Bahrain Medical Bulletin, Vol. 36, No. 3, September 2014

Risk for Obstructive Sleep Apnea among People with Diabetes

Jameel Nasser, MD, MSc* Fatima Habib, MD, MSc* Fatima Malallah, MD* Nada Darwish, MD* Ebtisam Rabie, MD*

ABSTRACT

Objective: The aim of this study is to identify people at high risk for Obstructive Sleep Apnea (OSA) and to evaluate the impact of OSA on the control of cardiovascular risk factors.

Design: A Cross-Sectional Study.

Setting: Four Primary Health Care Centers.

Method: Patients attending diabetes clinics in four health centers were screened for OSA by using the Berlin questionnaire. In addition, patients' medical records were reviewed for age, sex, body mass index (BMI), blood pressure, glycated hemoglobin, lipid profile, antihypertensive, hypoglycemic agents and previous OSA diagnosis.

Result: A total of 455 questionnaires were analyzed. All patients included were type 2. The mean age was 56.6 years. High risk for OSA was present in 173 (38%) patients. It was more common among females (P=0.013). There was no significant age difference (P=0.75). The risk of OSA increased significantly with BMI≥35 (P<0.001). No significant difference was found between low and high risk in the control of glycated hemoglobin, lipid profile, and the number of drugs used. Three (1.7%) patients from the high OSA risk and 2 (0.71%) from the low risk (282) had previous OSA diagnosis.

Conclusion: More than one-third of our patients were high risk for OSA. Screening for OSA among diabetics is lacking despite the presence of high number of at risk patients. Increasing awareness of the treating physicians is needed.

---

* Family Physician
Ministry of Health
Kingdom of Bahrain
Email: jnasser66@yahoo.com

INTRODUCTION

Obstructive Sleep Apnea (OSA) is a breathing disorder in which the affected person frequently stops breathing during sleep as a result of obstruction of the upper airways due to inadequate motor tone of the tongue and/or airway dilator muscles[1]. It is diagnosed by using overnight standardized, facility-based polysomnography to detect the frequency of apnea and hypopnea events. OSA is diagnosed when the apnea and hypopnea index (the number of events per hour) is greater than 15 or greater than 5 in a person who reports any of the following: unintentional sleep

episodes during wakefulness, daytime sleepiness, non-refreshing sleep, fatigue, insomnia, waking up breath holding, gasping, or choking, or the bed partner describing loud snoring, breathing interruptions or both during the patient's sleep[2].

Obstructive sleep apnea is a common primary health care problem[3-6]. Furthermore, OSA is associated with serious clinical conditions; it could worsen diabetes and blood pressure (BP)[7,8]. In addition, OSA increases the risks for stroke, heart failure, neuropathy, depression, road traffic accidents, cancer and mortality[9-14].

The relationship between diabetes and OSA is bidirectional. Obstructive sleep apnea is a risk factor for diabetes independent of traditional risk factors[15,16]. Furthermore, it has been found that the level of glycated hemoglobin increases linearly with the severity of OSA in non-diabetic individuals[17]. On the other hand, OSA is highly prevalent among people with diabetes[4,5,18-20].

Screening for OSA is important for various reasons. While OSA is common, it remains largely undiagnosed[4,5,20-22]. Presentation of OSA could be atypical[23,24]. Furthermore, OSA is commonly associated with known diabetic complications[4,9-11,25,26]. Lastly, screening and initiation of treatment may contribute to prevention and improved control of co-morbid conditions[16,27-29].

There are no studies about OSA among people with diabetes in the Kingdom of Bahrain.

The aim of this study is to identify people at high risk for OSA and to evaluate the impact of OSA on the control of cardiovascular risk factors.

METHOD

Four health centers were chosen randomly. Patients who attended diabetes clinics between 15 April to 15 July 2013 were invited to participate in the study. Patients were screened by using the Berlin questionnaire. This questionnaire has been validated for OSA screening in primary care and other settings[3,5,6,22,30-34]. The questionnaire has been validated in patients with diabetes[5,20]. The Arabic version of this questionnaire has recently been used in a similar study; the author has been contacted and permission was granted to use the Arabic version in our study[33].

