13 | -0.57 | -0.76 | -2.01 | -2.29 |
| Service business area | -0.42 | -0.59 | -1.66 | -1.75 | -0.61 | -0.74 | -2.22 | -2.30 |
| Combination area | 0.1 | -0.30 | -1.72 | -1.65 | 0.1 | -0.48 | -1.84 | -2.16 |
| Remote area | -0.01 | 0.09 | -1.24 | -1.83 | -0.12 | -0.47 | -1.58 | -2.28 |
| Hilly area | 0.19 | -0.75 | -0.40 | -1.11 | 0.17 | -0.38 | -1.23 | -2.31 |
| Aboriginal area | 0.16 | 0.02 | -0.30 | -0.22 | 0.12 | -0.41 | -0.69 | -1.36 |
| Chiayi | -1.10 | | -2.10 | | -1.01 | | -2.13 | |

comparison, the same table also showed the mean refractive index obtained in this study. Based on the figures shown in Table 2, we found, in general, that girls had higher mean refractive index (D) than boys and the severity worsened with years of investigation. Furthermore, boys in elementary schools of Chiayi County in 2013-2015 had the highest myopia (-1.10D). Girls in elementary schools of Chiayi County in 2013-2015 also had similar mild myopia in

second place (-1.01D), slightly trailing behind the Taipei area (-1.03D) in 2000. Boys in junior high schools in Chiayi County were in second place (-2.10D), with the first place being the Kaohsiung area (-2.26D) in 1995. Girls in junior high schools of Chiayi County were better than 4 areas (Taipei, Kaohsiung, provincial cities, and service business) in 1995, while they were better than most areas except the aboriginal area in 2000.

Table 3 and Figure 1 show the prevalence of myopia with respect to age group. There were no cases of moderate or high myopia at the age of 6. At age 7, there were only 1.13% with moderate myopia and 0.16% with high myopia. However, the trend for moderate and high myopia continuously climbed to 28.43% and 5.58%, respectively at the age of 15. The trend of mild myopia increased until 12 years old before the participants entered junior high schools. In 2001, Lin et al reported that the mean refractive index reached myopic status at the age of 8 and increased to -3.15D for boys and -4.12D for girls at the age of 18.[2] In our study, we found that the mean refractive index reached myopic status at the age of 6. Among the 6069 subjects, 870 reached moderate (-6D <SE = -3D) and high (SE = -6D) myopia at the age of 7 for boys and at the age of 8 for girls. Refractive index of -4.65D was reached at the age of 15 for both boys and girls (as shown in Table 4). This observation indicates that if we combined students with either moderate or high myopia into a single variable, then there would not have been much difference in mean refractive index (D) between boys and girls in Chiayi County in 2013-2015. Furthermore, the mean refractive index fell in the vicinity of the moderate myopia category.

Bonferroni test is a type of multiple comparison test used in statistical analysis. To compare any statistical significance among the different age levels, the *P* values of Bonferroni tests are shown in Table 5. The results revealed that there

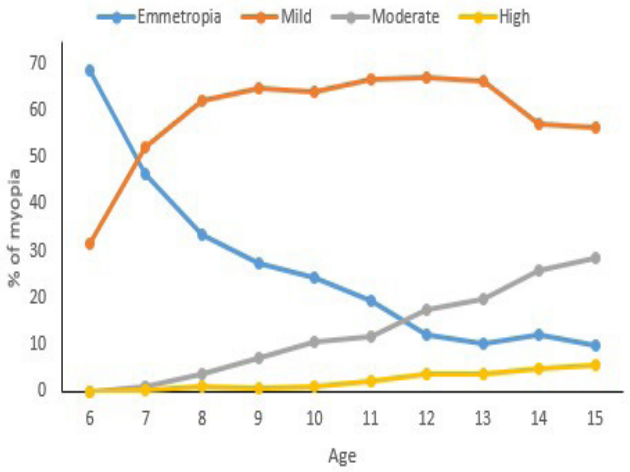


Fig. 1. Distribution of emmetropia, mild, moderate and high myopia with respect to ages.

were significant differences in the Bonferroni tests on mean refractive index when a schoolchild grew 1 or 2 years older. This deterioration was observed for schoolchildren aged 7 to 10 years old. Starting from 11 years old, there was no statistical significance.

Based on the examination data measured from the schoolchildren, we were also interested in analysing if other ocular indices, such as IOP, pupil distance, ocular alignments, or ocular height, affected myopia. ROC curves were calculated to assess the correlation between myopia and each ocular index. The area under the curve (AUC)—an index of discriminant validity—was the primary result of the ROC analyses. An AUC of 0.50 corresponding to test scores of ocular index cannot be discriminated, whereas an AUC of 1.00 indicates a perfect discrimination. Analytical results from ROC curves indicated that AUCs of IOP (0.444), pupil distance (0.418), ocular height (0.361) or ocular alignments (0.189) were smaller than the baseline

Table 3. Prevalence of Myopia in Each Age Group with Different Spherical Equivalent

| Age (Years) | Total No. (6069, %) | Emmetropia (SE ≥0D) (1421, %) | Mild Myopia (-3D <SE <0D) (3778, %) | Moderate Myopia (-6D <SE ≤-3D) (738, %) | High Myopia (SE ≤-6D) (132, %) |
|---|---|---|---|---|---|
| 6 | 79 (1.30) | 54 (68.35) | 25 (31.65) | - | - |
| 7 | 621 (10.23) | 289 (46.54) | 324 (52.17) | 7 (1.13) | 1 (0.16) |
| 8 | 730 (12.03) | 244 (33.42) | 452 (61.92) | 26 (3.56) | 8 (1.10) |
| 9 | 737 (12.14) | 201 (27.27) | 478 (64.86) | 53 (7.19) | 5 (0.68) |
| 10 | 870 (14.34) | 212 (24.37) | 558 (64.14) | 92 (10.57) | 8 (0.92) |
| 11 | 979 (16.13) | 190 (19.41) | 651 (66.50) | 116 (11.85) | 22 (2.25) |
| 12 | 887 (14.62) | 107 (12.06) | 593 (66.85) | 155 (17.47) | 32 (3.61) |
| 13 | 369 (6.08) | 37 (10.03) | 245 (66.40) | 73 (19.78) | 14 (3.79) |
| 14 | 403 (6.64) | 49 (12.16) | 230 (57.07) | 104 (25.81) | 20 (4.96) |
| 15 | 394 (6.49) | 38 (9.64) | 222 (56.35) | 112 (28.43) | 22 (5.58) |

SE: Spherical equivalent

Table 4. Mean Refractive Index (D) for Moderate and High Myopia from 870 Subjects

| Age (Years) | No. (%) | Boys (460) | | | Girls (410) | | |
|---|---|---|---|---|---|---|---|
| | | Moderate and High (460) | Moderate (392) | High (68) | Moderate and High (410) | Moderate (346) | High (64) |
| 7 | 8 (0.92) | -3.42 (8) | -3.29 (7) | -10.30 (1) | - | 0 | 0 |
| 8 | 34 (3.91) | -5.31 (20) | -3.87 (16) | -9.85 (4) | -5.49 (14) | -4.20 (10) | -10.29 (4) |
| 9 | 58 (6.67) | -4.25 (31) | -4.18 (28) | -6.04 (3) | -4.27 (27) | -3.93 (25) | -6.25 (2) |
| 10 | 100 (11.49) | -4.36 (53) | -4.04 (49) | -6.88 (4) | -4.29 (47) | -4.02 (43) | -7.59 (4) |
| 11 | 138 (15.86) | -4.77 (65) | -4.22 (53) | -7.03 (12) | -4.77 (73) | -4.42 (63) | -7.01 (10) |
| 12 | 187 (21.49) | -4.65 (86) | -4.08 (78) | -6.83 (8) | -4.63 (101) | -4.18 (77) | -7.24 (24) |
| 13 | 87 (10.00) | -4.50 (50) | -4.10 (40) | -7.19 (10) | -4.50 (37) | -3.90 (33) | -6.78 (4) |
| 14 | 124 (14.25) | -4.65 (71) | -4.06 (58) | -7.30 (13) | -4.63 (53) | -4.24 (46) | -7.00 (7) |
| 15 | 134 (15.40) | -4.68 (76) | -4.16 (63) | -7.35 (13) | -4.65 (58) | -4.13 (49) | -6.99 (9) |

Table 5. Bonferroni Tests of *P* Values between Ages

| Age (Years) | 6 | 7 | 8 | 9 | 10 | 11 | 12 | 13 | 14 | 15 |
|---|---|---|---|---|---|---|---|---|---|---|
| 6 | | 1 | 1 | 0.634 | 0.598 | 0.001 | <0.001 | <0.001 | <0.001 | <0.001 |
| 7 | 1 | | 1 | <0.001 | <0.001 | <0.001 | <0.001 | <0.001 | <0.001 | <0.001 |
| 8 | 1 | 1 | | 0.028 | 0.017 | <0.001 | <0.001 | <0.001 | <0.001 | <0.001 |
| 9 | 0.634 | <0.001 | 0.028 | | 1 | 0.003 | <0.001 | <0.001 | <0.001 | <0.001 |
| 10 | 0.598 | <0.001 | 0.017 | 1 | | 0.001 | <0.001 | <0.001 | <0.001 | <0.001 |
| 11 | 0.001 | <0.001 | <0.001 | 0.003 | 0.001 | | 0.117 | 1 | 0.046 | 0.002 |
| 12 | <0.001 | <0.001 | <0.001 | <0.001 | <0.001 | 0.117 | | 1 | 1 | 1 |
| 13 | <0.001 | <0.001 | <0.001 | <0.001 | <0.001 | 1 | 1 | | 1 | 0.968 |
| 14 | <0.001 | <0.001 | <0.001 | <0.001 | <0.001 | 0.046 | 1 | 1 | | 1 |
| 15 | <0.001 | <0.001 | <0.001 | <0.001 | <0.001 | 0.002 | 1 | 0.968 | 1 | |

of 0.50, except for BCVA, as shown in Figure 2. These results indicated that their relevance to myopia were less significant compared to BCVA. Among the calculated ROC values, BCVA had the highest AUC of 0.676 with myopia. This confirmed that myopia had effects on BCVA in schoolchildren. BCVA deteriorated with increasing myopia gradually.

