THE PREVALENCE OF ABNORMAL RESULTS OF ANNUAL INVESTIGATIONS AMONG DIABETIC PATIENTS WITH DIFFERENT RISK FACTORS

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Background: The basic theme of this study was to promote the use of risk approach and encourage selectivity in requesting laboratory investigations. The objective was to estimate the proportion of abnormal results obtained from routinely requested annual investigations among the whole study population, and the odds ratios of abnormal test results among patients with certain risk factors.

Patients and Methods: A total of 459 diabetic patients aged 12 years and over, attending the primary care clinics of a university hospital in Riyadh, Saudi Arabia, were included in the study. In this cross-sectional study, analysis of the association between patients' demographic characteristics and clinical findings (independent variables), and the results of the annual investigations were conducted. A multiple logistic regression analysis was carried out to identify certain independent variables associated with abnormal investigations.

Results: The proportion of patients who had abnormal electrocardiogram (ECG) was 23%, chest x-ray (CXR) 26%, and liver function test (LFT) 9%. High systolic blood pressure (BP) and age were found to be important determinants of abnormal ECG and CXR. Patients who had high systolic BP (>140 mm Hg) were found to be 2.39 times more likely to have abnormal ECG (OR=2.39), and their odds ratio of abnormal CXR was 2.33. Furthermore, for each 10-year increment in age, there was a 43% increased likelihood of abnormal ECG and 29% increase of abnormal CXR. Smokers were nine times more likely to have abnormal LFT (OR=9.26, 95% CI=2.29 to 37.5). The disease duration and obesity were not found to have an independent association with the possibility of having abnormal results.

Conclusion: The study results led to some tentative suggestions on guidelines for clinicians in their decision either to request annual investigations for all diabetic patients, or to restrict some investigations to certain groups of patients. This was discussed and compared with the findings from the literature and other authorities' recommendations.

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Key Words: Abnormal results, laboratory investigations, risk factors.

Non-insulin dependent diabetes mellitus (NIDDM) is a major public health problem in Saudi Arabia. The rapid urbanization and social and economic transformation of the country have been accompanied by changes in lifestyle and an increase in the incidence of the disease. While studies in the 1980s had shown a low prevalence of DM,[1-3] higher estimates of 12%-15% have been shown in recent studies.[4,5] This has made Saudi Arabia one of the high prevalence countries, according to the World Health Organization Ad Hoc Diabetes Reporting Group.[6] The age-standardized prevalence of DM is expected to be higher than the prevalence rate due to the fact that the Saudi population is relatively young. Many studies have clearly demonstrated the substantial cost of DM on the country's health budget.[7-9]

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Cost-benefit analysis of management and screening options should be utilized for more efficient use of resources and to reduce the cost of DM on the health system. Few studies have evaluated the cost effectiveness of diabetic investigations worldwide,[10] and none has been conducted in Saudi Arabia. Therefore, uncertainty exists regarding the yield and cost effectiveness of these tests.

Clinical practice guidelines (CPG) for the management of diabetic patients were developed to be used in the study primary health care (PHC) clinics, with the aim of having a standardized and scientifically sound management system among practicing physicians.[11] In 1988, doctors working in these clinics agreed to perform certain annual screening investigations[11,12] Glycosylated hemoglobin (HbA_{1c}) was to be requested each three months as an indicator of glycemic control. A literature review that summarized the essence of publications on diabetes and the PHCs recommended urine (micro) albumin, urine ketones, urine culture, glycated hemoglobin, serum creatinine, lipids and ECG to be requested at presentation and at an annual review.[13] The laboratory evaluations at the initial visit of a diabetic patient

TABLE 1. *The proportion of abnormal ECG, CXR and LFT for the study population, and the odds ratios of abnormal tests for different independent variables.*

Dependent variable	Independent variable	Categories	No. of Subjects	Proportion (%)	Estimated odds ratios	95% CI
ECG	Systolic BP	Normal systolic BP	212		1.0	
		High systolic BP	78	23.2	2.39	1.32-4.34
	Age	Ten-year increment in age	289	23.2	1.43	1.09-1.88
CXR	Systolic BP	Normal systolic BP	224		1.0	
		High systolic BP	68	26.4	2.33	1.28-4.25
	Age	Ten-year increment in age	292	26.4	1.29	0.99-1.69
LFT	Smoking	Non-smokers	436		1.0	
	status	Smokers <15 cig	11	8.9	9.26	2.29-37.50
	Sex	Males	211		1.0	
		Females	248	8.9	2.10	1.01-4.39

include fasting blood sugar (FBS), HbA_{lc}, fasting lipid profile, serum creatinine, urinalysis, urine culture (if indicated), thyroid function test and electrocardiogram (ECG).[14]

The objective of the study was to estimate the proportion of abnormal results of laboratory investigations routinely requested at initial visits and annually for the whole study population, and the estimated odds ratios of having abnormal test results among subgroups of the population who have certain risk factors. The ultimate aim of this exercise is to promote the use of risk approach in targeting patients for annual diabetes investigations.