The questionnaire is a self-report instrument that is focused on a set of known symptoms and clinical features associated with sleep apnea. One introductory question and four follow-up questions concerned snoring, witnessed apneas and the frequency of such events. Three questions addressed daytime sleepiness with a sub-question about drowsy driving. One question asked about history of high BP. Body Mass Index (BMI) is calculated based on self-reported height and weight of the participant. However in this study, we obtained the most recent BMI of the surveyed patients from their medical records.

High risk and lower risk groups for OSA are based on responses. Category 1, a positive score for risk is defined as frequent symptoms (more than three to four times per week or almost every day) in the questions about snoring and witnessed apneas; category 2, a positive score for risk is frequent symptoms in two or more questions about awakening sleepy, wake time sleepiness, and/or drowsy driving; category 3, a positive score for risk is defined as a self-report of high BP

and/or BMI of ≥30 kg/m^2. To score high for OSA, an individual's questionnaire must have had positive scores in two of the three categories or in all three. Those patients who denied having symptoms with such frequency, or who qualified in only one category are classified as low risk group[30].

In addition, we reviewed the patients' medical records for age, gender, BMI, BP, lipid profile, glycated hemoglobin (A1C), drugs used for hypertension and medications (oral and injectables) used to treat diabetes. We defined controlled BP, A1C, and lipid parameters according to recent American Diabetes Association (ADA) guidelines[36].

Data were analyzed by using SPSS software, version 20. Chi-squared test was used to assess the association between OSA and each of the following factors: age, gender, BMI, level of control of BP, A1C, lipid profile, antihypertensive and hypoglycemic drugs used. Multiple logistic regression model that included all the studied risk factors and OSA status as the dependent variable was set to determine the independent predictors for OSA. P-value less than 0.05 was considered statistically significant.

RESULT

We surveyed 484 patients. Twenty-nine questionnaires were excluded because they were incomplete. A total of 455 questionnaires were analyzed. All patients were type 2. The mean age was 56.6 years. Two hundred sixty-six (58.5%) were females. High risk for OSA was present in 173 (38%) patients, see table 1.

Table 1: Patients' Age Groups and Gender

Age group	Males	Females	Total
≤39	15(8)	16(6)	31(6.8)
40-49	21(11.1)	50(18.8)	71(15.6)
50-59	66(34.9)	99(37.2)	165(36.3)
≥60	87(46)	101(38)	188(41.3)
Total	189(100)	266(100)	455(100)

There was no significant gender difference between age groups (P value= 0.113). Risk for OSA was more common among females (113/173; 65%) and the association was statistically significant (P=0.013). There was no significant association between risk for OSA and age groups, see table 2.

Table 2: Risk for OSA by Age Groups

Age group	High OSA risk	Low OSA risk	Total	P value
≤39	11 (6.4)	20 (7.1)	31 (6.8)	0.756
40-49	31 (17.9)	40 (14.2)	71 (15.6)	
50-59	65 (37.6)	100 (35.5)	165 (36.3)	
≥60	66 (38.1)	122 (43.2)	188 (41.3)	

Total	173 (100)	282 (100)	455 (100)	

It was found that 397 (87.3%) patients were having BMI ≥25kg/m^2 and 264 (58%) were obese (BMI ≥30). One hundred and seventy one (171/264; 64.8%) obese patients were females. Only 25 (25/266; 9.4%) females were having normal BMI (<25). There was statistically significant association between BMI and OSA risk. The risk is lower in normal and overweight. However, it increased significantly with BMI ≥35, see table 3 and figure 1.

Table 3: BMI and OSA risk

BMI category(kg/m^2)	High risk	Low risk	Total	P value
≤24.9	10 (5.8)	32 (11.5)	42 (9.3)	0.00
25-29.9	38 (22.1)	98 (35.3)	136 (30.2)	
30-34.9	51 (29.6)	93 (33.5)	144 (32)	
35-39.9	44 (25.6)	31 (11.1)	75 (16.7)	
≥40	29 (16.9)	24 (8.6)	53 (11.8)	
Total	172* (100)	278** (100)	450 (100)	

