

Study of Risk Factor Cotributory in the Development of Diabetic Foot Ulceration

MUJAHID ALAM¹, SABAHAT JAVAID BUTT², KHIZAR HAYYAT³, ASSAM ARSHAD⁴, SAMEEA MUBARAK⁵

ABSTRACT

Aim: To determine and evaluate the risk factor which leads to the development of diabetic foot ulcers.

Plan and study design: This descriptive study was conducted at surgical department of Akhtar Saeed Medical and Dental college Lahore between 2012 to 2017.

Method: 250 patients with Diabetic foot problems were evaluated demographically, detailed history, clinical examination, Labortary findings, and diabetic complications. Glycemic control was determined on the basis of FBS and HBA1C. Foot problems were classified according to Wagner's Grading.

Results: Majority of the patients were male and belonged to rural background. Foot problems were more common in patients with age group above 50 and obese (BMI >25). Patients more likely to develop foot problems that had duration of diabetes more than 10 years and presence of significant foot deformities. Smoking, peripheral neuropathy and history of unrecognized trauma to foot were also contributory factors in the development of foot problems in diabetic populations.

Conclusions: Effective glycemic control, smoking cessation, protecting the foot by the trauma, presence of previous foot ulceration and awareness about diabetic foot problem to the patients reduced the chances of developing foot problems in diabetic patients. Primary care physician can play a vital role to decrease foot complications in diabetic population by educating them and examination of the foot on each visit to rule out peripheral neuropathies.

Keywords: Diabetic foot ulcers, Risk factor, Demographic factor, Laboratory investing, Smoking, Glycemic control.

INTRODUCTION

Foot problems are the most common cause of hospitalization in Diabetes mellitus. Many of these patients end up in amputations^{1,2,3}. These problems include ulceration, infections, gangrene and destruction of the deep tissue, in association with neurological abnormalities and various degree of peripheral vascular diseases in lower limb⁴. The principal contributory factors in the development of diabetic foot ulcers are neuropathy, peripheral vascular disease, poor glycemic control, duration of diabetes, repeated trauma, foot deformity, past h/o ulcers or amputations, visual impairment and cigarette smoking⁵. Foot ulcer can be prevented by addressing these factors. In addition, patient education for foot care, optimal blood sugar control, evaluation and correction of peripheral neuropathy and arterial insufficiency are mandatory^{6,7} to avoid

foot ulceration. It is estimated that Pakistan will be ranked 4th in the world with about 13.9 million people suffering from diabetes in 2030^{8,9}. The incidence of diabetic foot diseases is 4 to 10 percent whereas in Pakistan it is reported to be as high as 15%¹⁰. This incidence can be reduced by addressing the various causative factors. This study is conducted to find out various risk factors that causes the development of Diabetic foot ulcers. The aim of this study is to evaluate factors which lead to DFU.

MATERIAL AND METHOD

This descriptive study was conducted at surgical department of Akhtar Saeed trust teaching hospital, Lahore from Oct 2012 to Mar 2017. All Patients who reported in the OPD /Indoor with foot problems having Diabetes Mellitus were included in this study. Thorough history including duration of diabetes, it's treatment, residential area, educational level, history of coronary, cerebro-vascular, peripheral arterial disease, previous ulceration or amputation, abnormal sensation(parasthesia and numbness) in the peripheral leg, blurring of vision (retinopathy), peripheral edema (nephropathy), smoking, hypertension, previous vascular surgery and angioplasty, intermittent claudication and rest pain were asked. General physical examination, recording

¹Associate Professor, Department of Surgery, Akhtar Saeed Medical College, Lahore

²Associate Professor, Deptt. Of Pathology, Institute of Dentistry, CMH Lahore Medical College

