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Studies in preventive nephrology: blood pressure and proteinuria in the population

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Summary
The evolution of three generations of anti-hypertensive drugs has produced more than less effective therapy. Mild hypertension is a definite risk factor and it is responsible for the bulk of complications in the population and must be treated Community control of high blood pressure is feasible and effective. The third generation drugs seem to have specific reno-protective attributes

Keywords: *Blood pressure, predictive regression, cut-off level for hypertension.*

Introduction

The expanding pool of patients with end-stage renal failure (ESRF) remains a source of concern for all providers of health care for populations all over the world largely because the provision of currently effective management continues to strain available resources [1-5]. It is therefore becoming more obvious that urgent attention should be concentrated on its prevention rather than the management of end-stage disease [3,6]. It must however be admitted that the path to effective prevention of renal damage and ESRF remains largely uncharted and rather rudimentary. As part of our foundation efforts in the direction of preventive nephrology, we have studied proteinuria and blood pressure in a defined population. The results are presented in this brief report.

Population, materials and methods

Supervised self-urinalysis was carried out as part of a cross-sectional total population survey of the Faizia East Primary Health District (PHD) of Buraidah, the capital of the Gassim region of Saudi Arabia. Blood pressure was recorded in the same exercise. Details of methodology have already been given elsewhere [3].

Results

Detailed characteristics of the study population and the level of co-operation with the study team have already been supplied [3]. Table 1 shows the prevalence of proteinuria (using the dip stix method, in mg/dl) for the total population given in functional age groups. Out of a total population of 7,694 (Female: 3,852), information was not available in 1,534 (Female:580) subjects, mainly infants and children. About 5796 out of 6160 subjects examined (94.09%), were free of proteinuria. About 279 (4.53%), 60 (0.97%), and 25 (0.41%) were discovered to have proteinuria of 30 mg/dl; 100 mg/dl and 500 mg/dl, respectively. Using SPSS (Statistical Package for Social Sciences) progamme, and correcting for age, predictive regression curves were plotted for degree of proteinuria (Protdeg; Figs 1 & 2) against systolic and diastolic blood pressure. Mean and the 95% confidence interval are shown. Rsq for systolic blood pressure was 0.0131 and 0.0085 for diastolic. Although these represent very weak correlation, the p values indicated very high significance for both subsets of blood pressure ($p < 0.000001$). This is no doubt a result of the statistical power of the sample size. Projecting the regression curve to the base (y-axis), it will seem as if the proteinuria begins to appear in the

Table 1: Faizia east PHD, buraidah, gassim, KSA proteinuria (in mg/dl): total population in functional age groups

Age Groups	Nil	30	100	500	No Info.	Total
1-5	857	19	1	1	725	1603
6-12	1737	76	18	11	92	1934
13-49	2760	160	30	9	601	3560
50-69	363	21	8	4	94	490
70+	79	3	3	0	22	107
Total	5796	279	60	25	1534	7694
Effective %	94.09	4.53	0.97	0.41	-	(6160)

Chi Square = 43.92 (Excluding No Info.) d.f = 19 $p < 0.0001$

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population at the level of about 130 mm Hg systolic and 60 mm Hg diastolic blood pressure.

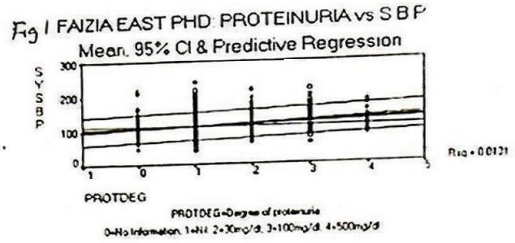

Fig.1: Faizia east phd: proteinuria vs sbp.

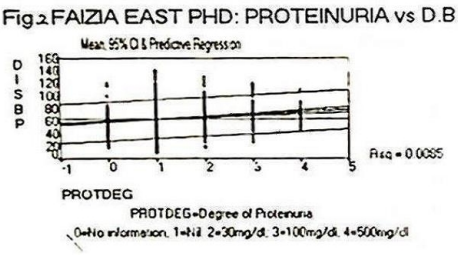

Fig.2: Faizia east phd: proteinuria vs d b p.

