Abdominal adiposity and metabolic alterations in hypertension - a case control study

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Indians are particularly susceptible to chronic diseases like hypertension, diabetes and coronary heart disease. Several Western studies have documented the role of obesity, especially the role of regional adiposity, and associated metabolic aberrations in the aetiopathogenesis of these chronic diseases. However, there is a paucity of information on the Indian sub-continent.

This study was therefore undertaken to investigate the role of regional adiposity and metabolic abnormalities in hypertension. Subjects, aged between 30-50 years, attending the out-patient department of Osmania General Hospital {1000 beds), which caters to middle and low income group of people located at Hyderabad City in India, were screened for hypertension. A total of 158 newly diagnosed subjects were selected along with 172 age and gender matched controls.

Body mass index (BMI), waist hip ratio (WHR), total body fat and percentage of body fat were calculated from the anthropometric parameters. Biochemical parameters like serum lipids and plasma glucose and insulin (at fasting as well as 2 h post load glucose) were determined in a subsample of 78 hypertensives and 74 controls.

Hypertensives had significantly higher body weight, body fat, BMI and WHR as compared to controls in both men and women. No differences were observed in lipid profile. Plasma glucose, fasting as well as 2 h post load, was significantly higher in both hypertensive men and women. Though there were no differences in plasma insulin at fasting, insulin level at 2 h post-load was elevated in hypertensive women. Higher glucose levels, despite elevated insulin levels, suggested insulin resistance. The calculated odds ratios revealed that increased BMI, WHR, plasma triglycerides, and 2 h post load glucose increased the risk for hypertension in both women and men. Insulin was identified as a risk factor only in women. These results suggest a role for regional adiposity and insulin resistance in the development of hypertension in the Indian sub-continent.

Key words: Abdominal obesity, hypertension, hyperlipidaemic, insulin resistance, men, women, India, Hyderabad, Andhra Pradesh

Introduction

Hypertension is one of the major risk factors for coronary artery disease and stroke. Its complications account for high morbidity and mortality in developed and developing countries[1]. Several investigators studied the role of obesity in hypertension and documented reduction in blood pressure with reduction in body weight[2,3]. Recently, body fat distribution has received much attention in health risk assessment of excess body weight. The terms 'apple' and 'pear' shapes have been put forward with 'apples' having more fat deposition in the abdomen (android), whereas 'pears' are more inclined to be large around the hip area (gynoid)[4]. It is reported that waist hip ratio (WHR), an indirect index of abdominal adiposity, is positively related to both systolic and diastolic blood pressure[5,6] and thus, increased WHR has been shown to be hazardous to health[7].

The distribution of body fat has been shown to be an important predictor of metabolic aberrations and cardio-vascular morbidity and mortality. It has been demonstrated that abdominal obesity is associated with hyper-insulinaemia, hypertriglyceridaemia, reduced concentration of high density lipoprotein (HDL) cholesterol and hypertension[8,9]. This constellation of features is described as "Syndrome X"[10].

Although obesity is known to be an important factor for determining the development of diseases such as coronary heart disease (CHD), hypertension and diabetes, there is limited information on its role in the aetiopathogenesis of these diseases in the Indian subcontinent[11-13]. Recent studies on Indian immigrants in UK have shown that Indians are more susceptible to these diseases than Europeans[14,15]. However, differences in known risk factors, such as smoking, elevated serum cholesterol, obesity and higher intake of calories, particularly from saturated fats could not account for higher prevalence of these diseases in Indians. Regional adiposity, hypertriglyceridaemia, insulin resistance and glucose intolerance were implicated as coronary risk factors in Indian immigrants[16-17].

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Both hypertension and obesity have been documented in India, but studies highlighting the relationship between the two are few. Practically no information is available on the role of distribution of body fat in relation to hypertension in Indians. A case control study was, therefore, undertaken with the objective to establish the relationship, if any, between obesity, abdominal fat and hypertension. In a sub-sample of individuals, its relation to metabolic aberrations was also assessed.