³Associate Professor, Deptt. Of Urology, Fatima Jinnah Medical College, Lahore

⁴Medical Officer, DHQ Sheikupura

⁵Consultant Gynaecologist, Nankana Hospital, Nankana

Correspondence: DR. Sabahat Javaid Butt; 46-A, Khuda Dad Street, Shalamar Town, Lahore E.mail: drsjbutt@yahoo.com, Cell: 0321-4270574; 0322-8400205

of blood pressure and anthropometric examination including BMI were done in all patients. Foot examination through touch and tuning fork was evaluated and abnormal sensation and visible foot deformities were noted. Foot ulcers were classified according to the Wagner's grade. The neurological assessment of the foot was done by 10g monofilament, vibration using 128-Hz tuning fork, pain sensations were noted by pinprick sensation, patellar and ankle reflexes were checked. Vascular status of the foot was assessed by palpating posterior tibial, dorsalis pedis, popliteal and femoral arteries. Ankle brachial pressure index (ABPI) were also recorded. Dermatological examination of the foot by colour, temperature, hair, nails, corn, callosity, fissure and toe web maceration were checked. Musculoskeletal assessment through the mobility of joints, foot deformities such as hallux valgus, flatfoot and toe deformities such as claw toe, hammer toe, Charcot foot and gait assessment were done. In patients who presented with osteomyelitis or cellulites, Bone to probe test was done to evaluate bone infection. Radiograph of the foot was taken to assess underlying bone involvement for osteomyelitis. Laboratory investigations including CBC/ESR, URINE C/E, URINE for microalbuminuria, HBA1C, fasting and 2 hours post-prandial blood glucose, serum albumin, serum lipid profile, serum creatinine level were conducted. Culture swab was taken and sent for culture and sensitivity before starting empirical antibiotics treatment.

Wound debridement done under suitable anesthesia to clear the wound from debris and promote wound healing. On pre-designed performa for data was filled and analyzed

RESULTS

A total number of 250 patients were included in this study. 179 patients were male and 71 patients were female. Maximum number of patients were in the age bracket of 50-59 years (100 patients,(Table 1).

Table 1: Age distribution (n=250)

Age (years)	n	%age
30-30	8	3.2
40-49	87	34.8
50-59	100	40
60-69	37	14.8
70-80	18	7.2

One hundred and sixty two patients had history of trauma (nail cutting, penetrating wound , punctured wound, corn and callosity, crush injuries, improper foot wearer etc.). This was an important initiating factor in the development of diabetic foot ulcer (DFU). 170 patients had diabetes of greater than 10 years

duration while 80 patients have duration of diabetes between 5 to 10 years. 162 patients had positive history of smoking while 88 patients had no h/o smoking. Majority of the patients had BMI >25(180 patients) while 70 had <25. Majority of patients with diabetic foot ulcer presented to us from rural area (165) than urban area. Majority of patients (170) lack awareness regarding diabetic foot problems. No awareness/information was given to them by their primary care physician.

The mean fasting plasma glucose level, 2 hours post-prandial glucose, HBA1c, creatinine, lipids were significantly higher in patients presented with foot problems due to diabetes

Table 2: Demographic presentation (n=250)

	n	%age
History of Trauma		
Yes	162	64.8
No	83	33.2
BMI		
>25	122	48.8
<25	128	51.2
Duration of Diabetic		
>5 Year	70	28
>10 Year	180	72
Smoking		
Yes	88	35.2
No	162	64.8
Residency		
Rural	155	62
Urban	95	38
Diabetic Foot problems		
Yes	80	32
No	170	68
S- Creatinine		
<1.2	105	42
>1.2	145	58
S-Albumin		
>3.2	37	14.8
<3.2	213	85.2
S-Lipid Profile		
Abnormal	176	70.4
Normal	74	29.6
HBA1C		
<7	85	34
>7	155	62
FBS		
>120 mg/dl	190	76
<120 mg/dl	60	24

Table 3 shows that majority of the patients had previous ulceration or h/o amputation. The presence of callosities, foot deformity and joint mobility were significantly higher. More than one foot deformity was present in DFU patients. Monofilament, vibration and pinprick sensation were lost in majority of patients who had DF problems and almost all who

had DFU. There was no significant decrease in ankle reflex. While majority of patients had palpable distal pulses

Table 3: Comparing between diabetic Foot patient with and without Foot ulcer in terms of diabetic foot examination (n=250)

Foot Examination	n	%age
Previous Foot Ulcers / Amputation		
Present	180	72
absent	70	28
Normal Foot Skin		
Foot Deformities	190	76
Callosity present	70	28
Charcot joint	45	18
Hammer toe	38	15.2
Flat Foot	30	12
Joint Mobility Limited	98	39.2
Neuropathy Monofilament		
Intact	45	18
Lost	205	82
Vibration		
Intact	45	18
Lost	205	82
Ankle Reflex		
abnormal	14	5.6
normal	236	94.4
Distal pulses		
Present	175	70
Absent	75	30