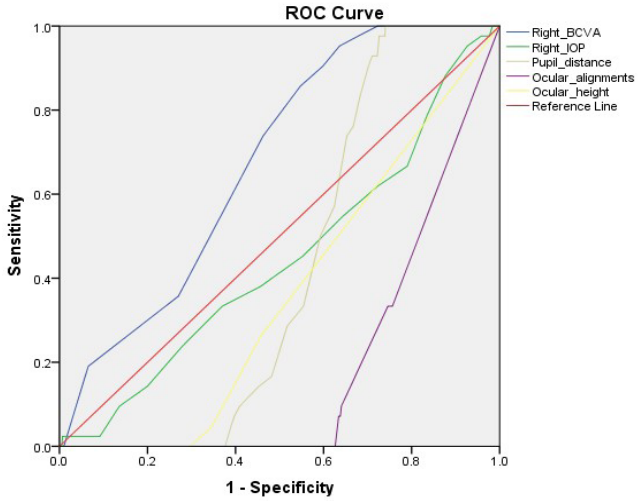


Fig. 2. ROC curves for different ocular conditions of the right eyes.

Furthermore, correlation coefficient was calculated to be 0.637 which indicated a positive correlation between BCVA and myopia. Also, Chi-squared ($\chi^2$) tests were used to determine that myopia had significant associations with BCVA and age levels—both with 95% confidence intervals (CI) 2.553, 2.713 and -0.284, -0.248, respectively, under $P$ <0.05. Table 6 shows the deteriorating BCVA with

Table 6. Effect of BCVA and IOP with Progressive Myopia of the Right Eyes

| Ages (Years) | Myopia | BCVA | IOP |
|---|---|---|---|
| 6 | 0.19 (± 0.95) | 0.96 (± 0.21) | 15.58 (± 4.36) |
| 7 | -0.22 (± 1.04) | 0.95 (± 0.26) | 15.76 (± 4.17) |
| 8 | -0.62 (± 1.50) | 0.91 (± 0.32) | 17.24 (± 4.51) |
| 9 | -0.92 (± 1.42) | 0.83 (± 0.39) | 16.85 (± 4.85) |
| 10 | -1.11 (± 1.53) | 0.83 (± 0.42) | 16.97 (± 4.68) |
| 11 | -1.39 (± 1.78) | 0.75 (± 0.44) | 17.38 (± 4.45) |
| 12 | -1.77 (± 1.86) | 0.69 (± 0.43) | 17.15 (± 4.29) |
| 13 | -1.89 (± 1.80) | 0.72 (± 0.53) | 18.12 (± 4.83) |
| 14 | -2.12 (± 2.01) | 0.67 (± 0.50) | 17.77 (± 5.72) |
| 15 | -2.31 (± 2.03) | 0.65 (± 0.53) | 17.29 (± 4.18) |

BCVA: Best corrected visual acuity; IOP: Intraocular pressure

progressive myopia in ages. At the age of 6, there was no myopia and the BCVA was close to 1 (BCVA = 20/20). Myopia started at the age of 7 and progressed with age, whereas BCVA deteriorated sharply with growing age (from 0.95 at age 7, down to 0.65 at age 15, a 31.57% drop). When the IOPs were considered for different age levels, they all fell within the range of 8 mmHg and 20 mmHg. A jump of IOP = 17.15 at age 12 to 18.12 at age 13 was potentially due to the fact that as schoolchildren transitioned from elementary school (sixth grade) to junior high school (seventh grade), more time was spent indoors studying. ROC curve from IOP in this study did not show impact on progressive myopia.

**Discussion**

This study investigated the prevalence and severity of myopia in Chiayi County, Taiwan based on examined data from elementary and junior high schools in 2013-2015. It is generally believed that myopia is more of a problem in urban areas where academically rigorous classes and higher demand for education are present.[2] In the past 15 years, there was hardly any survey or study done on myopia in Taiwan. In 2000, Lin et al studied about myopia and reported that the prevalence of high myopia (SE = -6D) at the age of 18 was 24%.[21,22] This study found that at the age of 7, the prevalence of myopia with a refractive index (D) was -0.22D, which increased to -1.77D at the age of 12, and then to -2.31D at the age of 15. Lin et al have studied myopia and revealed that in 1983, myopia started at the age of 10, in 1995 it was 9, and in 2000 it became 8. In contrast, this study during 2013-2015 found that myopia started at the early age of 7. Furthermore, this study found that the prevalence and severity of myopia in elementary schools in Chiayi County was higher than what was reported in the previous study by Lin et al in 2000.[2] In addition, girls had higher mean refractive index (D) than boys and the severity worsened with years of investigation. Furthermore, boys in elementary schools of Chiayi County in 2013-2015 had the highest myopia (-1.10D), as compared to the previous study. Girls in elementary schools also had similar mild myopia in second place (-1.01D), slightly trailing behind the Taipei area (-1.03D) in 2000. Boys in junior high schools in Chiayi County were in second place (-2.10D), with the first place being the Kaohsiung area (-2.26D) in 1995. Girls in junior high schools of Chiayi County were better than 4 areas (Taipei, Kaohsiung, provincial cities, and service business) in 1995 while they were better than most areas except the aboriginal area in 2000. This could be attributed to the fact that schoolchildren in the mountainous or aboriginal areas had more outdoor activities to touch green trees and grasses; therefore, milder myopia was expected as compared to most schoolchildren in other areas.

When studying the prevalence of myopia with respect to age group, we found there were 31.65% with mild myopia but there were no cases for moderate or high myopia at the age of 6. At age 7, the percentage of mild myopia increased to 52.17% and there were only 1.13% of moderate myopia and 0.16% of high myopia. The trend of mild myopia increased until 12 years old before they entered junior high school. The percentages of moderate and high myopia jumped to 17.47% and 3.61%, respectively at sixth grade (the final year of elementary school), then increased to 19.78% and 3.79% in the first year of junior high school, and this trend increased to 28.43% and 5.58%, respectively until the age of 15.

In general, girls had higher prevalence of myopia than boys at the elementary school level but the severity was overturned by boys in junior high schools. The role played by the environment in the development of myopia remained unclear.[23] The utilisation of computers or electronic devices in daily life has been a significant factor in the prevalence of myopia among children.[20,24] Dr Luke Lin, a retired professor at the National Taiwan University's College of Ophthalmology, said factors such as heavy workload at school, the stringent system of university entrance examinations, the possession and obsession of electronic devices all contributed to the epidemic of myopia.[15] In this study, we found that the onset of myopia started earlier and progressively worsened over the years among suburban schoolchildren. Specifically, this study found that the prevalence and severity of myopia in elementary schools was higher than the previous study. While we only mentioned computers and electronic devices as likely contributing factors to this trend, we realise that there are other potential risk factors. In fact, some scientific publications revealed that near-work activities might increase the prevalence of myopia as well. Hsu et al revealed that prevalence of myopia in second grade children in metropolitan Taipei was significantly associated with time spent on near-work activities every day. Further analysis on their study found that 6.2% of participants who spent more than 2 hours daily using cellphone, computer or tablet products tended to have a 41% higher risk of myopia than those who spent less than 2 hours on them.[24] Systematic review from Huang et al showed that near-work activities were associated with myopia and more diopter-hours of near-work might increase myopia prevalence. Specifically, they found that children with more near-work activities had an 80% higher risk of having myopia. Furthermore, myopic children spent more time reading, but not studying, using a computer, or watching television (TV) than non-myopic children.[25] Deng et al studied 147 children aged 6-18 years and found that during the school year, myopes spent less time on sports/outdoor activity than non-myopes. For non-myopes, the average

weekly TV hours (8.91 ± 5.95 hours/week) was significantly lower than in myopes (12.78 ± 9.28 hours/week).[26] Sherwin et al's findings from observational epidemiologic studies suggested that increasing time outdoors may be associated with a reduced risk of myopia and myopic progression.[27]

The risk is less for adult eyes which have a natural defense. As children's eyes are still developing, blue light is able to penetrate much easier and directly into the retina. One reason for the high prevalence of myopia in Taiwan is increasing workload from formal education and excessive usage of smartphones at a young age. Furthermore, with constant surfing on the Internet, watching TV, using computers and playing games on smartphones, the prevalence of myopia may exacerbate in schoolchildren. This study contributes to the investigation of prevalence of myopia in schoolchildren in an agriculture-based county in Taiwan and discusses how severe myopia was, as compared to the previous study in 2000.

## Conclusion

In conclusion, this study finds that myopia can occur at an age, as early as 7 years old and progressively worsens as a child ages. The prevalence and severity of myopia in schoolchildren has increased in the last 15 years.