Subjects and Methods

Patients, aged between 30-50 years, attending out-patient department of Osmania General Hospital, Hyderabad, (1000 beds) which caters to middle and low income group of people located at Hyderabad city in Andhra Pradesh, India, were screened for hypertension. 158 subjects (males (M) 74; females (F) 84) with diastolic blood pressure above 95mmHg on three consecutive occasions during an interval of 10 days were selected with their consent. In all the subjects, hypertension was detected for the first time. Normotensive subjects matched for age, gender and socio-economic status (M: 88; F: 84) were included to serve as controls. Both hypertensives and normotensives were not on any medication. All the subjects with known hepatic, renal disease and diabetes were excluded from the study. The study was approved by the Ethical Committee of the Institute.

Anthropometric measurements such as body weight, height and skinfold thickness were taken by using standard methods and equipment[18]. Waist circumference was taken one inch above the umbilicus and circumference of hip was measured at the level of maximum protrusion of the gluteal region. From these measurements, body mass index (BMI) and waist hip ratio (WHR) were calculated. From the measurements of fat fold thickness at three sites (triceps, subscapular and suprailiac), body density was assessed and body fat was computed[19].

Biochemical parameters like plasma glucose, insulin and serum lipids were determined in a subsample of subjects with normal (M: 32; F: 42) and high (M: 36; F: 42) blood pressure. After an overnight fast, blood samples were collected before and 2 h after a 75 g glucose load. From the fasting blood sample, serum cholesterol[20], HDL cholesterol[21] and triglycerides[22] were estimated. Plasma glucose[23] and insulin[24] were determined in both fasting and post glucose load blood samples.

The parameters were analysed separately for males and females. The difference between means in cases and controls were assessed by student 't' test. Pearson's product moment coefficients were calculated to identify the relationships between different parameters. Percentage frequency of subjects in each tertile was computed and significant differences between control and cases were tested, using chi-square test. Odds ratios were calculated to identify the anthropometric and biochemical risk factors for hypertension.

Results

The clinical profile of the subjects is presented in Table 1. There was no difference in the mean age between controls and cases, and as expected, cases had significantly higher ($P<0.001$) systolic, diastolic and mean arterial blood pressure as compared to controls. The anthropometric profile of hypertensives and controls is given in Table 2. Body weight, BMI, WHR, percentage of body fat and total body fat were significantly elevated in cases than controls.

Table 1. Mean age and blood pressures of controls and hypertensives.

	Men		Women	
	Controls (88)	Cases (74)	Controls (84)	Cases (84)
Age (years)	40.2 ± 0.8	42.8 ± 0.9	42.3 ± 0.7	42.9 ± 0.7
Blood pressure (mm/Hg)				
Systolic	117.9 ± 0.90	157.2 ± 1.43***	117.3 ± 1.12	159.0 ± 1.55***
Diastolic	78.0 ± 0.66	107.1 ± 1.09***	77.9 ± 0.73	106.7 ± 1.40***
Mean arterial	91.3 ± 0.66	123.8 ± 1.12***	91.1 ± 0.80	124.1 ± 1.31***

Values are Mean ± SE; *** $p<0.001$; ( ) No. of subjects

Table 2. Anthropometric profile of controls and hypertensives.

	Men		Women	
Anthropometric Parameters	Controls	Cases	Controls	Cases
	(88)	{74)	(84)	(84)
Weight (kg)	59.0 ± 1.3	63.9 ± 1.4**	55.3 ± 1.1	64.7 ± 1.4***
BMI (kg/m^2)	21.3 ± 0.6	23.5 ± 0.5***	23.9 ± 0.5	27.7 ± 0.5***
WHR	0.93 ± 0.01	0.98 ± 0.01***	0.92 ± 0.01	0.94 ± 0.10*
Total body fat (kg)	12.3 ± 0.7	15.4 ± 0.7**	20.4 ± 0.7	26.5 ± 0.7***
% of body fat	19.6 ± 0.7	23.4 ± 0.8***	36.1 ± 0.8	40.6 ± 0.5***

Values are Mean ± SE; * $P<0.05$; ** $P<0.01$; *** $P<0.001$; ( ) No. of subjects

Table 3. Biochemical parameters in controls and hypertensives.