*missing data for 1 patient;**missing data for 4 patients

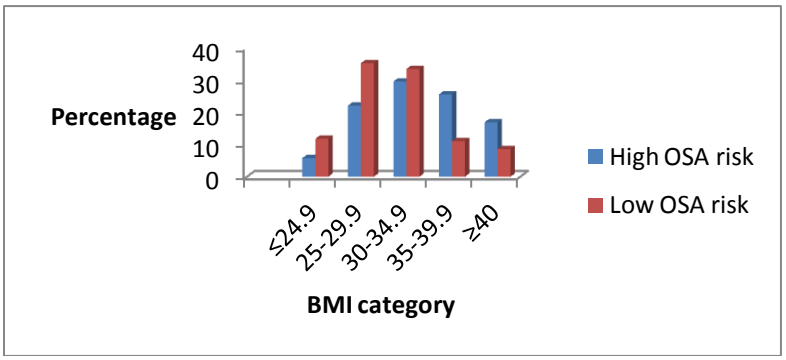

Figure 1: BMI and OSA Risk

Three hundred nine (67.9%) patients were on antihypertensive medications; hypertension was present in 131/173 (75.7%) patients who are at high risk for OSA. Thirty patients out of 309 (9.7%) were having uncontrolled BP (≥140/80); 16 (53.3%) patients were from high risk group. One hundred eight out of 309 (35%) patients were on 3 or more medications. There was no statistically significant difference in the number of antihypertensive medications used between low and high risk groups (P=0.31).

There was no statistically significant difference in A1C and lipid control between low and high OSA risk patients, see table 4.

Table 4: Diabetes, Lipid Control and OSA Risk

Indicator	High OSA risk	Low OSA risk	Total	P value
A1C<53*(mmol/mol)	73 (42.2)	116 (41.1)	189 (41.5)	0.450
A1C≥53	100 (57.8)	166 (58.9)	266 (58.5)	

Total	173 (100)	282 (100)	455 (100)	
LDL**<2.6(mmol/l)	101 (58.4)	184 (65.2)	285 (62.6)	0.086
LDL≥2.6	72 (41.6)	98 (34.8)	170 (37.4)	
Total	173 (100)	282 (100)	455 (100)	
TG***<1.7(mmol/l)	84 (48.6)	157 (55.7)	241 (53)	0.084
TG≥1.7	89 (51.4)	125 (44.3)	214 (47)	
Total	173 (100)	282 (100)	455 (100)	

*equivalent to 7% (ref.36), **Low Density Lipoproteins, ***Triglycerides

There was no significant difference in the number of anti-diabetic medications used between low and high OSA risk patients (P=0.825). Three (1.7%) patients out of 173 from high OSA risk and 2 (0.71%) out of 282 from low OSA risk had previous OSA diagnosis.

In the multiple logistic regressions model, BMI was found to be a significant predictor for OSA [P value<0.001, Odds ratio 0.674 (0.562-0.809)].

DISCUSSION

This study showed that over one-third of the patients are at high risk for OSA. It is more common among females. It is associated with moderate and severe obesity, but not with age, diabetes or lipid control. It was also found that OSA is mainly undiagnosed among the patients surveyed.

The prevalence of OSA (37.4%) found in this study is similar to a study using pulse oximetry; however, the prevalence in our study is likely to be underestimated because the prevalence of obesity in our study was 58% compared to 32%[37]. In a study using the Berlin questionnaire, the prevalence was 48%; most patients (96.8%) were either obese or hypertensive[5]. Obesity and hypertension are known risk factors for OSA which are prevalent among our study participants[18-20,38,39]. Indeed, obesity not only predicts OSA, but also its severity[40]. Furthermore, the presence of co-morbid obesity and hypertension among these patients increase the risk for OSA significantly[41]. In addition, females who constituted about 58% of our study's participants are more likely to present with atypical symptoms[23,39,42].

In this study, OSA was common in females. Male gender is a known risk factor for OSA as found in several studies[6,18,32,35,39]. The likely explanation for our finding is that most female patients (75.2%) were either peri-menopausal or menopausal (≥50 years), most of the high risk patients (75.7%) were in this age group. Male predominance usually disappears in older age and the risk for OSA increases with menopause[39,43-45]. In addition, about two-third of the obese patients in the study were females.

In this study, hypertension was present in about two-third of the patients, while 75% of the high risk group were hypertensive. Hypertension is strongly associated with OSA. It is an independent risk factor for OSA and patients with OSA are at higher risk to develop hypertension[46,47]. OSA was found to be the most common cause of secondary resistant hypertension[48]. Hence, the presence of resistant hypertension should urge the treating physician to evaluate the patient for OSA.