Table 4 shows type, side and site of patients who had diabetic foot ulcers, most common site were ulcers on the toe+, marginal ulcer both on the dorsum and plantar side⁴⁵, while alveolar ulcer³⁰ and ulcers on heel¹⁰. Right side affected more about 78(63%) than left side 47(37%). There were 40 neuropathic, 80 neuroischemic and only 5 were pure ischemic ulcers. Foot ulceration were graded according to Wagner Classification of Diabetic Foot. On grading, 38 patients had grade 0 ulcer, 42 had grade1 ulcer, 65 had grade 2 ulcer, 75 had grade 3 ulcers and 30 patients had grade 4 ulcers.

Table 4 Type and site of ulcer in Diabetic Foot patients (n=250)

Site of Ulcer	n	%age
Ulcer on Toe	80	64
Marginal ulcer	90	72
Involving planter & Dorsal		
Malleolar ulcer	60	48
Heel ulcer	20	16
Right Side	156	124.8
Left Side	74	59.2
Type of Ulcer		
Nuropathic	60	48
Neuro-ischemic	170	136
ischemic	20	16

Table 5 shows that age, sex and duration of diabetes were significantly related to diabetic foot problems. Cigarette smoking slightly increases the chances of DFU. Rural background, abnormal lipid profile HBA1C>7.5, FBS>120mg/dl, monofilament and vibratory sensation loss increase the chances of foot ulcer development in diabetic population. Previous foot ulceration, h/o trauma to foot, h/o previous amputation, foot deformities, increase the chances of foot ulcers. Majority of the patients belongs to rural population and they had no knowledge about foot care by himself neither treating physician inform about foot care.

Table 5: Odd ratio of different parameter as risk factor for foot problem in diabetic patients (n=250)

Parameter	n	%age
Age >50	155	62
Sex Male	179	71.6
Duration of DM >10	180	72
Smoking	162	64.8
BMI >25	160	64
Residence (Rural)	155	62
Serum Albumin < 2.5	213	85.2
S- Lipid profile	176	70.4
HBA1C >7.5	155	62
FBS	190	76
Previous Foot Ulceration / Amputation	180	72
Foot Deformities / Abnormal Foot Skin	165	66
Mono filament lost	205	82
vibration Test	205	82
Patient Education Level about Diabetic Foot Complication	170	68
Previous Trauma to Diabetic Foot	162	64.8

DISCUSSION

Foot problems are serious and disabling complication in diabetic population. The disability and possible progression to the loss (amputation) of digits and limbs make it a serious issue^{11,12}.

There was significant difference in diabetic patents for the development of foot problems with regards to age and sex. A significant factor in this study shows male predominance for the development of diabetic foot ulcer. This is in contrast to Kumar et al¹³ who describes no difference in the prevalence of DFU among male and female patients. Also a study carried out in Jordan¹⁴ shows 5% prevalence of diabetic related amputation, which occurred in both sexes equally. Several studies had shown a clear male predominance. Moss et al¹⁵ and Frakyberg et al¹⁶ explained that in general the prevalence of sensory neuropathy, peripheral vascular disease is lowered in women as compared to men^{17,18}. Various factors play a role in the affect of sex on diabetic foot;

these may include activity level, hormonal factors, smoking, vascular disease, neuropathy and degree of compliance^{19,20}.

In the current study, longer duration of diabetes >10 years was a significant risk factor in the development of Diabetic foot complications. This is in agreement with other studies who showed that longer duration of diabetes increase the chances of foot ulcers(21-26). This is because vascular complications and neuropathic complications (sensory, motor and autonomic) developed with passage of time²⁷.

H/O trauma was an important factor in the development of DFU. 162 patients suffered some sort of trauma that leads to the development of DFU. These results were redressed in the study by Mantey et al²⁸ which shows 4 out of five patients would develop DFU due to trauma.

In our study BMI is significantly increased in DFU, this had an association with a number of studies (29-30). This may be related to increase body weight which cause increase in planter pressure and lead to ulcer formation, however this association is not consistent³¹. This is contrary to Manter²⁸ who shows no association between BMI and DFU.