	Men		Women	
	Controls (32)	Cases (36)	Controls (42)	Cases (42)
Plasma Glucose (mg/dl)				
Fasting	79.9 ± 2.1	82.8 ± 4.3	74.7 ± 1.8	84.3 ± 3.7*
2 hr post load	103.2 ± 5.8	125.9 ± 8.7*	105.8 ± 4.7	120.1 ± 5.3*
Plasma insulin (μU/ml)				
Fasting	12.3 ± 1.8	12.6 ± 1.6	10.2 ± 0.7	11.2 ± 1.5
2 hr post load	87.0 ± 13.4	65.9 ± 11.3	32.0 ± 5.2	67.0 ± 9.4***
Serum lipids				
Total Cholesterol (mg/dl)	183.5 ± 5.9	193.5 ± 7.3	192.2 ± 5.9	194.3 ± 6.8
HDL Cholesterol (mg/dl)	36.4 ± 1.1	40.2 ± 1.6	37.3 ± 1.0	37.3 ± 1.2
% of HDL	20.4 ± 0.8	21.4 ± 0.9	20.7 ± 0.7	19.7 ± 0.6
Triglycerides (mg/dl)	106.7 ± 9.1	124.2 ± 8.2	113.4 ± 6.2	120.1 ± 6.3

Values are Mean ± SE; * $P<0.05$; *** $P<0.001$; ( ) No. of subjects

The tertile distribution of BMI and total body fat showed a significant difference between hypertensives and controls with higher proportion of cases being in third tertile as compared to controls in both men and women (Figures 1 and 2). The tertile distribution of WHR also showed significantly higher proportion of cases in the third tertile among males. A similar trend was observed in women. However, the differences were not significant (Figure 3). In addition, in each of the BMI tertiles cases had higher WHR as compared to controls in men. Such differences were not observed in women, although cases had higher WHR in first 2 tertiles (Figure 4).

Biochemical parameters of hypertensives and controls are presented in Table 3. Plasma glucose on fasting as well as plasma insulin after glucose load were significantly higher in cases as compared to controls in women. In

addition, 2 h plasma glucose was significantly higher in cases in both genders. However, there were no significant differences between cases and controls in fasting insulin and serum lipid profile.

Figure 1. Percentage distribution of controls and cases in BMI tertiles. Men ($p<0.01$) Women ($p<0.001$).

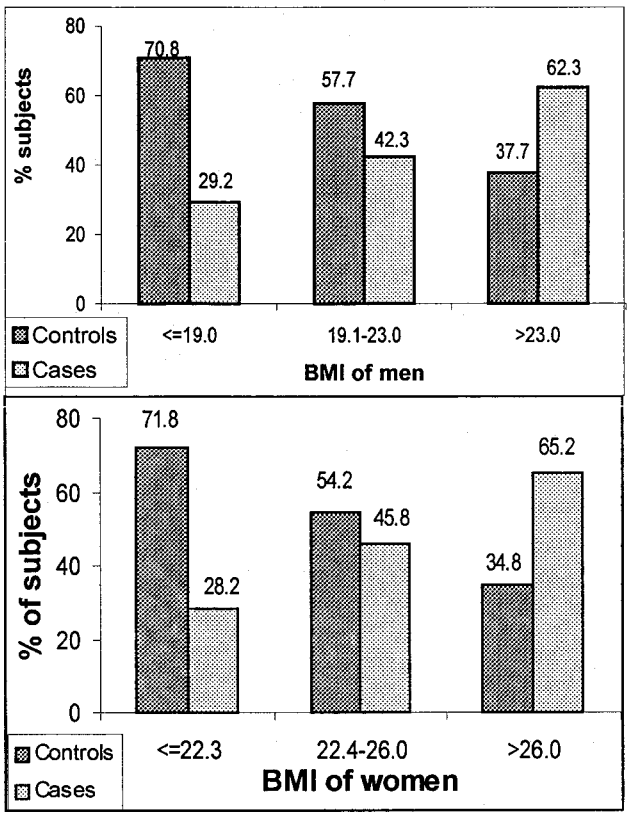


Figure 2. Percentage distribution of controls and cases in total body fat tertiles. Men ($p<0.01$), Women ($p<0.001$).