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REFERENCES

1. Lin LLK, Shih YF, Hsiao CK, Chen CJ. Prevalence of myopia in Taiwanese schoolchildren: 1983 to 2000. Ann Acad Med Singapore 2004;33:27-33.
2. Lin LLK, Shih YF, Hsiao CK, Chen CJ, Lee LA, Hung PT. Epidemiologic study of the prevalence and severity of myopia among schoolchildren in Taiwan in 2000. J Formosan Med Assoc 2001;100:684-91.
3. Ko LS, Liu HS, Yang YF. Study of the refraction on the primary school students in Taipei. J Formosan Med Assoc 1959;58:336-53.
4. Saw SM, Katz J, Schein OD, Chew SJ, Chan TK. Epidemiology of myopia. Epidemiol Rev 1996;18:175-87.
5. Liang YS, Lai IC, Loke TY, Chen TT. Preliminary report of ocular examination in school children. Trans Soc Ophth Sinicae 1984;23:1-7.
6. Hosaka A. The growth of the eye and its components: Japanese studies. Acta Ophthalmol Suppl 1988;185:65-8.
7. Hosaka A. Population studies – myopia experience in Japan. Acta Ophthalmol Suppl 1988;185:37-40.
8. Motegi S, Kunitomo N, Kumano CY, Chiu LY, Liaw KS, Hu TL, et al. Survey of the refractive status among Taiwanese aboriginals I. J Formosan Med Assoc 1944;43:778-90.
9. Motegi S, Kunitomo N, Kumano CY, Chiu LY, Liaw KS, Hu TL, et al. Survey of the refractive status among Taiwanese aboriginals II. J Formosan Med Assoc 1944;43:826-36.
10. Motegi S, Liaw KS, Kunitomo N, Hu TL, Kumano CY, Lee DH, et al. Survey of the refractive status among Taiwanese aboriginals III. J Formosan Med Assoc 1945;44:1-11.
11. Motegi S, Liaw KS, Kunitomo N, Hu TL, Kumano CY, Lee DH, et al. Survey of the refractive status among Taiwanese aboriginals IV. J Formosan Med Assoc 1945;44:71-81.
12. Chung CB, Huang WL, Sheu MM, Chen CW. Survey of refractive status of the eyes among the aboriginal primary school students of Wu-Tai and San-Ti Hsiung, mountain area of Ping-Tong Hsien. Trans Soc Ophth Sinicae 1983;22:21-5.
13. Chen NY, Chen CW, Huang WL, Lin CP, Lee CC. The refraction screening among primary school children in mountain area of Shiow-Lin Hsiang, Huea-Lian Hsien. Trans Soc Ophth Sinicae 1984;23:14-9.
14. Myopia now serious issue for young students: report. Taipei Times. May 15, 2014;5.
15. Kastner J. The problem with Taiwanese eyes. The Diplomat. March 12, 2015. Available at: https://thediplomat.com/2015/03/the-problem-with-taiwanese-eyes/. Accessed on 9 April 2018.
16. Lin LLK, Shih YF, Chen CJ, Hung PT, Hou PK. Epidemiologic study of ocular refraction among schoolchildren in Taiwan in 1983. Annual Reports of Department of Health, Executive Yuan, Taiwan, 1983.
17. Lin LLK, Shih YF, Chen CJ, Hung PT, Hou PK. Epidemiologic study of ocular refraction among schoolchildren in Taiwan in 1990. Annual Reports of Department of Health, Executive Yuan, Taiwan, 1990.
18. Lin LLK, Shih YF, Tsai CB, Chen CJ, Lee LA, Hung PT, et al. Epidemiologic study of ocular refraction among schoolchildren in Taiwan in 1995. Optom Vis Sci 1999;76:1-7.
19. Lin LLK, Chen CJ, Hung PT, Ko LS. Nation-wide survey of myopia among schoolchildren in Taiwan, 1986. Acta Ophthalmol Suppl 1988;185:29-33.
20. Saw SM, Chua WH, Hong CY, Wu HM, Chan WY, Chia KS, et al. Nearwork in early-onset myopia. Invest Ophthalmol Vis Sci 2002;43:332-9.
21. Lin LLK, Hung PT, Ko LS, Hou PK. Study of myopia among aboriginal school children in Taiwan. Acta Ophthalmol Suppl 1988;185:34-6.
22. Lin LLK, Hung PT, Ko LS. Survey of the refraction status among the primary school children in Taipei. Trans Soc Ophth Sinicae 1980;19:58-62.
23. Hsu SL, Chang CH, Lai YH, Wen MH, Cheng KC, Ho CK. Refractive status of mountain aborigine schoolchildren in southern Taiwan. Kaohsiung J Med Sci 2008;24:120-5.
24. Hsu CC, Huang N, Lin PY, Tsai DC, Tsai CY, Woung LC, Liu CJ. Prevalence and risk factors for myopia in second-grade primary school children in Taipei: a population-based study. J Chin Med Assoc 2016;79:625-32.
25. Huang HM, Chang ST, Wu PC. The association between near work activities and myopia in children–a systematic review and meta-analysis. PLoS One 2015;10:e0140419.
26. Deng L, Gwiazda J, Thorn F. Children's refractions and visual activities in the school year and summer. Optom Vis Sci 2010;87:406-13.
27. Sherwin JC, Reacher MH, Keogh RH, Khawaja AP, Mackey DA, Foster PJ. The association between time spent outdoors and myopia in children and adolescents: a systematic review and meta-analysis. Ophthalmology 2012;119:2141-51.

# Arrival of *Candida auris* Fungus in Singapore: Report of the First 3 Cases

**Dear Editor,**

*Candida auris* is an emerging fungus that is of increasing global concern. Healthcare-associated outbreaks and cases have been reported in 5 continents[1-2] and the number of countries involved is growing. This is alarming as *C. auris* is commonly multidrug-resistant with some isolates displaying pan-resistance to the available antifungal drugs.[3] Here, we report the first 3 cases of *C. auris* isolated from a tertiary hospital in Singapore. Table 1 summarises the clinical characteristics, management, outcome and antifungal susceptibilities of these cases.

## Case 1

The first case was detected back in 2012. A 52-year-old local-born Chinese lady was transferred from India following a road traffic accident. She sustained multiple bilateral lower limb fractures. External fixation was performed for the right femur fracture in India and the patient received multiple

Table 1. Clinical Characteristics, Management, Outcome and Antifungal Susceptibilities of the 3 Cases of *Candida auris*

| **Case/Year** | **1/2012** | **2/2016** | **3/2017** |
|---|---|---|---|
| Transferred from overseas hospital/country | Yes/India | Yes/Bangladesh | Yes/Bangladesh |
| Main diagnosis | Traumatic fractures | Metastatic carcinoma | Infective exacerbation of COPD |
| CP-CRE screening*/type of carbapenemase(s)† identified | Positive/NDM-1 | Positive/NDM and OXA-232 | Positive/OXA-232 |
| *C. auris* isolation site | Right femur tissue | Blood | Blood |
| Antifungal therapy | | | |
| Prior *C. auris* isolation | Yes. Fluconazole for 10 days. | Yes. Fluconazole was given in Bangladesh. Duration not known. | Not known back in Bangladesh. Not given upon arrival in Singapore. |
| Post *C. auris* isolation | Yes. Fluconazole for 6 days before *C. auris* antibiogram was known. | Yes. Anidulafungin for 1 day prior discharge to Bangladesh. | No. Palliative care. |
| Outcome | Survived | Not known | Death |
| **Antifungal Susceptibility Testing** | **Antifungal MIC in µg/ml (Interpretation)‡** | | |
| Fluconazole | 256 (R) | ≥256 (R) | 256 (R) |
| Voriconazole | 1 (NA) | 1 (NA) | 2 (NA) |
| Itraconazole | 0.25 (NA) | 0.12 (NA) | 0.12 (NA) |
| Posaconazole | 0.06 (NA) | 0.06 (NA) | 0.06 (NA) |
| Caspofungin | ≥8 (R) | 0.06 (S) | 0.12 (S) |
| Anidulafungin | 0.5 (S) | 0.12 (S) | 0.12 (S) |
| Micafungin | 0.25 (S) | 0.12 (S) | 0.06 (S) |
| Amphotericin B | 2 (R) | 2 (R) | 1 (S) |
| Flucytosine | 0.25 (NA) | ≤0.06 (NA) | ≤0.06 (NA) |

COPD: Chronic obstructive pulmonary disease; CP-CRE: Carbapenemase-producing carbapenem-resistant *Enterobacteriaceae*; MIC: Minimum inhibitory concentration; NA: Not available; NDM: New Delhi metallo-β-lactamase; OXA: Oxacillinase; R: Resistance, S: Susceptible

*Screening was performed from stool or rectal swab on admission.
†NDM and OXA.
‡There are currently no established susceptibility breakpoints for *C. auris*. Interpretation is based on the US CDC tentative MIC breakpoints for *C. auris* (Centres for Disease Control and Prevention. Recommendations for identification of *Candida auris*. Available at: https://www.cdc.gov/fungal/diseases/candidiasis/recommendations.html. Accessed on 1 February 2018.) Fluconazole ≥32 µg/ml (R), amphotericin B ≥2 µg/ml (R), anidulafungin ≥4 µg/ml (R), caaspofungin ≥2 µg/ml (R), micafungin ≥4 µg/ml (R).

antibiotics prior to transferring to Singapore for further management at day 5. Patient underwent external fixation to the left tibia fracture in Singapore on the following day with the right external fixator left in-situ. Unfortunately, the wound at the pin track site of the right femur shaft fracture was infected and intraoperative tissue cultures grew multiple organisms including *C. auris* on hospital day 78. Both antibiotics and antifungal were initiated. However, fluconazole was discontinued after 1 week when *C. auris* was tested to be resistant to it (Table 1). Due to an improvement in the inflammatory markers, no further antifungal drug was given. Blood cultures remained sterile throughout the hospitalisation. Patient was discharged 4 months later with the wounds healing well.

**Case 2**

A 24-year-old Bangladeshi male flew to Singapore in 2016 to seek further medical management. He had been admitted to 3 hospitals in Bangladesh for a total of 21 days for metastatic carcinoma of unknown origin and was given antibiotics including fluconazole before transferring to Singapore. Chemotherapy was initiated upon arrival but patient turned septic and was cultured and covered with antibiotics. Anidulafungin was added subsequently when blood culture taken at day 9 grew *C. auris* (Table 1). However, the patient discharged against medical advice and returned to Bangladesh the following day.

**Case 3**

A 69-year-old United States' male citizen suffered infective exacerbation of chronic obstructive pulmonary disease (COPD) while touring in Bangladesh in late 2016. He was admitted into the intensive care unit (ICU) in Bangladesh and treated with broad-spectrum antibiotics before transferring to Singapore in early 2017 for further management.

The patient suffered from a series of medical complications including cardiac arrest and brain infarcts during his hospitalisation here. Septic workup grew *C. auris* from the blood culture taken on day 9 of admission (Table 1). Antifungal therapy was not initiated as patient was not for active management after discussion with family members. He deteriorated rapidly and passed away shortly after.

The identification of *C. auris* was confirmed by sequencing of the internal transcribed spacer (ITS). Antifungal susceptibilities were performed using Sensititre™ YeastOne® microdilution panel (TREK Diagnostic Systems Ltd, Thermo Scientific). Although there are currently no established Clinical Laboratory Standard Institute (CLSI) and European Committee for Antimicrobial Susceptibility Testing (EUCAST) susceptibility breakpoints for *C. auris*, the United States Centers for Diseases Control and Prevention (US CDC) does provide tentative minimum inhibitory concentration (MIC) breakpoints for certain antifungals as a general guide.[4] It must be emphasised that these breakpoints are not definitive and an elevated MIC does not necessarily preclude the use of an antifungal drug. *C. auris* isolates uniformly display high fluconazole MICs and about one-third of them have raised MICs to voriconazole and amphotericin B which are similar to the cases here.[5-6] As such, echinocandins are the empiric drugs of choice for *C. auris* infections, although they have no activity against *C. auris* biofilms.[6] Coincidentally, all 3 cases were screened positive for carbapenemase-producing carbapenem-resistant *Enterobacteriaceae* (CP-CRE) and were isolated with contact precautions (Table 1).