In our study, we concluded that smoking is mild risk factor in the development of DFU. Smoking cause PAD (peripheral arterial disease) which is associated with DFU(32). This observation was supported by other studies(24-33). Similar to the results in this study Moss et al¹⁵ found that smoking was predictive of diabetic ulceration. The results failed to show any association between foot complications in diabetes and smoking (34).

In this study, it was found that previous ulceration and amputation increase the chances of further ulcer development. Different studies supported that previous ulcers^{25,35,36} and previous lower limb amputation increase the chances of further lesions^{12,24,25,27,35,37,38}. This may be loss of protective sensation due to neuropathy³⁹ and peripheral vascular disease.

Our study demonstrated that peripheral neuropathy was an important contributory factor in the development of DFU. Different studies confirm our results that peripheral neuropathy is the most important factor in the development of foot ulcer^{32,35,36,40,41}. Diabetic neuropathy leads to sensory, motor and autonomic instability. Patients suffering from sensory neuropathy are unable to recognize trauma while motor neuropathy leads to muscle atrophy and foot deformities whereas autonomic instability leads to dry skin, fissure and callus formation^{42,44,45}.

Poor glycemic control was an independent risk factor in our study for the development of ulcers. This

finding was supported by other studies^{22,26,45}. Previous studies showed that high levels of HBA1C is an important factor in the development of foot ulcer due to neuropathy and microvascular complications^{24,27,38,43,46}. In our study, foot deformities, callosity and joint immobility are risk factors for the development of foot ulcer. This was also supported by previous studies^{25,35,40,42,47}. In contrast Alex et al³⁶ describes that foot deformities were a non contributory factor in the development of foot ulcers.

In this study diabetic foot ulcer are more common in rural population due to lack of education, more physical work, walking bare foot, and improper foot wear. Lack of awareness for foot care in diabetic population is also an important contributory factor for the development of ulcers⁴⁸.

CONCLUSION

This study concluded that poor glycemic control leads to peripheral neuropathy. Longer duration of Diabetes, male gender, rural population, increased BMI, abnormal lipid profile foot deformities and trauma to the foot unrecognized by patient leads to an increased risk of diabetic foot complications. Lack of self-awareness for foot care in diabetic patients and also the primary care physician does not normally evaluate the patient regarding this complication. All these risk factor are preventable, correctable and controllable. By early prevention and treatment, we are able to save our patients from the suffering of diabetic foot ulcer and later amputation

REFERENCES

1. Boulton AJ, Vileikyte L; The diabetic foot; The scope of the problem. *J Fam Pract* 499(Suppl. 11);53-58,2000
2. Levin M, Pathophysiology of diabetic foot lesions, IN *Clinical Diabetes Mellitus. A Problem Oriented Approach*. Davidson JK, Ed. New York, Theime Medical, 1991. p 504-510.
3. Boulton AJ, Vileikyte L, Rangnarsen-Tennvall G, Apelqvist J; The global burden of diabetic foot disease, *Lancet* 366;1719-1724,2007-
4. International consensus on the diabetic foot and practical guideline on the management and prevention of diabetic foot, consultative section of the IDF; 200712
5. American Diabetes Association, Standards of medical care in Diabetes-2013 *Diabetes Care* 2013;36;S11-S66
6. Edmonds M, Foster A. The use of antibiotics in the diabetic foot. *Am J Surg* 2004; **187**:25S-28S.
7. Veves A, Falanga V, Armstrong DG, Sabolinski ML. Graft skin, a humankind equivalent, is effective in the management of non infected neuropathic Diabetic foot ulcers: a prospective randomized multicenter clinical trial. *Diabetes Care* 2001; **24**:290-295.
8. FAGILA E, Favales F, Morabito A, New ulceration, new major amputation and survival rates in diabetic subject hospitalized for foot ulceration from 1990-1993. *Diab Care*. 2001;24(1);78-83.
9. Abbott CA, Carrington AL, Ashe H, North-west Diabetes Foot Care Study, et al. The North West Diabetic Foot Care Study;