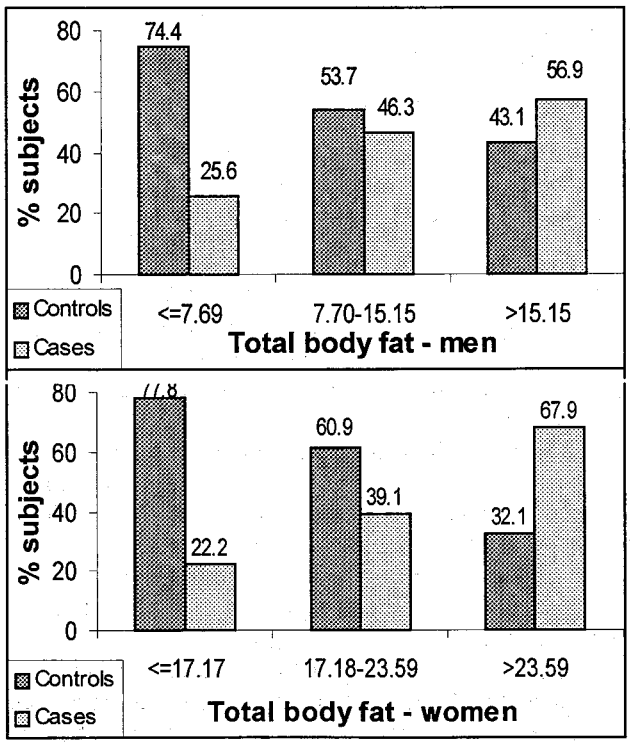


Figure 3. Percentage distribution of controls and cases in WHR tertiles. Men ($p<0.001$), Women ($p>0.05$ - <0.10).

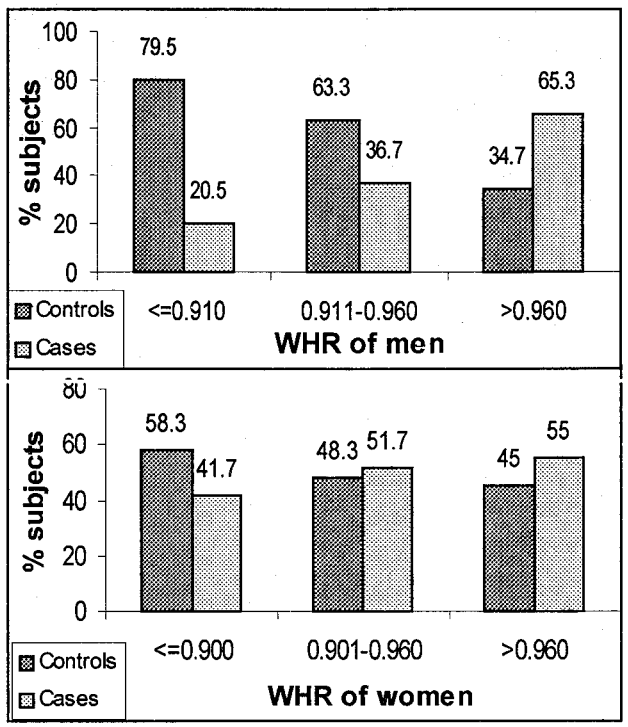
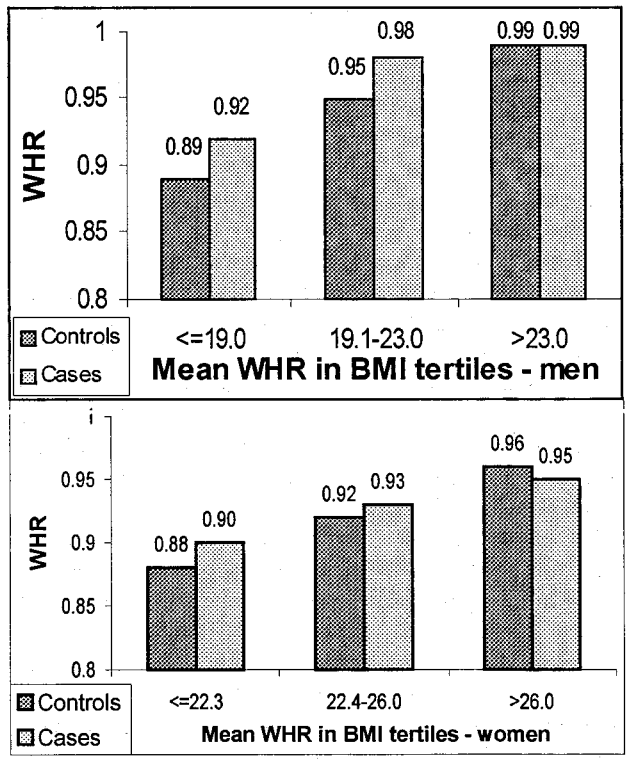


Figure 4. Mean WHR in BMI tertiles. Men ($p<0.01$) Women (NS).