*C. auris* has not been previously reported in Singapore.[7] These 3 cases all appear to be imported. This highlights the need for a screening policy for *C. auris* in patients transferred from overseas hospitals, especially from countries reported to have this yeast in order to prevent its establishment and spread within the institution. Despite our first case in 2012 and not doing active surveillance, we were fortunate not to experience any outbreaks of *C. auris* infection during this period. This may be due to the heightened infection control for all 3 cases which were screened positive for CP-CRE. The isolation of CP-CRE may also indicate the high probability of co-colonisation with *C. auris* in patients transferred from overseas hospitals. This was not surprising as some of these countries were reported to have high incidence of CP-CRE too.[8] With the propensity of *C. auris* to cause outbreaks in healthcare settings,[2,9] institutions may have to do risk assessment to consider including this fungus into their screening protocols and further strengthen infection control measures to prevent it from becoming a major global public health issue.

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REFERENCES

1. Schelenz S, Hagen F, Rhodes JL, Abdolrasouli A, Chowdhary A, Hall A, et al. First hospital outbreak of the globally emerging Candida auris in a European hospital. Antimicrob Resist Infect Control 2016;5:35.
2. Public Health England. Guidance: Candida auris: laboratory investigation, management and infection prevention control. Available at: https://www.gov.uk/government/publications/candida-auris-laboratory-investigation-management-and-infection-prevention-and-control. Accessed on 6 September 2017.

3. Lockhart SR, Etienne KA, Vallabhaneni S, Farooqi J, Chowdhary A, Govender NP, et al. Simultaneous emergence of multidrug- resistant Candida auris on 3 continents confirmed by whole-genome sequencing and epidemiological analyses. Clin Infect Dis 2017;64:134-40.
4. Centres for Disease Control and Prevention. Recommendations for identification of Candida auris. Available at: https://www.cdc.gov/fungal/diseases/candidiasis/recommendations.html. Accessed on 1 February 2018.
5. Kathuria S, Singh PK, Sharma C, Prakash A, Masih A, Kumar A, et al. Multidrug-resistant Candida auris misidentified as Candida haemulonii: characterization by matrix-assisted laser desorption ionization–time of flight mass spectrometry and DNA sequencing and its antifungal susceptibility profile variability by Vitek 2, CLSI broth microdilution, and Etest method. J Clin Microbiol 2015;53:1823-30.
6. Lu PL, Liu WL, Lo HJ, Wang FD, Ko WC, Hsueh PR, et al. Are we ready for the global emergence of multidrug-resistant Candida auris in Taiwan? J Formos Med Assoc 2018;117:462-70.
7. Tan TY, Tan AL, Tee WS, Ng SY. A retrospective analysis of antifungal susceptibilities of Candida bloodstream isolates from Singapore hospitals. Ann Acad Med Singapore 2008;37:835-40.
8. Lee CR, Lee JH, Park KS, Kim YB, Jeong BC, Lee SH. Global dissemination of carbapenemase-producing Klebsiella pneumonia: epidemiology, genetic context, treatment options, and detection methods. Front Microbiol 2016;7:895.
9. Centres for Disease Control and Prevention. General information about Candida auris. Available at: https://www.cdc.gov/fungal/diseases/candidiasis/candida-auris-qanda.html. Accessed on 6 September 2017.

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# Camera Cover Perforation after Arthroscopic Surgery

**Dear Editor,**

To maintain sterility during arthroscopic surgery, arthroscopic cameras may be used either sterilised or enveloped in a sterile cover. Before the development of autoclavable arthroscopic cameras, sterilising arthroscopic cameras in glutaraldehyde had been the acceptable method of practice in many centres around the globe. However, case reports of suspected gas gangrene cases following arthroscopic surgery[1-2] had raised concern regarding the effectiveness and safety of this disinfection method. We use the word 'disinfection' here because it had been shown that soaking instruments in glutaraldehyde solution for 15 to 20 minutes could eliminate all types of bacteria and viruses, but not spores.[3]

In the report by Ketterl[2] the patient presented with compartment syndrome and was presumptively treated for gas gangrene based on radiological findings. Although the gram stain revealed gram positive bacilli, no positive cultures were obtained. Therefore, the infection may not necessarily have been due to a clostridial infection.

Standard arthroscopic cameras are temperature-sensitive and thus not amenable to autoclave sterilisation due to the high temperature. The use of autoclavable arthroscopic cameras seems like an attractive option, but given the high frequency at which arthroscopic surgeries are performed, duplication of these expensive modern cameras are required to allow adequate turnover between cases, resulting in escalating costs.

Other options include ethylene oxide and plasma sterilisation. However, while they are effective and do not require a long sterilisation processes, they are also relatively costly.

Therefore, most centres still utilise standard arthroscopic cameras, either disinfected with glutaraldehyde or covered with sterile plastic arthroscopic camera covers. Although convenient and relatively cheap, the reliability of these covers is unproven.

Glutaraldehyde soaking of arthroscopic cameras was the sterilisation/disinfection method-of-choice at our institution until 2005, when concerns regarding the potential of postoperative infection by spore-forming bacteria was raised.[1-2] Despite its many advantages, glutaraldehyde had limitations due to its ineffectiveness against spore-forming bacterium. Sterile arthroscopic camera covers had replaced our standard of practice since then, believed to be offering a safe, relatively cheap and reliable alternative to glutaraldehyde. A prospective randomised study conducted by Werner et al reported a staggering leakage rate of 74% out of the 90 sterile covers analysed in their study.[4] We aimed to determine the integrity of sterile arthroscopic camera covers used at our institution.

**Materials and Methods**

Forty-three sterile arthroscopic camera covers (Fairmont Medical, Australia) were analysed in a prospective study at our institution's Ambulatory Surgery Centre. Data recorded include the performing surgeon, type and duration of surgery. The type of surgery included both knee and shoulder arthroscopies. The average duration was 61 minutes, with a range from 20 to 150 minutes.

Covers were immediately removed from the camera postarthroscopy and filled with water to a level of about 70 cm. The junction between the built-in camera adapter and plastic sleeve was labelled as Zone C. Zone B and A marked the level from the adapter-plastic junction to 25 cm and from 25 to 50 cm, respectively. The area above the 50 cm mark was labelled as the pre-zone (Figs. 1 and 2).

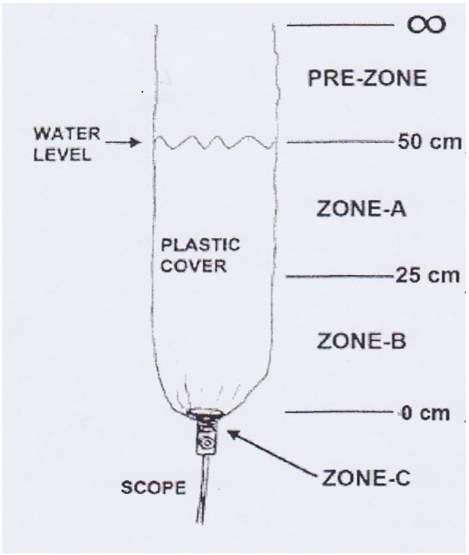


Fig. 1. Diagram of testing setup.

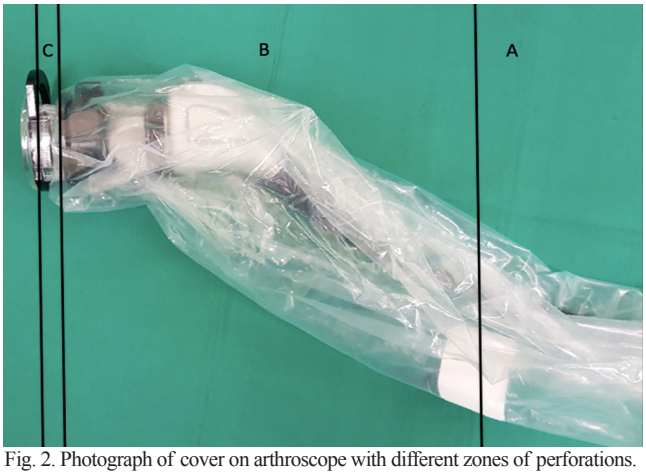

Fig. 2. Photograph of cover on arthroscope with different zones of perforations.

Perforations were documented as 'small' where leakage was detected with no visible perforation, 'medium' for perforations up to 1 mm and 'large' for perforations larger than 41 mm. All testing were conducted by the same personnel to maintain consistency and standardisation. In addition, 15 unused covers were analysed as controls. Testing of the control unused covers was carried out in a similar manner to the covers used during arthroscopy.

The statistical analysis was performed using 1-way analysis of variance (ANOVA) with posthoc Dennett pairwise comparison. Statistical software SPSS v17.0 was utilised.

## Results

A total of 81% (35 out of 43) of covers analysed postarthroscopy had 1 to 3 perforations. A total of 49 perforations were recorded in our study (Zone A = 14%, Zone B = 41%, Zone C = 43%). One cover was found to have 1 perforation in the pre-zone (Table 1).

Most small and medium sized perforations were found in Zone C and most large perforations were found in Zone B. Only the difference in percentage of leakage rate between Zone A and Zone B was found to be statistically significant ($P = 0.026$) (Table 2).

No correlation was found between the duration and type of surgery with the number or size of perforations. The number and size of perforations was also found to be independent of the performing surgeon. None of the 15 new covers in the control group had perforations. At 3 months follow-up, there were no cases of postoperative infection.

Table 2. Comparison between Zones of Perforation

| Comparisons | *P* Value |
|---|---|
| Zone A vs zone B | 0.026 |
| Zone A vs zone C | 0.054 |
| Zone B vs zone C | 0.998 |

## Discussion

Sterile plastic arthroscopic camera covers, thought to be a cost-effective and reliable alternative to glutaraldehyde, may not be the perfect solution after all. The high rate of perforation found by Werner et al[4] and our study is indeed of concern.

Our analysis had shown that most perforations occurred at Zones C and B (area from junction of camera adaptor to 25 cm proximal along the plastic sleeve). This could perhaps be because the 2 zones were the areas under most mechanical stress from manipulation by the operator. Furthermore, majority of the large sized perforations occurred in Zone B where the operator's hand made direct contact with the plastic drape.