Patients and Methods

This cross-sectional study was conducted in the PHC clinics of King Abdulaziz University hospital in Riyadh, Saudi Arabia. The records of all diabetic patients aged 12 years and over were reviewed. No other exclusion criteria were used, and a total of 459 patients were included. The study focused on the annual investigations that included creatinine level, cholesterol, triglycerides, liver function tests (LFT), HbA_{lc}, urine dipstick, 24-hour urine for protein and glomerular filtration rate (GFR), chest x-ray and ECG.

The associations between patients' demographic characteristics and other risk factors, and the results of laboratory investigations were analyzed. The data were entered into the Epi Info statistical program (version 5.01B). They were later transferred to General Linear Interaction Models (GLIM) statistical program to perform the multiple logistic regression and models fitting to the data for each dependent variable (response).

The dependent and independent variables were classified and converted into categorical data based on objective measurable thresholds or lab range, except ECG, and CXR, which were considered abnormal if an abnormal feature was found regardless of the prognostic or clinical value of the finding.

Results

The total number of patients included in the study was 459. The majority of the study population were Saudis and illiterate. Women outnumbered men (1.2:1), and about two-thirds were above 50 years of age. Most of the patients had had the disease for less than 10 years and were treated with oral hypoglycemics, and around 12% were treated with insulin. About 5% were smokers. Abnormal ECG findings included left atrial dilation in seven patients, left ventricular hypertrophy (LVH) in six, sinus tachycardia in six, ischemic changes in six, premature ventricular contractions (PVC) in five, sinus bradycardia in four, old myocardial infarction (MI) in three, and poor R-wave progression in two patients. Abnormal CXR findings included unfolded aorta among 17 patients, cardiac enlargement in 13, increased pulmonary markings in six, inflammatory and fibrotic changes in five, pulmonary collapse in two, and tuberculous calcification in three patients. Abnormal LFT findings were mostly raised liver enzymes in 35 patients and raised alkaline phosphatase in twelve patients.

The data for the dependent and independent variables were complete for the 459 patients except for the 24-hour urine for protein (27 patients), ECG (289 patients) and CXR (292 patients). There was no statistically significant difference in the demographic characteristics of patients who performed ECG and CXR and those who did not. For the 24-hour urine for protein, no model could fit. It had no significant relationship with any of the independent variables; the number of patients for whom 24-hour urine for protein result was available was too small (27 patients).

The proportion of abnormal ECG, CXR and LFT among the whole study diabetic population was 23.2%, 26.4% and 8.9%, respectively (Table 1). Using multiple logistic regression analysis, the significant positive determinants of abnormal ECG and abnormal CXR were high systolic blood pressure and age (i.e., the effect remained significant after control for other possible confounding variables.) For

TABLE 2. *The magnitude of change in serum creatinine level* and HbA_{1c} in association with different independent variables.*

Independent variables	Categories	No. of subjects	Proportion (%)	Magnitude of increment	95% CI
		Serum creatinine			
Age	Ten-year increment in age	459	3.1	3.1 μmol/L increment in level of creatinine	1.92-4.28
		HbA_{1c}			
Age	Ten-year increment in age	459	59	0.21 increment in level of HbA_{1c}	0.08-0.35

*Serum creatinine level is considered abnormally high if it is ≥120 μmol/L.