Significant positive correlations were observed between various anthropometric parameters such as body weight, BMI, WHR and % body fat and blood pressure among both genders (Table 4). In addition, post load plasma insulin in women was also significantly ($P<0.05$) correlated to systolic ($r=0.209$), diastolic ($r=0.302$) and mean arterial ($r=0.266$) blood pressure.

Table 4. Correlation between anthropometric parameters and blood pressure.

	Men (162)			Women (168)		
	Systolic	Diastolic	Arterial	Systolic	Diastolic	Arterial
Weight	0.254***	0.232***	0.245***	0.328***	0.323***	0.333***
BMI	0.321***	0.285***	0.305***	0.344***	0.356***	0.360***
WHR	0.390***	0.334***	0.363***	0.204**	0.218**	0.273***
% of body fat	0.335***	0.289***	0.314***	0.392***	0.362***	0.384***

** P<0.01; *** P<0.001 ( ) No. of subjects.

From the odds ratios, it was evident that higher body weight, BMI, WHR and total body fat were found to increase the risk for hypertension in both genders. Among biochemical parameters, plasma glucose at both time points, triglycerides, postload plasma insulin were found to increase the risk for hypertension in women. In addition, triglycerides and post load glucose were also found to increase the risk for hypertension in men (Table 5).

Table 5. Odds ratios for hypertension in 3rd tertile of anthropometric and biochemical parameters.

	Men			Women		
Parameters	t3	95% Confidence Intervals		t3	95% Confidence Intervals	
		Lower	Upper		Lower	Upper
Anthropometric						
Bodyweight	2.27	1.03	4.97	5.99	2.47	14.49
BMI	4.01	1.78	9.01	4.77	2.02	11.22
WHR	7.29	2.91	18.21	1.71	0.79	3.68
Total body fat	3.83	1.60	9.15	7.39	2.97	18.34
Biochemical						
Total Cholesterol	1.02	0.32	3.19	1.13	0.41	3.12
HDL Cholesterol	1.88	0.56	6.21	0.53	0.17	1.58
Triglycerides	3.98	1.06	14.67	2.03	0.67	6.14
Glucose(F)	0.93	0.28	3.01	1.89	0.63	5.65
Glucose(P)	2.50	0.66	9.38	2.86	0.90	9.06
Insulin(F)	1.25	0.34	4.48	0.82	0.28	2.34
Insulin(P)	0.47	0.13	1.67	4.33	1.38	13.56

F = Fasting; P = Post Prandial; Odds ratio > 1.5 is considered as risk

Discussion

Several studies in recent years have documented that Indians are particularly susceptible to chronic diseases such as hypertension, coronary artery disease and diabetes[12,13]. The reported prevalence rates of hypertension in urban population are not very much different from that of developed countries[11]. Although risk factors associated with these diseases have been evaluated in developed countries, information in Indian sub continent has not been explored in depth. In the present study, an attempt has been made to evaluate the risk factors associated with hypertension, adopting the case control approach.

The mean diastolic blood pressure of hypertensives both in men and women, indicates that majority of subjects had moderate hypertension. Since the mean ages of controls and cases both in men and women were similar, the observed differences either in anthropometric or biochemical parameters could not be attributed to differences in age.

The association between blood pressure, and physical parameters such as body weight, BMI and other indices of obesity based on skin fold thickness have been studied[11,25]. Such parameters, though complex, have been related to fatal and nonfatal cardiovascular events. However, the correlation coefficients of these different relationships were found to be constantly small, indicating that the association between overweight and blood pressure is complex.