Manufacturers of sterile arthroscopic camera covers should re-evaluate their design to address the issue of perforations at the junction between the built-in camera adapter and plastic sleeve (Zone C), and consider reinforcing the initial 25 cm from the adapter-plastic junction (Zone B) to reduce the perforation rate.

While standard glutaraldehyde disinfection may not sufficiently sterilise the arthroscopic equipment, the published infection rates were still low. The incidence of infection postarthroscopy is reported to be around 1% or less.[5-11] Staphylococcal and streptococcal infections were still the most common pathogens involved in infection, and thus glutaraldehyde disinfection may be sufficient to prevent most infections. While glutaraldehyde disinfection may not be proven to result in higher infection rates, the discerning surgeon may have to consider other methods of maintaining sterility, be it with ethylene oxide, plasma sterilisation, or with sterile plastic arthroscopic camera covers.

The question remains as to why there was such a low incidence of infection despite the high leakage rate found in sterile arthroscopic camera covers used in arthroscopic surgery. The use of copious and continuous irrigation during arthroscopic surgery may perhaps minimise or eliminate

Table 1. Table of Perforations by Zones

| | Pre-Zone | Zone A (S) | Zone A (M) | Zone A (L) | Zone B (S) | Zone B (M) | Zone B (L) | Zone C (S) | Zone C (M) | Zone C (L) |
|---|---|---|---|---|---|---|---|---|---|---|
| | 1 | 3 | 2 | 2 | 7 | 1 | 12 | 10 | 4 | 7 |
| Total by region | 1 (2%) | | 7 (14%) | | | 20 (41%) | | | 21 (43%) | |

L: Large; M: Medium; S: Small

joint contamination. Another explanation may be due to the fact that arthroscopic surgery is minimally invasive, utilising small incisions for access, thus minimising outside contamination and at the same time minimising tissue trauma and necrosis.

In between cases, it was the standard practice for the camera heads and cables to be wiped with a solution containing detergent and disinfectant. This helped in removing gross contaminant and in reducing bacterial load on the equipment, potentially minimising the risk of infection despite the perforations, even though the equipment was not handled in a sterile manner.

Currently, there are no direct studies comparing the incidence of postoperative infection between the use of glutaraldehyde disinfection and the use of sterile arthroscopic camera covers. However, given the low incidence of postarthroscopy infections, large numbers are required to prove any differences in postoperative infection rates.

As we strive to improve on current standards and practices, there is still a need to provide better sterilisation instead of mere disinfection for elective surgical procedures, and hence there is a need for surgeons, operating theatres and hospitals to consider different methods of maintaining sterility.

## Conclusion

The alarmingly high rate of perforations found in sterile plastic arthroscopic camera covers postarthroscopy raises concern regarding its reliability in the maintenance of sterility in clinical practice. Although the rate on infection is low, surgeons and their hospitals may want to consider other options to maintain sterility, since the perforation rate, and hence potential for infection, is high.

REFERENCES


1. Bernhang AM. Clostridium pyarthrosis following arthroscopy. Arthroscopy 1987;3:56-8.
2. Ketterl R, Beckurts T, Kovacs J, Stuebinger B, Hipp R, Claudi B. Gas-gangrene following arthroscopic surgery. Arthroscopy 1989;5:79-83.
3. Herzberg W. Problems with the sterilisation and the maintenance of sterility of arthroscopic instruments: a comparison of different types of camera drapes. Knee Surg Sports Traumatol Arthrosc 1993;1:223-5.
4. Werner CM, Necas T, Schneeberger AG. Defects of camera covers after arthroscopic surgery. J Shoulder Elbow Surg 2006;15:199-202.
5. Clement RC, Haddix KP, Creighton RA, Spang JT, Tennant JN, Kamath GV. Risk factors for infection after knee arthroscopy: analysis of 595,083 cases from 3 United States databases. Arthroscopy 2016;32:2556-61.
6. Yeranosian MG, Petrigliano FA, Terrell RD, Wang JC, McAllister DR. Incidence of postoperative infections requiring reoperation after arthroscopic knee surgery. Arthroscopy 2013;29:1355-61.
7. Salzler MJ, Lin A, Miller CD, Herold S, Irrgang JJ, Harner CD. Complications after arthroscopic knee surgery. Am J Sports Med 2014;42:292-6.
8. Yeranosian MG, Arshi A, Terrell RD, Wang JC, McAllister DR, Petrigliano FA. Incidence of acute postoperative infections requiring reoperation after arthroscopic shoulder surgery. Am J Sports Med 2014;42:437-41.
9. Weber SC, Abrams JS, Nottage WM. Complications associated with arthroscopic shoulder surgery. Arthroscopy 2002;18:88-95.
10. Moen TC, Rudolph GH, Caswell K, Espinoza C, Burkhead Jr WZ, Krishnan SG. Complications of shoulder arthroscopy. J Am Acad Orthop Surg 2014;22:410-9.
11. Fong SY, Tan JL. Septic arthritis after arthroscopic anterior cruciate ligament reconstruction. Ann Acad Med Singapore 2004;33:228-34.



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# Delusion of Parasitosis: A Descriptive Analysis of 88 Patients at a Tertiary Skin Centre

**Dear Editor,**

Delusions of parasitosis (DoP) is a form of mono-symptomatic hypochondriacal delusional disorder of bodily infestation. Patients present to the dermatologist with a fixed false belief of infestations of the body. They may share similar characteristics such as ritualistic behaviour to rid themselves of their infestations. Although the pathophysiology is unclear, it is likely to be multifactorial including genetics, organic factors, premorbid traits, acute triggers, and social vulnerability.[1] The main challenge is starting these patients on appropriate treatment as they do not have insight to their problem and are often otherwise normal. The mainstay of treatment are antipsychotics, though the addition of antidepressants might be useful. In the present study, we describe the novel combination of risperidone and fluoxetine in the management of such patients.

## Materials and Methods

We conducted a retrospective review to study the demographic characteristics, symptomatology, comorbidities, associated psychiatric disorders and treatment outcome of patients seen in a tertiary dermatology institute. Patients with a diagnosis of DoP seen at the National Skin Centre, Singapore, over a 9-year period between January 2004 and December 2012 were included. They were identified through: the electronic medical records, with diagnoses containing 'delusion' or 'parasitosis'; and from electronic pharmacy prescriptions of risperidone; and from the Psychodermatology Clinic patient database. All patients were managed in the joint Psychodermatology Clinic and concurrently by a psychiatrist and a dermatologist.

## Results

*Patient Demographics and Symptoms*

Eighty-eight patients with DoP were identified. There were 52 (59%) females and 36 (41%) males. The ethnic composition was 87% Chinese, 5% Malay, 5% Indian and 3% others—there were more Chinese patients seen compared to the general population of Singapore (74%). The mean age was 61.4 ± 13.0 years.

The delusions were of infestation (86/88, 98%) and fibres (2/88, 2%). They experienced symptoms in/under the skin (80/88, 91%), inside body orifices (4/88, 5%), in the body (3/88, 3%) and in the hair/scalp (1/88, 1%). Thirty-seven patients (42%) reported an event triggering the onset of symptoms, including exposure to new home/office environments (14%) and animals (9%), and travelling (9%).

Thirty-eight (43%) presented with the classical "matchbox"sign, with specimens in containers. 'Folie a deux' involving a family member was present in 7 (8%) patients. Sixty (68%) and 32 (36%) patients displayed excessive cleaning of oneself and their environment, respectively. In the Asian context, these patients rid themselves of the parasites by: kerosene and oil to the scalp/hair (3/88), joss sticks (1/88), smoking parasites with charcoal (1/88), and Chinese herbs and vinegar (1/88). Twenty (23%) patients engaged in self-mutilation using instruments (12/88), caustic agents (5/88) and heat (3/88) (Fig. 1).

*Clinical Presentation and Investigations*

The main skin signs manifested were: excoriations in 37 patients (42%) and irritant contact dermatitis in 29 (33%). Nineteen (22%) patients had no skin signs. In patients with excoriations, most of these occurred in a generalised distribution (41%), followed by limbs (15%), face (10%), scalp (6%), and trunks (1%). Half had

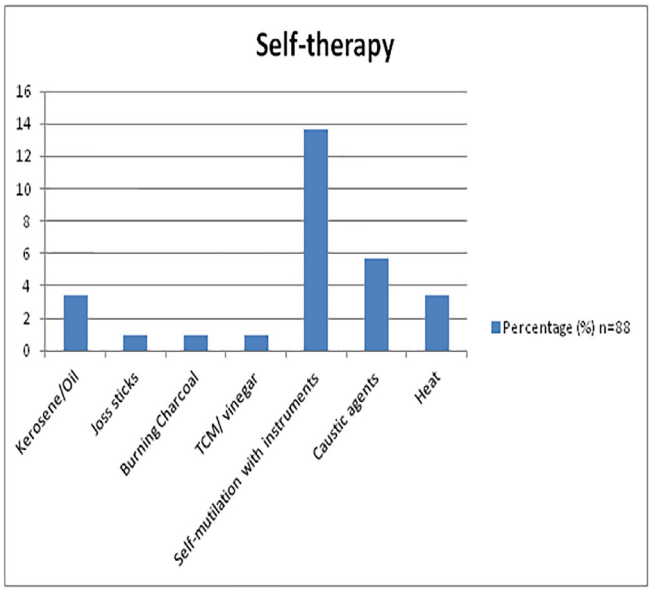


Fig. 1. Chart showing the various methods used by patients to rid themselves of their perceived infestation.

accompanying medical comorbidities (Fig. 2), including diabetes (15/88), hyperlipidaemia (16/88), hypertension (21), renal impairment (5/88), non-diabetes endocrine disorders (3/88), and haematological disease (3/88). Ten (11%) patients had pre-existing skin diseases, of whom 8 (9%) had endogenous eczema or psoriasis. Fourteen patients (16%) had psychiatric comorbidities, including 8 with schizophrenia, 6 with depression, and 3 with bipolar disorders. Three (3%) patients were found to have suicidal tendencies. Ten (11%) patients had associated psychodermatoses, including 3 who had trichotillomania, 5 with dermatitis artefacta and 2 with neurotic excoriations. Over half of the patients underwent investigations: blood tests in 47 (54%), scrapings were done to exclude scabies and fungus in 35 (40%), and skin biopsy to differentiate serious disorders, in 10 (12%).