TABLE 3. *The magnitude of change in blood triglycerides and cholesterol levels for different independent variables.*

Independent variables	Categories	No. of subjects	Proportion (%)	Magnitude of change in triglyceride	95% CI
		A) Triglycerides			
Type of diabetes mellitus	On diet only On oral drugs	48 355	68.4	0 0.64 mmol/L increment in triglycerides	0.28-1.01
Type of diabetes mellitus	On diet only On insulin	48 56	68.4	0 0.29 mmol/L increment in triglycerides	–0.18-0.75
		B) Cholesterol			
Age	10-year increment in age	459	57.7	0.26 mmol/L increment in cholesterol	0.16-0.35
Sex	Males Females	211 248	57.7	0 0.25 mmol/L increment in cholesterol	0.05-0.46
Nationality	Non-Saudi Saudi	93 366	57.7	0 0.33 mmol/L increment in cholesterol	0.07-0.58

patients with high systolic BP, the odds ratio of abnormal ECG was 2.39 and abnormal CXR was 2.33. Furthermore, for each 10-year increment, there was a 43% increased risk of abnormal ECG and 29% increase in abnormal CXR. Smokers were nine times more likely to have abnormal LFT (OR = 9.26, 95% CI 2.29 to 37.5).

Creatinine level (index of renal function) greater than 120 μmol/L was found in only a small proportion (3.1%) of the study population (Table 2), and it increased significantly in association with age increment. For each 10 years of age increment, there was a 3.1 μmol/L increment of creatinine level. HbA_{lc} was above the normal range (>8.0) for the majority (59%) of the study population, and was significantly directly associated with age. More than half of the study population had high cholesterol (>5.2 mmol/L) and triglyceride (>1.4 mmol/L) levels (Table 3). Triglyceride levels were, on average, 0.64 mmol/L higher among patients on oral hypoglycemics and 0.29 mmol/L higher among patients on insulin compared with patients on diet only. On the other hand, cholesterol levels increased in accordance with age (each 10-year increment of age was associated with 0.26 mmol/L increment of cholesterol level). It was also higher among women and Saudis.

Discussion

The basic theme of the present study was to promote the use of risk approach, by looking at the prevalence of abnormal investigation results among different population subgroups. Limited resources could be used more efficiently by restricting investigations to some readily identifiable high-risk groups. The final decision to initiate a test depends on the balance between cost (money, discomfort, etc.) and benefit (reduction of morbidity and mortality).[16] As there is no scientific basis for determining exchange rates between money and discomfort on one hand and people's health and survival on the other, it becomes clear that the decision should be looked at as a guideline rather than a precise measure.

The study was conducted in a university hospital in Riyadh, the capital city of Saudi Arabia. Apart from age and level of literacy, the demographic characteristics of the study population were similar to those of patients seen in the primary health care (PHC) setting. The older age of the study population than that of the general population could be attributed to the nature of the disease. Furthermore, older Saudis are known to have a higher rate of illiteracy than younger ones.[15]

The fact that the study was based in a practice that already had in existence the clinical practice guidelines (CPG) led to a better compliance with performing the annual tests than if it had been compared with retrospective studies. Although CXR and ECG were not performed on all patients, we were reassured by finding that there was no statistically significant difference in the demographic characteristics of the group of patients who had the CXR and ECG and the group that did not.

Multiple logistic regression was used in the study analysis. The association of the investigation results was tested against all the independent variables (e.g., age, gender, BP, duration of disease, BMI, etc.). The finding of association is likely to be real and significant, as the possible confounding factors were controlled. It is noteworthy and contrary to expectations that the duration of the disease and obesity (BMI) did not have a significant independent association with the possibility of having abnormal results of all investigations tested. Regarding the BMI, the presence of confounding factors (e.g., age) could be the explanation.

One limitation of the study was that the classification of the ECG and CXR into normal and abnormal was not based on clear-cut measurable criteria. ECGs and CXRs with abnormal features were classified as abnormal regardless of their prognostic or clinical value. Nevertheless, it could be argued that including all the ECG and CXR abnormalities is useful to avoid misclassification and to reduce inaccuracy.

The extremely low compliance rate with the 24-hour urine test for protein and GFR was a point of concern. It is not recommended as a routine annual test, as it is an expensive test and associated with low compliance rate. Although only a small proportion of patients had high serum creatinine levels, it is still recommended to do annual creatinine (particularly for the elderly), as it is relatively cheap, of great prognostic value and probably acceptable to patients, as was shown by the high compliance rate in our study. Since accurately measuring renal function in routine clinical practice is difficult,[17] other tests to screen for diabetic nephropathy, e.g., sensitive urine dipsticks for protein and urinary albumin-creatinine ratio, should be evaluated. One commercially available method tested for measuring urinary albumin in the range of 15 to 200 mg/dL in random spot urine was found to have a high sensitivity (95.5%) and specificity (91.5%).[18] The present study results are in line with evidence from PHC literature[13] and consensus groups,[19] which recommend annual creatinine and urinalysis, while 24-hour urine for protein and GFR is not recommended.