Generally, it is known that Indians have lower body weight, BMI and body fat as compared to Westerners[26]. In the present study, although most of the anthropometric parameters of both cases and controls were within normal limits, cases had higher values for each of these parameters. More recently, regional adiposity has been recognised as a greater health hazard than a simple increase in body weight or BMI. Long term follow up studies have shown that high WHR (>1.0 in men and >0.8 in women) is associated with increased morbidity and mortality for several chronic diseases such as myocardial infarction, stroke, diabetes and cancer in both genders[7,27,28]. In the present study, WHR is significantly associated with systolic, diastolic and mean arterial blood pressure. This is in line with several other studies which have also shown that WHR is independently correlated with blood pressure in males and females[29]. It has been shown that with increasing BMI and WHR, there was an increase in the prevalence of hypertension and hypercholesterolaemia alone or in combination[30,31].

Higher WHR observed in cases than controls suggests a role for abdominal adiposity in the inception and progression of disease. Further, hypertensives, particularly men, had higher WHR in each of the BMI tertiles, compared to controls, suggesting that for any given degree of overweight, individuals with higher WHR are more prone to hypertension. Thus the abdominal body fat distribution appears to be a major risk factor for hypertension.

Apart from obesity, either general or regional, hypertension is closely linked with metabolic abnormalities such as glucose intolerance, hyperinsulinaemia, insulin resistance and abnormal lipid profile[17,32]. Significant positive associations between hypertension, impaired glucose tolerance and plasma insulin levels have been demonstrated, which suggest insulin resistance[15]. Using more sophisticated clamp technique, many investigators have shown the presence of insulin resistance in hypertension[10,33].

In several other studies, fasting and 2 h plasma glucose, and 2 h plasma insulin were significantly associated with death from cardiovascular disease[34,35]. In the present study, in hypertensive women both insulin and plasma glucose are elevated, suggesting insulin resistance. However, in men, only the 2 h plasma glucose is higher, which gives an indirect indication of insulin resistance.

Based on Western data, National Cholesterol Education Programme[36] recommends cholesterol levels above 240 mg/dL as a risk factor for CHD. However, several studies have demonstrated that Indians are susceptible to hypertension and CHD even with cholesterols levels as low as 180 mg/dL[11,37]. In the present study, there was no significant difference in serum cholesterol levels between controls and cases. However, odds ratios reveal that triglycerides were also a risk factor for hypertension in both men and women.

Our study attempts to elucidate the possible metabolic consequences of excess body fat accumulation distribution in the pathogenesis of hypertension. Despite normal body weight, our results highlight the importance of regional adiposity in Indian subjects. In addition, it suggests that

hypertension and its sequelae are probably mediated through insulin resistance and atherogenesis. Primary prevention attempts must, therefore, be directed towards maintenance of ideal body weight, blood glucose and triglyceride levels.

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高血壓患者的腹部肥胖症和代謝改變 —— 病例及對照的研究

摘要

印度人特別易患的慢性疾病是高血壓，糖尿病和冠心病。雖然在印度次大陸的報導是不足的，但是在若干西方的研究已經証實肥胖症，特別是局部肥胖症的作用，同時把這些慢性病的發病機理和代謝異常聯系起來。

該研究探討了高血壓病人的局部肥胖和代謝改變。作者在印度海德拉巴（Hyderabad）市 Osmenia 總醫院（1000 病床）門診部選擇了 158 位中等或偏低收入的、新診斷爲高血壓的病人爲對象，同時選擇了 172 位年齡和性別相配的正常人爲對照。

從生理測量參數計算體重指數（BMI）、腰臀圍比例（WHR）、總體脂肪和體脂百分率，從 78 位高血壓病人和 74 位正常人測定血清脂類、血漿葡萄糖和胰島素（空腹和葡萄糖負荷 2 小時後）等生化參數。

高血壓男女的體重、體脂、BMI 和 WHR 較正常人明顯增加，脂類兩組沒有差異。高血壓男女的血漿葡萄糖（空腹和葡萄糖負荷 2 小時後）較正常人明顯增高。雖然空腹時血漿胰島素沒有差異，但是高血壓婦女在葡萄糖負荷 2 小時後是升高的，血漿胰島素與葡萄糖水平同時升高，被認爲是抗胰島素性的結果。BMI、WHR、血漿甘油三酯、葡萄糖負荷後 2 小時的增加將增加男女二者高血壓的危險。胰島素被認爲只是婦女的危險因素。這些結果指出局部肥胖症和抗胰島素性在高血壓形成中的作用。

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