Discussion

The above results could have been dismissed as spurious since large sample size can sometimes produce such levels of significance but the following reasons should compel us to carefully look into the possible epidemiological importance of the findings.

1. Haemodynamic consequences of blood pressure on the structure of the glomerulus and other target organs is, among others, directly related to its level.
2. The Modification of Diet in Renal Disease (MDRD) study has shown significant correlation between blood pressure and reduction in GFR which continues in patients with blood pressure below 140/90, suggesting that it may be necessary to lower the operational blood pressure below this level to preserve renal function [7-8].
3. Vascular lesions, arteriolar and pre-arteriolar necrosis, normally seen in systemic hypertension have been reported in 54–82% of "normotensive" young patients with glomerulonephritis [9-11]. "... Accordingly, arterioles and glomeruli may be sensitive to haemodynamic stress at blood pressure levels less than those considered hypertensive." When these lesions are present in the absence of "hypertension or any other recognised causes like IgA or systemic lupus, it is customary to term such lesions as primary nephropathy named according to histological pattern - sclerosis, membranous, proliferative, etc. The clear suggestion is that, in the control of blood pressure aimed at the prevention of progressive renal injury and failure, consideration may have to be given to the issue of initiation of antihypertensive therapy at blood pressure levels hitherto considered normal.
4. Hypertension by itself, in the absence of obesity and NIDDM, is now recognised as a state of insulin resistance. Further, and perhaps significantly, Saad et al (1991), found, in the "normotensive" Caucasian, correlation between blood pressure and plasma insulin levels [12].

Thus, it would appear that many defined consequences of hypertension are present at levels below the currently accepted cut-off points. With these as background, it becomes possible to explain at least in part, some of the rather odd observations which had been recorded since the beginning of the Framingham era of co-ordinated studies of blood pressure. Patients under antihypertensive drug treatment do continue to have a higher morbidity and mortality than untreated people with similar levels of blood pressure [13]. It has been difficult to demonstrate a protective effect of antihypertensive therapy on renal function save in a small number of patients with diabetic nephropathy. "... With or without good control of blood pressure, renal function may deteriorate in perhaps 15% over a period of 5 years, more frequently in black patients than in white [13-14]." Projection of hypertension-related disease in the middle-aged residents of the United States showed that blood pressure control did not seem to reduce the progression of renal failure [15] and seemed in fact to increase the pathology [16].

If we accept the role of the auto-immune component in the pathogenesis of progression of renal damage, it becomes relatively easy to explain these findings. Once the critical degree of damage has been effected (by hypertension-induced haemodynamic stress), progression is at least in part, if not largely, dependent on the activities of the body immune mechanism in attacking the damaged tissue which is no longer recognised as self. In other words if the haemodynamic damage had been effected before antihypertensive is commenced, subsequent reduction of level of blood pressure can hardly be expected to be the only mitigating factor in its progression.

The implication of these, in the context of preventive nephrology, is that the level at which intervention should begin in the management of blood pressure needs to be revised downwards. The level of about 130/60 mm Hg suggested by this study can only be regarded as preliminary.

To arrive at this level, it is to be noted that evidence of early renal damage, proteinuria, has been used. It would appear that using clinical evidence of target organ damage (myocardial hypertrophy, renal size, plasma creatinine, anaemia, stroke, etc.) appear late in the evolution of the disease and can only produce high and inappropriate operational definition of hypertension. This would explain why research observations have shown that antihypertensive drug therapy did not seem to have mitigated renal damage. If organ damage is to be prevented, appropriate operational definition of hypertension should be based on the earliest evidence of haemodynamic stress. This, in our opinion, should be microalbuminuria and we suggest that by tracking this in the community an accurate cut-off point can be defined.

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