*Treatment and Follow-up*

The patients were treated with medications for 7.7 months, and followed-up for 21.2 months. Thirty-nine (44%) patients were prescribed a combination of risperidone and fluoxetine, 15 (17%) risperidone, 2 (2%) fluoxetine. These were started on low doses and titrated upwards as most patients were elderly. Thirty-two (36%) patients did not receive medications. Adverse effects such as extrapyramidal side effects and drowsiness were observed in 22 (39%) patients—20 from risperidone and 2 from fluoxetine. There were no major side effects and in 15 patients, the side effects improved after the dose was reduced.

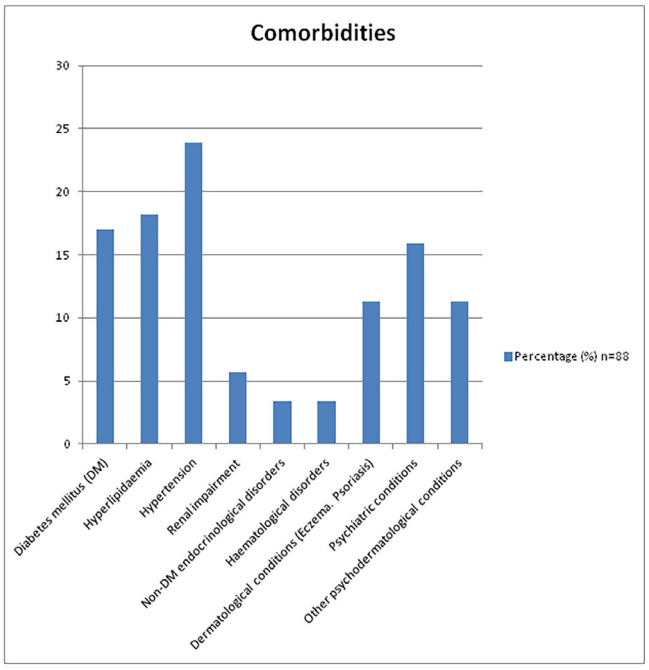


Fig. 2. Chart showing the underlying comorbidities.

Twenty-nine (33%) patients defaulted follow-up without starting treatment. In the 59 (67%) patients who started treatment, 43 (73%) had improved clinically. Sixteen (27%) had no improvement. Of those who responded, clinical improvement was observed by 3.7 ± 7.5 months. When treatment was discontinued or tapered, 10 (23%) of these patients relapsed within 2 years. It is known that patients do relapse on stopping medication.

## Discussion

The majority of our patients were Chinese females who presented with characteristic symptoms and features seen in patients with DoP. Perhaps unique to our local context was the use of abrasive agents such as kerosene for self-therapy.

A fairly high percentage (33%) of our patients defaulted follow-up even though drugs were not prescribed. Indeed, treatment of DoP is challenging and much of this difficulty lies in having a trusting relationship with the patient. Physicians need to learn how to cope with psychiatric patients by displaying active listening skills and showing interest in their concerns. However, in the case of DoP, it is important not to collude with the patient and offer them hope in dealing with their problem. Due to the nature of the condition and ethical considerations, randomised controlled trials are lacking regarding the management of DoP. A systematic review indicates that antipsychotic agents remain the treatment of choice.[2] Atypical or second-generation antipsychotic agents such as risperidone, olanzapine or amisulpride in age-appropriate doses are commonly used to treat DoP.[3]

Pimozide—which is effective in up to 80%—has limited availability. This is related to its adverse extrapyramidal side effects, including tardive dyskinesia which may be irreversible.[4] It may also prolong the QT interval, which limits its use.

In this study, 39 (44%) of the patients received a combination of risperidone and fluoxetine and 22/39 (56%) of them improved clinically. This is comparable to other reported remission rates of 25%-69% with risperidone.[5,6,7] Previous studies have suggested that combining an atypical antipsychotic drug and a selective serotonin reuptake inhibitor (such as fluoxetine) work synergistically to promote the release of dopamine in prefrontal areas.[8] This has been shown in animal studies as well where the coadministration of risperidone and fluoxetine increased the extracellular level of cortical dopamine, serotonin and noradrenaline.[9] This may potentially reduce the risk of side effects by allowing lower doses of each drug used.

## Conclusion

In conclusion, this retrospective study of 88 patients with delusions of parasitosis represents a large number of

patients reported in South East Asia (and maybe worldwide) from a dermatological clinic. The unique combination of risperidone and fluoxetine appears to be efficacious without major adverse events. More studies will be helpful to improve the management of this condition.

REFERENCES


1. Freudenmann RW, Lepping P. Delusional infestation. Clin Microbiol Rev 2009;22:690-732.
2. Lepping P, Russell I, Freudenmann RW. Antipsychotic treatment of primary delusional parasitosis : systematic review. Br J Psychiatry 2007;191:198-205.
3. Lepping P, Freudenmann RW. Delusional parasitosis: a new pathway for diagnosis and treatment. Clin Exp Dermatol 2008;33:113-7.
4. Elmer KB, George RM, Peterson K. Therapeutic update: use of risperidone for the treatment of monosymptomatic hypochondriacal psychosis. J Am Acad Dermatol 2000;43:683-6.
5. Freudenmann RW, Lepping P. Second-generation antipsychotics in primary and secondary delusional parasitosis: outcome and efficacy. J Clin Psychopharmacol 2008;28:500-8.
6. Ahmad K, Ramsay B. Delusional parasitosis: lessons learnt. Acta Derm Venereol 2009;89:165-8.
7. Kulkarni K, Arasappa R, Prasad MK, Zutshi A, Chand PK, Murthy P, et al. Risperidone versus olanzapine in the acute treatment of persistent delusional disorder: a retrospective analysis. Psychiatry Res 2017;253:270-3.
8. Quintin P, Thomas P. Efficacy of atypical antipsychotics in depressive syndromes. Encephale 2004;30:583-9.
9. Kamińska K, Golembiowska K, Rogóż Z. Effect of risperidone on the fluoxetine-induced changes in extracellular dopamine, serotonin and noradrenaline in the rat frontal cortex. Pharmacol Rep 2013;65:1144-51.



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# An Unexpected Cause of Trauma-related Myocardial Infarction: Multimodality Assessment of Right Coronary Artery Dissection

**Dear Editor,**

Blunt cardiac injury refers to injury sustained due to blunt trauma to the heart. It encompasses a spectrum of pathologies ranging from myocardial contusion; myocardial, pericardial and valvular rupture/aneurysm to coronary artery injuries (dissection, thrombosis or rupture). The clinical manifestations range from clinically silent, transient arrhythmias, to acute myocardial infarction (AMI) and sudden cardiac death. The true incidence of blunt chest injury is unknown as reported rates vary greatly in the literature, ranging between 8% and 71%.[1]

**Case Report**

A 28-year-old male cyclist sustained blunt chest injury during a road traffic accident. Apart from transient loss of consciousness during the accident, he remained haemodynamically stable thereafter.

The electrocardiograph (ECG) (Fig. 1) showed Q waves and 2 mm ST elevation in leads II, III and aVF (inferior leads) with reciprocal ST depression in leads I and aVL (lateral leads), suspicious for an inferior myocardial infarction. Another ECG performed 30 minutes later showed persistent Q waves in the inferior leads but interval resolution of ST elevation in the inferior and lateral leads. A contrast-enhanced non-cardiac-gated thoracic computed tomography (CT) scan showed fractures of the upper ribs and right transverse process of the 7th cervical vertebra, small mediastinal haematoma, lung contusions and bilateral pneumothoraces. The troponin I increased from 10 ng/dL to >72,000 ng/dL (normal range 0-39 ng/dL). Subsequent serial ECGs revealed T wave inversion in leads III, aVF and V1, suggestive of an evolving subendocardial myocardial infarction.

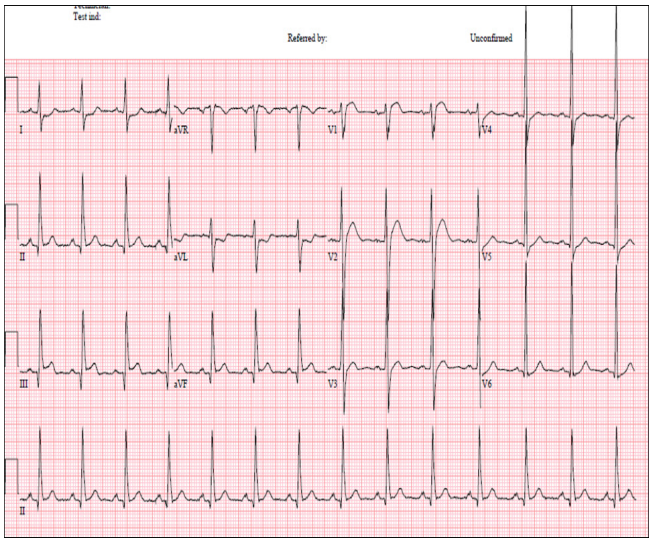


Fig. 1. A 12-lead ECG showed 2 mm ST elevation in leads II, III and aVF with reciprocal ST depression in leads I and aVL, suspicious for an inferior myocardial infarction.

Transthoracic echocardiogram showed inferoseptal and inferior regional wall motion abnormality. No pericardial effusion was detected (Fig. 2). Retrospectively, subendocardial hypoenhancement of the inferoseptal and inferior wall of the left ventricle was seen in the initial thoracic CT scan (Fig. 3). This was in keeping with myocardial infarction in the right coronary artery (RCA)

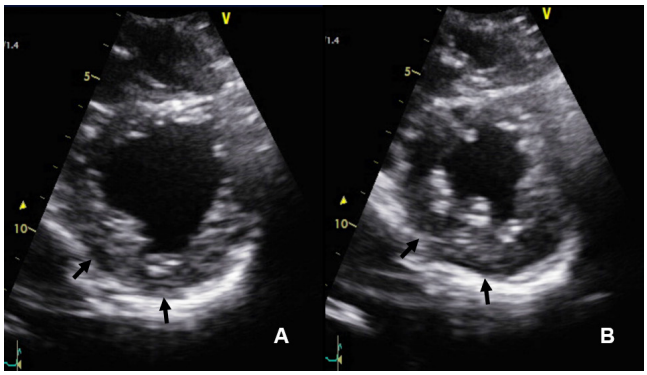


Fig. 2. Short axis images from echocardiogram in ventricular diastole (image A) and systole (image B) showed regional wall motion abnormality in the inferoseptal and inferior wall (arrows). No pericardial effusion was detected.