High systolic BP and age could be used as a guideline for clinicians to decide for which patients they should request ECG and CXR. Some authorities[13,19] recommend performing ECG but not CXR at the initial visit. DM is a known risk factor for acquiring tuberculosis.[20] Saudi Arabia is a developing country with a relatively high prevalence of tuberculosis, especially among the elderly.[21] The fibrotic changes noted among the CXR of five patients may represent an old TB infection. Tuberculin test needs further investigations.

The high proportion of abnormal ECG (23%) and CXR (26%) in our study indicates the need for screening all diabetic patients at first visit with CXR and ECG. As most of the abnormalities in the ECG and CXR are not expected to change within a short period of time, it seems appropriate to restrict routine annual investigations to patients aged above 50, or those with high systolic BP (140 mm Hg). Furthermore, information obtained from a careful history and physical examination during follow-up should be the basis of predicting abnormal results. The need for requesting stress ECG should be investigated in this community. In one study in the West, it was found that 20% of newly diagnosed NIDDM had coronary heart disease.[22] Another study found a high prevalence of asymptomatic myocardial ischemia in diabetics, but the noninvasive screening using stress ECG and 24-hour ECG recording was associated with a high false-positive rate.[23]

The association of smoking and abnormal LFT should be investigated in future studies. Daily exposure of rats to cigarette smoke showed increased lipid peroxidation in the liver. The glutamic-oxaloacetic transaminase (GOT), gamma-GTP, total bilirubin and LDH values were significantly higher than those in the control group.[24] For the nonsmoking diabetic population, the yield of routine annual LFT is low and unjustified. This is in line with recommendations made in other reports.[13,19] However, the current study found a high association between the patient's smoking status and abnormal LFT result. For this reason, we recommend restricting LFT screening for the smoking patients at initial visit. Abnormal LFT results could be utilized in patients' education to quit smoking. Nonsmoking patients may need screening with LFT only if there are other clinical indications (e.g., on starting with metformin or if there is enlarged or fatty liver).

HbA_{1c} is usually used as an index of blood glucose control. It is not meant as a screening test but was included in the study to determine the group at risk of undesirable glucose control. The finding of positive association with age means that, in general, older patients have worse glycemic control than the young. The beneficial effects of effective glycemic control on chronic complications of diabetes had been established for both type I[25,26] and type II DM.[27] It has been shown that the HbA_{1c} level is correlated with the development of retinopathy.[26,27] So the question is not whether HbA_{1c} is worthwhile or not, but which group of patients has worse glycemic control, as reflected by HbA_{1c} results. The older age group (with a high HbA_{1c}) probably needs more efforts and closer monitoring to achieve better glycemic control.

The high prevalence of elevated triglycerides and cholesterol levels prompted the need for the whole study population to be tested for these. The serum lipids profile has a strong prognostic value and merits intervention, primarily nutritional.[14] However, one may argue that there is no evidence that the detection of high cholesterol or triglycerides improves the clinical outcome. The ADA recommends fasting lipids profile at initial visit, while others recommend lipids profile at initial visit and annual review for younger patients (<65 years).

Based on the findings of this study, and with evidence from the literature, certain investigations are recommended for all patients at the annual visits. These are urinalysis, serum creatinine, lipids and HbA_{1c}. On the other hand, ECG and CXR should be done for all patients at the initial visit and thereafter, should be restricted to patients over 50 years of age and patients who have a systolic BP of >140 mm Hg. LFT should be confined to smokers.

Further prospective data are needed to develop cost-effective and at-risk population diagnostic strategies. The clinical utility of urine culture, thyroid function test, stress ECG, tuberculin test and different methods to screen for diabetic nephropathy (e.g., urine dipsticks, urinary albumin

to creatinine ratio) needs evidence-based analysis of their cost effectiveness to help in the development of CPG for the management of diabetic patients.

