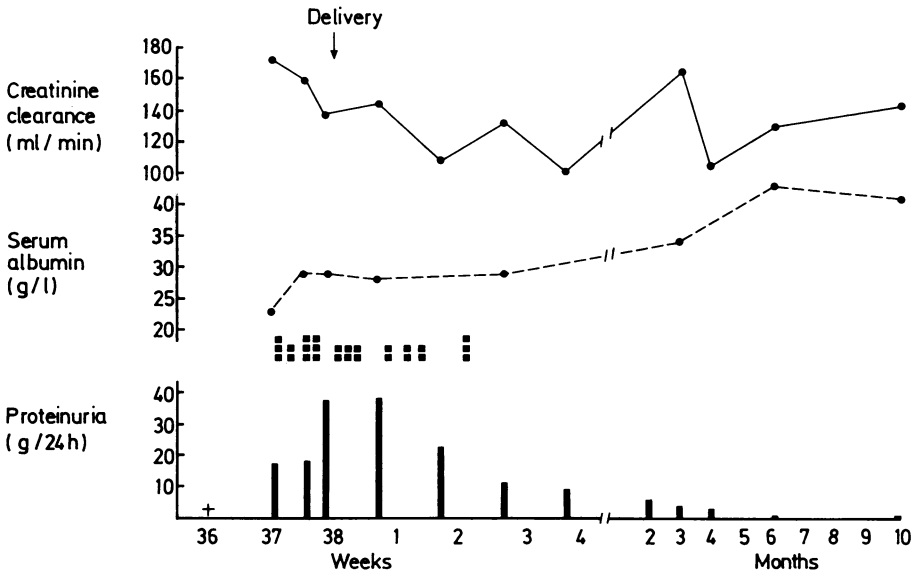
Severe transient nephrotic syndrome in diabetic pregnancy

The nephrotic syndrome is uncommon in pregnancy, probably complicating fewer than one in 1000 pregnancies.[1] In the absence of pre-existing clinical renal disease the cause is probably pre-eclampsia in most patients. Diabetic glomerulosclerosis has been noted as a possible cause but no evidence offered about its frequency.[1] We report a case of severe transient nephrotic syndrome in a pregnant diabetic patient subsequently followed up for over one year.

Case report

A 29 year old woman with a history of insulin dependent diabetes for 19 years presented at 10 weeks' gestation in her second pregnancy. The previous pregnancy had been normal, with no proteinuria or hypertension. At 11 weeks' gestation her renal function was assessed: there was no proteinuria and creatinine clearance was 78 ml/min. Blood pressure was normal (120/70 mm Hg) and booking glycosylated haemoglobin value satisfactory (8·4%; non-diabetic range 5·5-8·5%). There was no evidence of diabetic retinopathy or neuropathy.



Serum albumin concentrations, creatinine clearance, and 24 hour proteinuria before and after delivery. ■=20 g albumin concentrate given intravenously.

Diabetes was managed with twice daily injections of highly purified porcine insulins (Velosulin and Insulatard; Nordisk, Gentøfte), and regular home blood glucose monitoring was undertaken (Reflomat; Boehringer Mannheim).

Pregnancy proceeded uneventfully for the next six months, the patient attending the combined antenatal and diabetic clinic fortnightly and achieving good diabetic control. At 34 weeks routine urine analysis showed no proteinuria. Two weeks later Albustix testing disclosed 1+ proteinuria; blood pressure was 120/70 mm Hg and the glycosylated haemoglobin value 7·9%. After a further week (37 weeks' gestation) she had pronounced peripheral oedema and 4+ proteinuria; blood pressure was 130/90 mm Hg and serum albumin concentration 23 g/l. Urinary protein excretion of 16·3 g/24 h and creatinine clearance of 171 ml/min were recorded (figure). Albumin 220 g was given by intravenous infusion over the next four days, the serum albumin concentration rising to 29 g/l but proteinuria increasing to 37·0 g/24 h. Blood pressure was mildly raised, never higher than 135/90 mm Hg. Platelet count, serum urate concentration, serum complement values, and the antistreptolysin O titre were all normal. Electrophoresis of the urinary protein suggested glomerular leakage with no evidence of protein selectivity.

Prompt elective delivery was planned but at 38 weeks the patient went into labour spontaneously and delivered a healthy boy weighing 2710 g. The placenta was normal macroscopically and on microscopical examination and the baby had no complications in the neonatal period. The mother was managed by administration of oral frusemide and intravenous albumin concentrate (figure). Proteinuria declined rapidly, the creatinine clearance remaining static. Blood pressure was slightly raised four days after delivery (150/100 mm Hg) and was controlled with metoprolol 50 mg daily; the drug was stopped after three weeks and blood pressure was normal thereafter. Three months after delivery proteinuria was 4·0 g/24 h, creatinine clearance 165 ml/min, and the serum albumin concentration 34 g/l. Sixteen months after delivery proteinuria had dropped to 0·58 g/24 h with creatinine clearance 106 ml/min.

Comment

A true incidence for the development of the nephrotic syndrome in pregnancy is difficult to assess. Standard textbooks quote figures of less than 0·1%,[1] and more recent observational studies have found incidences of 0·05%[2] and 0·08%.[3] Many aetiologies have been observed, including acute and chronic glomerulonephritis and pre-eclampsia.

In our patient the aetiology of the transient nephrotic syndrome was uncertain, as we did not think that renal biopsy was justified before delivery and the patient declined biopsy afterwards. The very acute onset late in pregnancy and rapid resolution after delivery must be explained and these factors together with the normal complement concentrations and antistreptolysin O titre make acute glomerulonephritis unlikely.

Pre-eclamptic nephropathy would account for the mode of onset and speed of resolution; nevertheless, in the largest series of patients with the nephrotic syndrome due to pre-eclampsia all 13 patients had severe hypertension (>170/110 mm Hg) and a pronounced rise in the serum urate concentration, neither of which occurred in our patient.[4] The persistently high creatinine clearance during the nephrotic phase also contrasts with the reduced creatinine clearance (<100 ml/min) seen in a group of patients with pre-eclamptic nephropathy,[2] and overall it seems unlikely that pre-eclampsia would explain the nephrotic syndrome in our patient. Schreiner suggested that hypersensitivity to products of conception may produce the "nephrotic syndrome of pregnancy," probably by an effect on glomerular basement membrane charge,[1] while other workers have proposed a simple mechanical effect of the gravid uterus compressing the inferior vena cava and producing renal vein thrombosis.[3]

Transient nephrotic syndrome complicating a diabetic pregnancy has not previously been reported. While the mechanisms outlined above may be implicated, it may also be that the combined stimuli to renal hyperfiltration of diabetes and pregnancy produce transient glomerular damage, especially in kidneys already damaged subclinically by prolonged diabetes. Whatever the mechanism, the successful outcome of the pregnancy in our patient and the good renal function persisting beyond one year of follow up show that severe nephrotic syndrome late in diabetic pregnancy does not necessarily herald a rapid decline in maternal renal function.

1 Schreiner GE. The nephrotic syndrome—nephrosis of pregnancy. In: Strauss MB, Welt LG, eds. *Diseases of the kidney*. Boston: Little Brown and Co, 1963:389-93.
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3 Wallace MR, Smedley MG. The transient nephrotic syndrome of pregnancy. *NZ Med J* 1970;**71**:208-12.
4 First MR, Ooi BS, Jao W, Pollak VE. Pre-eclampsia with the nephrotic syndrome. *Kidney Int* 1978;**13**:166-77.

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