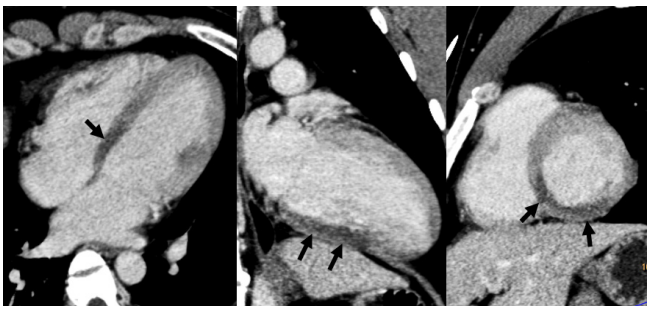

Fig. 3. Multiplanar reformats of the non-cardiac gated CT thorax images in the 4-chamber, 2-chamber and short axis views of the heart showed extensive subendocardial hypoenhancement involving the inferoseptal and inferior wall of the left ventricle (arrows), in keeping with myocardial infarction in the RCA territory.

territory. Since the patient remained well without any signs and symptoms to suggest an AMI, an initial diagnosis of cardiac contusion was made.

The patient was managed conservatively but 5 days following admission, the cardiovascular magnetic resonance imaging (CMR) (Fig. 4) showed features of acute myocardial infarction in the RCA territory. Late gadolinium enhancement (LGE) images showed LGE at the basal and mid-cavity inferoseptal and inferior left ventricular wall (RCA territory). The early gadolinium enhancement images showed subendocardial hypointense foci in the above myocardial segments, indicative of microvascular obstruction (no reflow phenomenon). There was moderate to severe hypokinesia in the same segments on the cine gradient echo images.

CT coronary angiogram (CTCA) (Fig. 5) showed proximal RCA dissection with the true lumen being compressed by the false lumen. As there was good distal runoff in the RCA and the patient remained asymptomatic, no invasive imaging or intervention was performed. The patient was treated medically with a plan to return for follow-up assessment and imaging.

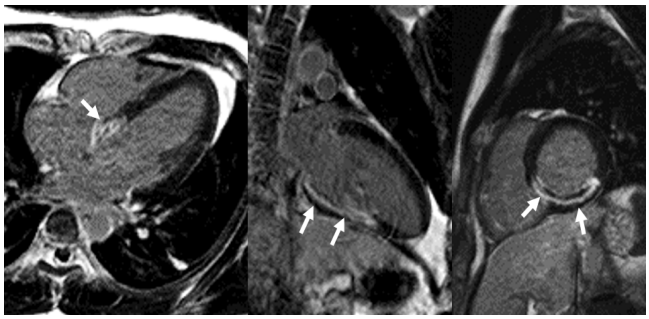

Fig. 4. Corresponding 4-chamber, 2-chamber and short axis late gadolinium CMR images showed LGE in the basal to mid cavity inferoseptal and inferior wall of the left ventricle (arrows), corresponding to the findings on the initial non-cardiac-gated thoracic CT scan. Subendocardial foci of hypointensity within the RCA territory myocardial infarction is in keeping with no reflow phenomenon, also known as microvascular obstruction.

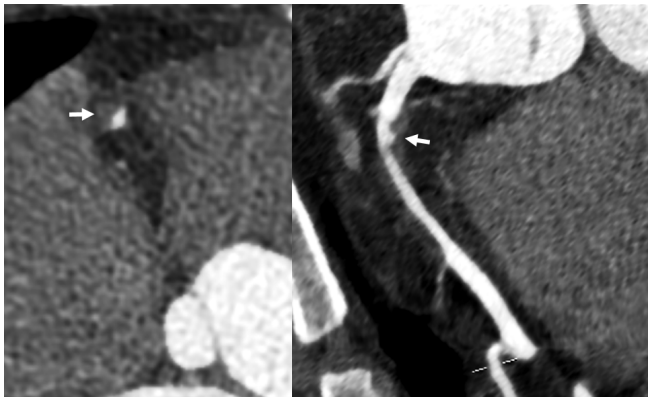

Fig. 5. Multiplanar reformatted images of the RCA from a 3rd generation dual-source CT coronary angiogram study 5 days after the trauma showed irregular severe luminal narrowing of the true lumen of the proximal RCA secondary to mass effect from the false lumen (arrows), in keeping with a dissection. A small outpouching of contrast proximally was suspicious for an intimal tear. There was good distal run-off with contrast present in the mid and distal RCA.

## Discussion

The sequelae from blunt chest injury can vary from a simple arrhythmia to myocardial rupture. Coronary artery dissections are exceedingly rare in the clinical context of blunt chest injury. Autopsy studies of blunt chest trauma have revealed that injuries to the heart and coronary arteries are present in 20% and less than 2% of the study cohort respectively.[2] The mortality rate is high—ranging from 13.8% to 43.1%[3]—and is dependent on the severity of blunt chest injury assessed using the abbreviated injury score.

Traumatic coronary artery dissections are exceedingly rare. The most frequently injured vessel is the left anterior descending artery (71.4%) followed by the RCA (19%), left main coronary artery (6.4%) and left circumflex artery (3.2%).[4] The pathogenesis of acute AMI following trauma-induced coronary artery dissection is unclear, but shearing forces during the traumatic episode may produce a small intimal tear which subsequently initiates the process of thrombus formation.

Clinical manifestations of coronary dissection and cardiac contusion are variable and often overlap. It is often difficult to establish an accurate diagnosis because chest pain can be overshadowed by concomitant injuries. We recommend that patients with i) ECG changes suggestive of ongoing myocardial ischaemia, such as evolving and focal myocardial infarction, ii) unresolving or worsening chest pain, iii) persistent elevation or rising troponin I and; iv) worsening cardiogenic shock should undergo further non-invasive cardiac imaging such as CMR or CTCA.

There are no specific recommendations regarding the choice of advanced cardiac imaging modalities for assessing blunt chest injury currently.[5] With the widespread availability of multi-detector CT scanners, CTCA can now be easily performed for diagnostic imaging in patients with significant trauma and cardiac injury. It is fast, non-invasive and provides good quantitative and qualitative assessment of the coronary arteries and aortic root. CTCA can accurately identify the location and extent of coronary injury and differentiate between plaque rupture, thrombus, dissection or external compression.[6] This negates the potential risks of catheter-related injury, including propagation of the coronary artery dissection. Although CTCA exposes the patient to ionising radiation, the radiation dose can be as low as below 1 millisievert (mSv) (equivalent to less than 50 chest x-rays) using the latest CT scanners.[7] CMR is a useful complementary non-ionising imaging modality, which can distinguish myocardial infarction from myocardial contusion.

The management of coronary artery dissection from blunt chest injury remains controversial because of their rare occurrence. Percutaneous coronary intervention, coronary artery bypass grafting, thrombolysis and conservative medical treatment in the setting of AMI associated with blunt chest injury, have all been reported with good clinical outcomes.[8-9] Our patient was managed medically with good clinical recovery.

## Conclusion

AMI secondary to coronary artery dissection is a rare complication from blunt chest injury, but it carries high morbidity and mortality. Vigilance and a high index of suspicion are necessary when managing patients with blunt chest injury. Timely intervention may be vital for myocardial recovery and prevention of further progression of coronary artery dissection. CTCA should be utilised as a form of non-invasive imaging during the investigation of blunt chest injury in the appropriate clinical context. We propose that in haemodynamically stable patients with a high clinical suspicion of cardiac injury, CTCA should be performed.

REFERENCES


1. Parr MJ. Blunt cardiac injury. Minerva Anestesiol 2004;70:201-5.
2. Pretre R, Chilcott M. Blunt trauma to the heart and great vessels. N Engl J Med 1997;336:626-32.
3. Hanschen M, Kanz KG, Kirchhoff C, Khalil PN, Wierer M, Van Griensven M, et al. Blunt cardiac injury in the severely injured – a retrospective multicentre study. Plos One 2015;10:e0131362.
4. Christensen MD, Nielsen PE, Sleight P. Prior blunt chest trauma may be a cause of single vessel coronary disease; hypothesis and review. Int J Cardiol 2006;108:1-5.
5. Clancy K, Velopulos C, Bilaniuk JW, Collier O, Crowley W, Kurek S, et al. Screening for blunt cardiac injury: an Eastern Association for the Surgery of Trauma practice management guideline. J Trauma Acute Care Surg 2012;73:S301-6.
6. Malbranque G, Serfaty JM, Himbert D, Stegj PG, Laissy JP. Myocardial infarction after blunt chest trauma: usefulness of cardiac ECG-gated CT and MRI for positive and aetiologic diagnosis. Emerg Radiol 2011;18:271-4.
7. Halliburton SS, Abbara S, Chen MY, Gentry R, Mahesh M, Raff GL, et al. SCCT guidelines on radiation dose and dose-optimization strategies in cardiovascular CT. J Cardiovasc Comput Tomogr 2011;5:198-224.
8. Ucar FM, Sen F, Karamanliogli M, Cagli K. Airbag inflation-related left main coronary artery dissection, localized aortic dissection and aortic valve dehiscence in a patient with previous coronary artery surgery. Int J Cardiol 2014;173:118-9.
9. Keresztesi AA, Asofie G, Jung H. Traumatic coronary dissection: case presentation and literature review. Journal of Interdisciplinary Medicine 2016;1:282-6.