References

1. Fatani HH, Mira SA, El-Zubier AG. Prevalence of diabetes mellitus in rural Saudi Arabia. Diabetes Care 1987;10:180-3.
2. Fatani HH, Mira SA, El-Zubier AG. Prevalence of diabetes mellitus in urban Saudi Arabia. In: Nitiyanant W, Hayanrat A, Vannasaeng S, editors. Diabetes Mellitus: Proceedings of the Third World Congress on Diabetes Mellitus in the Tropics and Developing Countries, December 2-5, 1984. Bangkok, Thailand. Bangkok: Crystal House Press, 1985: 8-16.
3. Bacchus RA, Bell JI, Madkour M, Kilshaw B. The prevalence of diabetes mellitus among male Saudi Arabs. Diabetologia 1982;23: 330-2.
4. National Chronic Metabolic Diseases Survey. Ministry of Health and King Saud University, Kingdom of Saudi Arabia.
5. El-Hazmi MAF, Warsy A, Al-Swailem A, et al. Diabetes mellitus and impaired glucose tolerance in Saudi Arabia. Ann Saudi Med 1996;16: 381-5.
6. King H, Rewers M. WHO Ad Hoc Diabetes Reporting Group. Global estimates for prevalence of diabetes mellitus and impaired glucose tolerance in adults. Diabetes Care 1993;16:157-77.
7. Roesler J, et al. Economic cost of diabetes mellitus, Minnesota, 1988. MMWR 1991;40:229.
8. American Diabetes Association. Direct and indirect costs of diabetes in the United States in 1987. Washington: American Diabetes Association, 1988.
9. British Diabetic Association. Diabetes in the United Kingdom. London: BDA, 1996.
10. British Diabetic Association. Counting the cost: the real impact of non insulin dependent diabetes. London: BDA, 1996.
11. Al Faris EA. Guidelines for the management of diabetic patients in Saudi health centres. J Fam Comm Med 1997;4:12-24.
12. Al-Faris EA. Diabetes mellitus. The Scientific Committee of Quality Assurance in Primary Health Care. Quality Assurance in Primary Health Care Manual. Riyadh: Dar Al-Hilal Printing Press, 1991:197-225.
13. Lauritzen T. Diabetes care by the primary health care team: a review of the literature with some recommendations for the future. In: Marshall SM, Home PD, Rizza RA, editors. The Diabetes Annual/9. Amsterdam: Elsevier Science B.V., 1995.
14. Kerr CP. Improving outcomes in diabetes: a review of the outpatient care of NIDDM patients. J Fam Pract 1995;40:63-75.
15. Saudi Arabia Family Health Survey 1995. Khoja TA, Farid SM, editors. Riyadh: Ministry of Health, 1997.
16. Backett EM, Davies AM, Petros Barrazia A. The risk approach in health care. Geneva: World Health Organization, 1984.
17. McElduff A, Shuter B, Cooper R, Davies L, Fulcher G, Hoschl R, et al. Measuring renal function in patients with diabetes mellitus. J Diabetes Complications 1997;11:225-9.
18. Williams BT, Ketchum CH, Robinson CA, Bell DS. Screening for slight albuminuria: a comparison of selected commercially available methods. South Med J 1990;83:1447-9.
19. American Diabetes Association. Standards of medical care for patients with diabetes mellitus. Diabetes Care 1989;12:365-8.
20. Boucot KR, Cooper DA, Dillon EC, et al. Tuberculosis among diabetics. The Philadelphia Survey. Rev Tubercul 1952 (Suppl);65: 127.
21. Al-Kassimi FA. Review of tuberculosis in Saudi Arabia. Saudi Med J 1994;15:192-5.
22. Gall M, Rossing P, Skott P, Damsbo P, Vaag A, Bech K, et al. Prevalence of micro- and macroalbuminuria, arterial hypertension, retinopathy and large vessel disease in European type 2 (non-insulin-dependent) diabetic patients. Diabetologia 1991;34:655-61.
23. Koistinen MJ. Prevalence of asymptomatic myocardial ischaemia in diabetic subjects. BMJ 1990;301:92-5.
24. Watanabe K, Eto K, Furuno K, Mori T, Kawasaki H, Gomita Y. Effect of cigarette smoke on lipid perodixation and liver function tests in rats. Acta Med Okayama 1995;49:271-4.
25. The Diabetes Control and Complications Trial Research Group. The effect of intensive treatment of diabetes on the development and progress of long-term complication in IDDM. N Engl J Med 1993; 329:977-86.
26. Reichard P, Bengt-Yngve N, Rosenquist U. The effect of long-term intensified insulin treatment on the development of microvascular complications of diabetes mellitus. N Engl J Med 1993; 329: 304-309.
27. Klein R. Hyperglycemia and microvascular and macrovascular disease in diabetes. Diabetes Care 1995;18:258-68.