- incidence of, and risk factor for, new diabetic foot ulceration in a community-based patient cohort. *Diabet Med* 2002; **19**:377-384.
10. Khalid Mahmood, S, Tahseen Akhtar, Abu Talib, Badar Abbasi, Siraj-ul-Salekeen and Iftikhar Haider Naqvi. Clinical profile and Management outcome of Diabetic Foot Ulcers In a Tertiary Care Hospital ; *Journal of the College of Physicians and Surgeons Pakistan* 2008, vol ,18(7);408-412.
 11. Leese GP, Reid F, Green V, McAlpine R, Cunningham S, Emslie-Smith AM, *et al*. Stratification of foot ulcer risk in patients with diabetes: a population-based study. *Int J Clin Pract* 2006; **60**:541-545.
 12. Crawford F, Inkster M, Kleijnen J, Fahey T. Predicting foot ulcers in patients with diabetes: a systematic review and meta-analysis. *Q J Med* 2007; **100**:65-86
 13. Kumar S, Ashe HA, Parnell LN. The prevalence of foot ulceration and its correlates in type 2 diabetic patients: a population-based study. *Diabet Med* 1994; **11**:480-484.
 14. Jbour AS, Jarrah NS, Radaideh AM. Prevalence and predictors of diabetic foot syndrome in type 2 diabetes mellitus in Jordan. *Saudi Med J* 2003; **24**:761-764.
 15. Moss SE, Klein R, Klein BE. The prevalence and incidence of lower extremity amputation in a diabetic population. *Arch Intern Med* 1992; **152**:610-616
 16. Frykberg RG, Lavery LA, Pham H. Role of neuropathy and high foot pressures in diabetic foot ulceration. *Diabetes Care* 1998; **21**:1714-1719.
 17. Beach KW, Strandness DE. Arteriosclerosis obliterans and associated risk factors in insulin-dependent and non-insulin dependent diabetes. *Diabetes* 1980; **29**:882-888.
 18. Alolado JC, Pacy PJ, Beevers M. Risk factors for peripheral vascular disease in hypertensive subjects with type 2 diabetes mellitus. *Diabet Med* 1992; **9**:904-907.
 19. Armstrong DG, Todd WF, Lavery LA. The natural history of acute Charcot's arthropathy in a diabetic foot specialty clinic. *Diabet Med* 1997; **14**:247-43.
 20. Lavery LA, Armstrong DG, Vela SA. Practical criteria for screening patients at high risk for diabetic foot ulceration. *Arch Intern Med* 1998; **158**:157-162.
 21. Reiber GE. Epidemiology of foot ulcers and amputations in the diabetic foot. In: Bowker JH, Pfeifer MA, eds. *The diabetic foot*. 6th ed. St Louis: Mosby; 2011; 13-32
 22. Ali SM, Basit A, Sheikh T, Mumtaz S, Hydrie MZ. Diabetic foot ulcer — a prospective study. *J Pak Med Assoc* 2001; **51**:78-81.
 23. JR Brownrigg, J Davey, PJ Holt, WA Davis, MM Thompson, KK Ray, RJ Hinchliffe. The association of ulceration of the foot with cardiovascular and all-cause mortality in patients with diabetes: a meta analysis. *Diabetologia* 2012; **55**:2906-2912.
 24. SK Shahi, A Kumar, S Kumar, SK Singh, SK Gupta, TB Singh. Prevalence of diabetic foot ulcer and associated risk factors in diabetic patients from north India. *J Diabet Foot Complications* 2012; **4**:83-91
 25. Cowley MS, Boyko EJ, Shofer JB, Ahroni JH, Ledoux WR. Foot ulcer risk and location in relation to prospective clinical assessment of foot shape and mobility among persons with diabetes. *Diabetes Res Clin Pract* 2008; **82**:226-232.
 26. Nyamu PN, Otieno CF, Amayo EO, McLigeyo SO. Risk factors and prevalence of diabetic foot ulcers at Kenyatta National Hospital, Nairobi. *East Afr Med J* 2003; **80**:36-43.
 27. Merza Z, Tesfaye S. The risk factors for diabetic foot ulceration. *Foot* 2003; **13**:125-129.
 28. Mantey I, Foster AV, Spencer S. Why do foot ulcers recur in diabetic patients? *Diabet Med* 1999; **16**:245-249
 29. Boyko EJ, Ahroni JH, Stensel V. A prospective study of risk factors for diabetic foot ulcer. The Seattle Diabetic Foot Study. *Diabetes Care* 1999; **22**:1036-1042.