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# Multiple Erythematous Plaques with Palpable Purpura in a Febrile Patient

A 71-year-old Malay man was admitted to the Medicine department with complaints of swelling of the left submandibular area with sore throat and rashes for 1 month. His past medical history included hypertension, hyperlipidaemia, bilateral cataracts and haemorrhoids. The rash started on his arms and rapidly progressed to involve the trunk and lower limbs. He denied taking any new medications and was well prior to these symptoms. On examination, he was persistently febrile and had an enlarged 6 cm x 6 cm left submandibular lymph node. He also had multiple erythematous and dusky plaques over his trunk and limbs (Fig. 1). Computed tomography (CT) scan of the neck, thorax, abdomen and pelvis revealed enlarged bilateral cervical, right intraparotid, axillary, obturator, iliac, aortocaval and para-aortic lymph nodes. Further investigations revealed a normocytic and normochromic anaemia, an elevated leukocyte count of 13.9 x $10^9$/L with lymphocytosis and raised serum levels of immunoglobulin (Ig)A, IgG and IgM. A detailed infection screen including multiple blood cultures was negative. Skin biopsy demonstrated superficial and deep, perivascular and periadnexal infiltration by atypical, medium-sized lymphoid cells which stained positive for CD3, CD4 and CD10 (Fig. 2). Cervical lymph node core biopsy showed diffuse effacement of nodal architecture with atypical lymphocytes showing CD2, CD3 and CD4 positive cells with scattered CD10 positivity (Fig. 3). There was also reduced CD7 and CD5 staining which is consistent with neoplastic aberrancy, and the proliferation index was raised. CD23 staining showed some follicular dendritic cells juxtaposed against high endothelial venules. Epstein-Barr virus-encoded small ribonucleic acid (EBER) was not detected in both biopsies. Bone marrow trephine biopsy showed hypercellular trilineage haematopoiesis without any immunohistochemical evidence of lymphomatous involvement. During his hospitalisation,

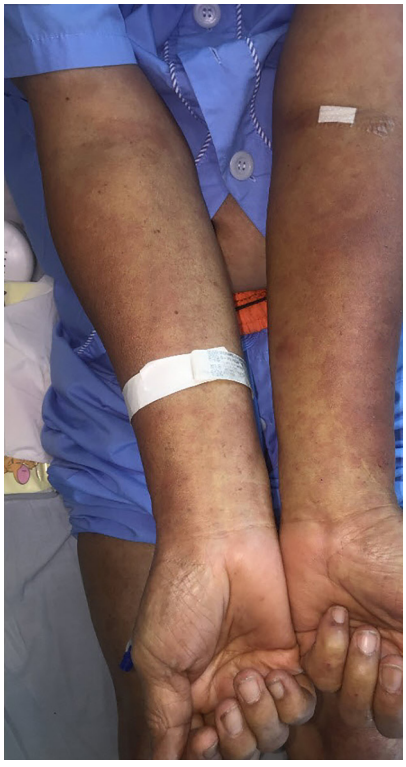

Fig. 1. Erythematous plaques over the patient's upper limbs.

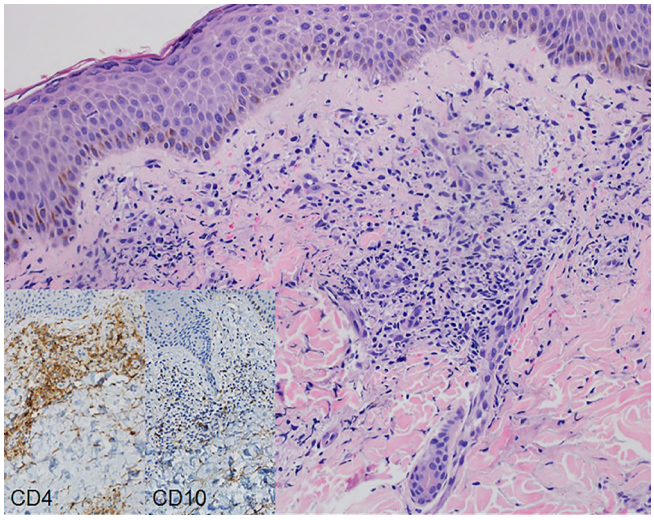


Fig. 2. Superficial dermal perivascular polymorphous lymphoid infiltrate with atypical lymphoid cells (haematoxylin and eosin, 40x) which are immunoreactive to CD4 and CD10.

the patient developed new onset rapidly progressive palpable purpura over his lower legs (Fig. 4). Biopsy of these lesions for histology and direct immunofluorescence revealed leukocytoclastic vasculitis with IgA and C3 deposits within the blood vessels, without any atypical lymphocytes. The patient was started on chemotherapy with the cyclophosphamide, doxorubicin, etoposide, vincristine and prednisolone (CHEOP) regime, which led to complete and rapid resolution of his skin lesions.

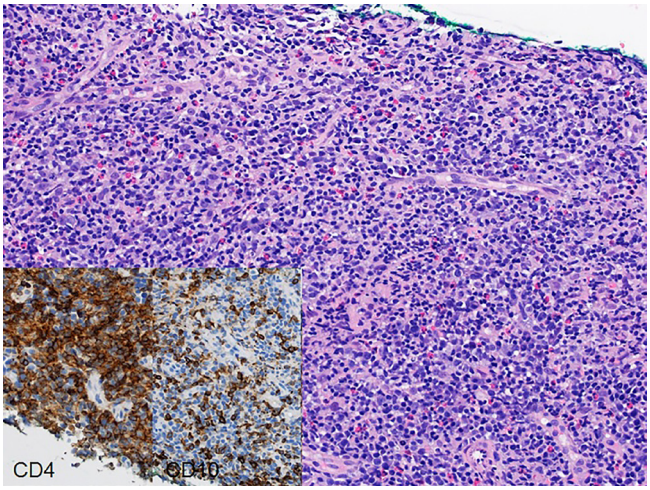


Fig. 3. Polymorphous lymphoid infiltrate with some eosinophils and larger lymphoid cells (haematoxylin and eosin, 40x) which are immunoreactive to CD4 and CD10 (400x).

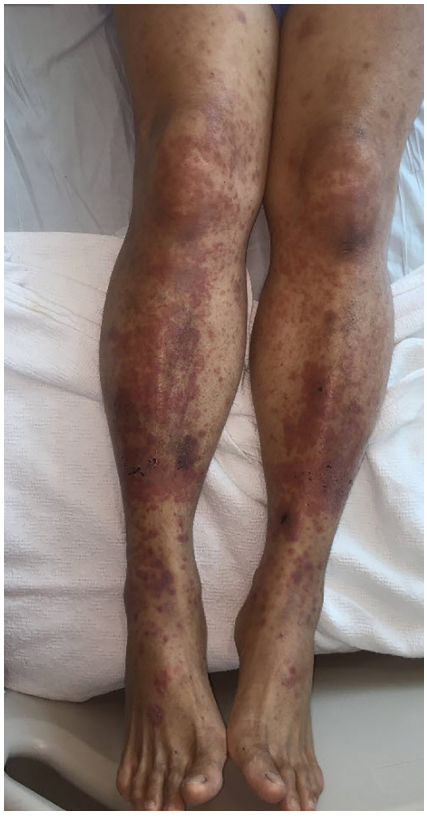

Fig. 4. Purpuric lesions over the patient's legs.

What is your diagnosis?

A. Lupus erythematosus
B. Sarcoidosis
C. Angioimmunoblastic T-cell lymphoma (AITL) with vasculitis
D. Adverse drug reaction
E. Septic vasculitis

**Discussion**

AITL is a distinct subtype of peripheral T-cell lymphoma affecting older patients and has an aggressive clinical course.[1] It arises from the malignant transformation of follicular T helper cells. Epstein-Barr virus (EBV) has been implicated in the pathogenesis, although this was not found in our patient. Other factors recently described to be important in the pathogenesis include vascular endothelial growth factor (VEGF) and over production of the CXCL13 cytokine.[2] The latter is responsible for B-cell activation and causes the polyclonal hypergammaglobulinaemia (as seen in our patient) frequently found in AITL. This also causes other manifestations of immune dysregulation including haemolytic anaemia, cold agglutins and autoantibodies.[1] Recently, novel mutations in *RHOA* genes as well as in epigenetic factors like *TET2*, *IDH2* and *DNMT3A* have been identified in AITL subsets.[3] On histology, it is noted to cause effacement of lymph node architecture and formation of high endothelial venules. Immunohistochemistry reveals the expression of CD4 and CD10 on the neoplastic T-cells.[2] The absence of granulomas, interface changes and any bacteria rule out the other diagnoses.

AITL frequently presents with fever, weight loss, generalised lymphadenopathy and hepatosplenomegaly. Skin manifestations have been reported in 21% to 49% cases of AITL and include maculopapular eruptions, erythroderma and nodules, as well as urticarial and vasculitic lesions. IgA-related paraneoplastic manifestations including vasculitis have been described in relation to haematologic and solid tumour malignancies.[4] However, IgA vasculitis in association with AITL is very rare with only 1 published case report so far.[5] It is not clear why this association exists, but immunological defects have been postulated, especially since immunoregulatory dysfunction is commonly found in AITL. The fact that our patient's purpuric lesions developed shortly after his initial presentation and resolved promptly with chemotherapy suggests that the vasculitis may have been causally linked to his AITL.

The presence of IgA-related autoimmune manifestations in adulthood warrants a workup for underlying malignancy. In our patient, the vasculitis developed after the onset of his

Answer: C

skin and systemic manifestations. However, it is possible for vasculitis to occur before or even concomitantly with the primary malignancy.

To our knowledge, this is the second case report of AITL with associated IgA vasculitis. We would also like to highlight the significance of IgA vasculitis in an adult when it can be a harbinger of an underlying malignancy.

REFERENCES

1. Federico M, Rudiger T, Bellei M, Nathwani BN, Luminari S, Coiffier B, et al. Clinicopathologic characteristics of angioimmunoblastic T-cell lymphoma: analysis of the International Peripheral T-Cell Lymphoma Project. J Clin Oncol 2013;31:240-6.
2. Dunleavy K, Wilson WH, Jaffe ES. Angioimmunoblastic T cell lymphoma: pathobiological insights and clinical implications. Curr Opin Hematol 2007;14:348-53.
3. Rodríguez-Cortés J, Palomero T. The curious origins of angioimmunoblastic T-cell lymphoma. Curr Opin Hematol 2016;23:434-43.
4. Taintor AR, Leiferman KM, Hashimoto T, Ishii N, Zone JJ, Hull CM. A novel case of IgA paraneoplastic pemphigus associated with chronic lymphocytic leukemia. J Am Acad Dermatol 2007;56:S73-6.
5. Sugaya M, Nakamura K, Asahina A, Tamaki K. Leukocytoclastic vasculitis with IgA deposits in angioimmunoblastic T cell lymphoma. J Dermatol 2001;28:32-7.

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