The study showed that A1C is almost similar between low and high risk group while lipids control was worse in high risk group but did not reach statistical significance. However, the level of control is far from optimal level as found in a recent study[49]. While some studies found that treatment of OSA improves A1C, the results are inconsistent[7,29,50].

The strong association between OSA and metabolic syndrome components on one hand and the presence of mixed results about the efficacy of OSA treatment (especially in mild to moderate cases) highlights the importance of screening[51]. Unfortunately, this study found that only 2 patients from high risk group had previous OSA diagnosis. However, under-diagnosis is a consistent finding in primary care settings[4,5,21,22,52]. This could be related to lack of awareness of the treating physicians about OSA and its consequences[53].

CONCLUSION

More than one-third of our patients were high risk for OSA. Screening for OSA among diabetics is lacking despite the presence of high number of at risk patients. Increasing awareness of the treating physicians is needed.

Author Contribution: All authors share equal effort contribution towards (1) substantial contributions to conception and design, acquisition, analysis and interpretation of data; (2) drafting the article and revising it critically for important intellectual content; and (3) final approval of the manuscript version to be published. Yes.

Potential Conflicts of Interest: None.

Competing Interest: None. **Sponsorship:** None.

Submission Date: 16 January 2014. **Acceptance Date:** 10 May 2014.

Ethical Approval: Approved by the Research Committee for Primary Healthcare, MOH, Bahrain.

REFERENCES

1. Park JG, Ramar K, Olson EJ. Updates on Definition, Consequences, and Management of Obstructive Sleep Apnea. Mayo Clin Proc 2011; 86(6):549-54.
2. Epstein LJ, Kristo D, Strollo PJ Jr, et al. Clinical Guideline for the Evaluation, Management and Long-Term Care of Obstructive Sleep Apnea in Adults. J Clin Sleep Med 2009; 5(3):263-76.
3. BaHammam AS, Alrajeh MS, Al-Jahdali HH, et al. Prevalence of Symptoms and Risk of Sleep Apnea in Middle-Aged Saudi Males in Primary Care. Saudi Med J 2008; 29(3):423-6.
4. Burgess KR, Havryk A, Newton S, et al. Targeted Case Finding for OSA within the Primary Care Setting. J Clin Sleep Med 2013; 9(7):681-6.
5. Cass AR, Alonso WJ, Islam J, et al. Risk of Obstructive Sleep Apnea in Patients with Type 2 Diabetes Mellitus. Fam Med 2013; 45(7):492-500.
6. Netzer NC, Hoegel JJ, Loube D, et al. Prevalence of Symptoms and Risk of Sleep Apnea in Primary Care. Chest 2003; 124(4):1406-14.
7. Aronsohn RS, Whitmore H, Van Cauter E, et al. Impact of Untreated Obstructive Sleep Apnea on Glucose Control in Type 2 Diabetes. Am J Respir Crit Care Med 2010; 181(5):507-13.
8. He QY, Feng J, Zhang XL, et al. Elevated Nocturnal and Morning Blood Pressure in Patients with Obstructive Sleep Apnea Syndrome. Chin Med J (Engl) 2012; 125(10):1740-6.
9. Rice TB, Foster GD, Sanders MH, et al. The Relationship between Obstructive Sleep Apnea and Self-Reported Stroke or Coronary Heart Disease in Overweight and Obese Adults with Type 2 Diabetes Mellitus. Sleep 2012; 35(9):1293-8.
10. Gottlieb DJ, Yenokyan G, Newman AB, et al. A Prospective Study of Obstructive Sleep Apnea and Incident Coronary Heart Disease and Heart Failure: The Sleep Heart Health Study. Circulation 2010; 122(4):352-60.
11. Tahrani AA, Ali A, Raymond NT, et al. Obstructive Sleep Apnea and Diabetic Neuropathy. A Novel Association in Patients with Type 2 Diabetes. Am J Respir Crit Care Med 2012; 186(5):434-41.
12. Feng J, Chen BY, Chiang AA. Significance of Depression in Obstructive Sleep Apnea Patients and the Relationship between the Comorbidity and Continuous Positive Airway Pressure Treatment. Chin Med J (Engl) 2010; 123(12):1596-602.
13. De Mello MT, Narciso FV, Tufik S, et al. Sleep Disorders as a Cause of Motor Vehicle Collisions. Int J Prev Med 2013; 4(3):246-57.
14. Marshall NS, Wong KK, Cullen SR, et al. Sleep Apnea and 20-year Follow-up for All-cause Mortality, Stroke, and Cancer Incidence and Mortality in the Busselton Health Study Cohort. J Clin Sleep Med 2014; 10(4):355-62.
15. Wang X, Bi Y, Zhang Q, et al. Obstructive Sleep Apnoea and the Risk of Type 2 Diabetes: A Meta-Analysis of Prospective Cohort Studies. Respirology 2013; 18(1):140-6.
16. Nannapaneni S, Ramar K, Surani S. Effect of Obstructive Sleep Apnea on Type 2 Diabetes Mellitus: A Comprehensive Literature Review. World J Diabetes 2013; 4(6):238-44.