 30. Ctercteko GC, Dhanendran M, Hutton WC. Vertical forces acting on the feet of diabetic patients with neuropathic ulceration. *Br J Sur* 1981; **68**:608-614.
 31. Cavanagh PR, Sims DS, Sanders LJ. Body mass is a poor predictor of peak plantar pressure in diabetic men. *Diabetes Care* 1991; **14**:750-755
 32. Levin ME. Pathogenesis and general management of foot lesions in the diabetic patient. In: Bowker JH, Pfeifer MA, eds. *The diabetic foot*. 6th ed. St Louis: Mosby; 2011. 219-260.
 33. G Chellan, S Sri Kumar, AK Varma, TS Mangalanandan, KR Sundaram, RV Jayakumar, *et al*. Foot care practice – the key to prevent diabetic foot ulcers in India. *Foot* 2012; **22**:298-302.
 34. Coppini DV, Young PJ, Weng C. Outcome on diabetic foot complications in relation to clinical examination and quantitative sensory testing: a case-control study. *Diabet Med* 1998; **15**:765-771.
 35. Stephanie Wu, DG Armstrong. Risk assessment of the diabetic foot and wound. *Int Wound J* 2005; **2**: 17-24.
 36. R Alex, B Ratnaraj, B Winston, DN Samson Devakiruba, C Samuel, J John, *et al*. Risk factors for foot ulcers in patients with diabetes mellitus — a short report from Vellore, South India. *Indian J Community Med* 2010; **35**:183-185.
 37. Rathur HM, Boulton AJM. The diabetic foot. *Clin Dermatol* 2007; **25**:109-120.
 38. Lavery LA, Armstrong DG, Wunderlich RP, Mohler MJ, Wendel CS, Lipsky BA. Risk factors for foot infections in individuals with diabetes. *Diabetes Care* 2006; **29**:1288-1293.
 39. Rogers LC, Driver VR, Armstrong DG. Assessment of the diabetic foot. In: Krasner D, Rodeheaver GT, Sibbald RG, eds. *Chronic wound care: a clinical source book for healthcare professionals*. 4th ed. Malvern, PA: HMP Communications; 2007; 549-555.
 40. KS Reid, BD Martin, F Duerksen, LE Nicolle, M Garrett, JN Simonsen, *et al*. Diabetic foot complications in a northern Canadian Aboriginal Community. *Foot Ankle Int* 2006; **27**:1065-1073.
 41. C Formosa, A Gatt, N Chockalingam. Diabetic foot complications in Malta: prevalence of risk factors. *Foot* 2012; **22**:294-297.
 42. Abbott CA, Carrington AL, Ashe H, Bath S, Every LC, Griffiths J, *et al*. The North-West Diabetes Foot Care Study: incidence of, and risk factors for, new diabetic foot ulceration in a community-based patient cohort. *Diabet Med* 2002; **19**:377.
 43. T Dinh, F Tecilazich, A Kafanas, J Doupis, C Gnardellis, E Leal, *et al*. Mechanisms involved in the development and healing of diabetic foot ulceration. *Diabetes* 2012; **61**:2937-2947.
 44. Steed DL. Wounds in people with diabetes: assessment, classification, and management. In: Krasner D, Rodeheaver GT, Sibbald RG, eds. *Chronic wound care: a clinical source book for healthcare professionals*. 4th ed. Malvern, PA: HMP Communications; 2007; 537-54
 45. M Dubský, A Jirkovská, R Bem, V Fejfarová, J Skibová, NC Schaper, BA Lipsky. Risk factors for recurrence of diabetic foot ulcers: prospective follow-up analysis of a Eurodiale subgroup. *Int Wound J* 2012; **10**:555-561.
 46. Martín Borge V, Herranz de la Morena L, Castro Dufourny I, Fernández, Martínez A, Pallardo Sánchez LE. Diabetic foot and risk factors [in Spanish]. *An Med Interna* 2007; **24**:263-266.
 47. Birke JA, Franks BD, Foto JG. Ulceration of the first metatarsal head in diabetes mellitus. *Foot Ankle Int* 19. First ray joint limitation, pressure, and 95; **16**:277-284.
 48. Andrew J.M. Boulton ,DavidG. Armstrong. Stephen F. Albert, Robert G. ,Frykberg, Richardg Hellman, M.Sue Kirkman, Comprehensive foot Examination and Risk Assesment, *Diabetes Care*, volum 31 NO8 ,August 2008.1679-1685.