17. Pamidi S, Wroblewski K, Broussard J, et al. Obstructive Sleep Apnea in Young Lean Men Impact on Insulin Sensitivity and Secretion. Diabetes Care 2012; 35(11):2384-9.
18. Einhorn D, Stewart DA, Erman MK, et al. Prevalence of Sleep Apnea in a Population of Adults with Type 2 Diabetes Mellitus. Endocr Pract 2007; 13(4):355-62.
19. Foster GD, Sanders MH, Millman R, et al. Obstructive Sleep Apnea among Obese Patients with Type 2 Diabetes. Diabetes Care 2009; 32(6):1017-9.
20. West SD, Nicoll DJ, Stradling JR. Prevalence of Obstructive Sleep Apnoea in Men with Type 2 Diabetes. Thorax 2006; 61(11):945-50.
21. Heffner JE, Rozenfeld Y, Kai M, et al. Prevalence of Diagnosed Sleep Apnea among Patients with Type 2 Diabetes in Primary Care. Chest 2012; 141(6):1414-21.
22. Bailes S, Baltzan M, Rizzo D, et al. Sleep Disorder Symptoms are Common and Unspoken in Canadian General Practice. Fam Pract 2009; 26(4):294-300.
23. Glidewell RN, Roby EK, Orr WC. Is Insomnia an Independent Predictor of Obstructive Sleep Apnea? J Am Board Fam Med 2012; 25(1):104-10.
24. Jose B, Ali A, Begum S, et al. Obstructive Sleep Apnoea as a Cause of Headache Presenting to the Emergency Department. QJM 2011; 104(12):1087-9.
25. Banerjee D, Leong WB, Arora T, et al. The Potential Association between Obstructive Sleep Apnea and Diabetic Retinopathy in Severe Obesity—the Role of Hypoxemia. PLoS One 2013; 8(11):e79521.
26. Tahrani AA, Ali A, Raymond NT, et al. Obstructive Sleep Apnea and Diabetic Nephropathy A cohort study. Diabetes Care 2013; 36(11): 3718-25.
27. Buchner NJ, Sanner BM, Borgel J, et al. Continuous Positive Airway Pressure Treatment of Mild to Moderate Obstructive Sleep Apnea Reduces Cardiovascular Risk. Am J Respir Crit Care Med 2007; 176(12):1274-80.
28. Marin JM, Agusti A, Villar I, et al. Association between Treated and Untreated Obstructive Sleep Apnea and Risk of Hypertension. JAMA 2012; 307(20):2169-76.
29. Dawson A, Abel SL, Loving RT, et al. CPAP Therapy of Obstructive Sleep Apnea in Type 2 Diabetics Improves Glycemic Control during Sleep. J Clin Sleep Med 2008; 4(6):538-42.
30. Netzer NC, Stoohs RA, Netzer CM, et al. Using the Berlin Questionnaire to Identify Patients at Risk for the Sleep Apnea Syndrome. Ann Intern Med 1999; 131(7):485-91.
31. Bouloukaki I, Komninos ID, Mermigkis C, et al. Translation and Validation of Berlin Questionnaire in Primary Health Care in Greece. BMC Pulm Med 2013; 13:6.
32. Khazaie H, Najafi F, Rezaie L, et al. Prevalence of Symptoms and Risk of Obstructive Sleep Apnea Syndrome in the General Population. Arch Iran Med 2011; 14(5):335-8.
33. Chung F, Yegneswaran B, Liao P, et al. Validation of the Berlin Questionnaire and American Society of Anesthesiologists Checklist as Screening Tools for Obstructive Sleep Apnea in Surgical Patients. Anesthesiology 2008; 108(5):822-30.
34. Abrishami A, Khajehdehi A, Chung F. A Systematic Review of Screening Questionnaires for Obstructive Sleep Apnea. Can J Anaesth 2010 M; 57(5):423-38.
35. Mahboub B, Afzal S, Alhariri H, et al. Prevalence of Symptoms and Risk of Sleep Apnea in Dubai, UAE. Int J Gen Med 2013; 6:109-14.
36. American Diabetes Association. Standards of Medical Care in Diabetes—2014. Diabetes Care 2014; 37(1):S14-S80.
37. Schober AK, Neurath MF, Harsch IA. Prevalence of Sleep Apnoea in Diabetic Patients. Clin Respir J 2011; 5(3):165-72.

38. Shim U, Lee H, Oh JY, et al. Sleep Disorder and Cardiovascular Risk Factors among Patients with Type 2 Diabetes Mellitus. Korean J Intern Med 2011; 26(3):277-84.
39. Lee W, Nagubadi S, Kryger MH, et al. Epidemiology of Obstructive Sleep Apnea: a Population-based Perspective. Expert Rev Respir Med 2008; 2(3):349-364.
40. Dacal Quintas R, Tumbeiro Novoa M, Alves Pérez MT, et al. Obstructive Sleep Apnea in Normal Weight Patients: Characteristics and Comparison with Overweight and Obese Patients. Arch Bronconeumol 2013; 49(12):513-7.
41. Drager LF, Genta PR, Pedrosa RP, et al. Characteristics and Predictors of Obstructive Sleep Apnea in Patients with Systemic Hypertension. Am J Cardiol 2010; 105(8):1135-9.
42. Alotair H, Bahammam A. Gender Differences in Saudi Patients with Obstructive Sleep Apnea. Sleep Breath 2008; 12(4):323-9.
43. Bixler EO, Vgontzas AN, Lin HM, et al. Prevalence of Sleep-disordered Breathing in Women. Effects of Gender. Am J Respir Crit Care Med 2001; 163(3 Pt 1):608-13.
44. Resta O, Caratozzolo G, Pannacciulli N, et al. Gender, Age and Menopause Effects on the Prevalence and the Characteristics of Obstructive Sleep Apnea in Obesity. Eur J Clin Invest 2003; 33(12):1084-9.
45. Kapsimalis F, Kryger M. Sleep Breathing Disorders in the U.S. Female Population. J Womens Health (Larchmt) 2009; 18(8):1211-9.
46. Sjöström C, Lindberg E, Elmasry A, et al. Prevalence of Sleep Apnoea and Snoring in Hypertensive Men: A Population Based Study. Thorax 2002; 57(7):602-7.
47. Marin JM, Agusti A, Villar I, et al. Association between Treated and Untreated Obstructive Sleep Apnea and Risk of Hypertension. JAMA 2012; 307(20):2169-76.
48. Pedrosa RP, Drager LF, Gonzaga CC, et al. Obstructive Sleep Apnea: The Most Common Secondary Cause of Hypertension Associated With Resistant Hypertension. Hypertension 2011; 58(5):811-7.
49. Nasser J, Habib F, Al Tajer B, et al. Risk Factors for Diabetic Retinopathy in Patients Attending Primary Care Settings. Bahrain Med Bull 2014; 36(1):9-13.
50. Surani S, Subramanian S. Effect of Continuous Positive Airway Pressure Therapy on Glucose Control. World J Diabetes 2012; 3(4): 65-70.
51. Tanigawa T. Obstructive Sleep Apnea: Its Prevention and Screening May Contribute to the Prevention of Hypertension, Diabetes and Cardiovascular Diseases. EPMA J 2011; 2(1):83-9.
52. Mold JW, Quattlebaum C, Schinnerer E, et al. Identification By Primary Care Clinicians of Patients With Obstructive Sleep Apnea: A Practice-Based Research Network (PBRN) Study. J Am Board Fam Med 2011; 24(2):138-45.
53. BaHammam AS. Knowledge and Attitude of Primary Health Care Physicians towards Sleep Disorders. Saudi Med J 2000; 21(12):1164-7.