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Clinically significant newly presenting autoimmune thrombocytopenic purpura in adults: a prospective study of a population-based cohort of 245 patients

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Summary. The true incidence and prognosis of autoimmune thrombocytopenic purpura (ITP) in adults is unknown. We present the results of a prospective study in a population-based cohort of newly presenting adults (≥ 16 years) with ITP and platelet count of $< 50 \times 10^9$/l, which took place between 1 January 1993 and 31 December 1999 in the former Northern Health Region in the UK (population 3·08 million). A total of 245 cases were confirmed by bone marrow examination with a median follow-up of 60 months (range 6–78 months). There were 134 females/111 males (1·2:1). Overall incidence was 1·6 per 10^5 per annum. Absolute incidence was similar for both sexes, with highest age-specific incidence in those aged > 60 years. Thirty patients (12%) presented with frank bleeding, and 28% were asymptomatic. Forty-five patients (18%) received no treatment, and 135 (55%) received first-line treatment only. Thirty patients (12%) underwent splenectomy. There were four deaths (1·6%) from bleeding and/or the complications of therapy in this cohort, but only one was in the acute phase of the illness. The majority of patients (155 out of 245) achieved remission (platelet count $> 100 \times 10^9$/l), with a further 59 (24%) in partial remission with no symptoms (platelet count $30–100 \times 10^9$/l). This population-based study suggests that the traditional view of adult ITP as being a predominantly chronic disease that preferentially affects females needs to be modified.

Keywords: autoimmune thrombocytopenic purpura, adults, cohort study, incidence, splenectomy.

Autoimmune thrombocytopenic purpura (ITP) was first described in 1735 by Werlhof (Editorial, 1963), who described a young woman with sudden onset of spontaneous petechiae, ecchymoses and mucous membrane haemorrhage. In the American Society for Haematology guidelines (George *et al*, 1996), ITP is defined as 'isolated thrombocytopenia with no clinically apparent associated conditions or other causes of thrombocytopenia'. It is thus a condition that, to a large extent, is a diagnosis of exclusion of, for example, human immunodeficiency virus infection, systemic lupus erythematosus, lymphoproliferative disorders, myelodysplasia, agammaglobulinaemia, drug-induced thrombocytopenia, alloimmune thrombocytopenia, congenital/hereditary non-immune thrombocytopenia, relying on the presence of thrombocytopenia and an otherwise normal full blood count, with no clinically apparent associated conditions or drug therapy that may cause thrombocytopenia (George *et al*, 1998).

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Although ITP in adults is not considered to be rare, the true incidence of the disorder is unknown. Although several demographic studies have been carried out in children, current estimates of the incidence among adults are taken from studies with patients diagnosed between 1936 and 1985 (Jacobs & Wood, 1986; Cortelazzo *et al*, 1991; Kaufman *et al*, 1993) or are extrapolated from the data on children. These studies report an excess of females, with a peak age of incidence around 40 years (Doan & Bouroncle, 1960).

Clinical observation and experience indicate a spectrum of manifestations ranging from trivial bruising to catastrophic haemorrhage. The incidence of fatal haemorrhage is as high as 10·4% according to some studies (Stasi *et al*, 1995; George *et al*, 1996; Frederiksen & Schmidt, 1999). The literature suggests that older patients appear to have more severe bleeding manifestations (Cortelazzo *et al*,

1991). It has been reported that ≈43% of patients achieve a remission with a platelet count of $>100 \times 10^9$/l, thus implying that the majority of patients have a continuous or relapsing chronic disease state (George *et al*, 1995).

Clinical experience and anecdote supported by some published data led us to believe that the true demographic features of this disease differ from the published literature. This led the members of the Northern Region Haematology Group to initiate an audit. Prospective collection of data from adult patients with ITP within the Northern Health Region of England was commenced on 1 January 1993. The intention of the audit was to provide a current review of demographics, clinical manifestations and response to treatment in ITP. It is a prospective population-based cohort study allowing assessment, within this defined population, of the effect of changes in management introduced over the last half-century and thus provides a more contemporaneous review of ITP than that found in published texts (which mostly reflects practice before 1970).

PATIENTS AND METHODS

All patients with ITP aged 16 years and over presenting between 1 January 1993 and 31 December 1999 within the Northern Health Region of England (population 3·08 million) were registered prospectively by the haematologist who made the diagnosis.

Eligibility criteria. For the purposes of this audit, the diagnosis of ITP required exclusion of other haematological pathology by bone marrow aspirate and biopsy. The date of diagnosis was considered to be the date of the marrow biopsy. Patients with platelet counts $\geq 50 \times 10^9$/l were excluded from the audit as they were considered to be clinically less problematic. Patients with gestational and therapy-related thrombocytopenia and all those with a proven cause for thrombocytopenia, e.g. drug related, were also excluded. Infection-associated cases were not excluded from the cohort. Eligible cases therefore had presumed autoimmune but otherwise idiopathic thrombocytopenia.

Clinical details. Full presenting details were obtained from the hospital notes of all registered new cases of ITP. Information collected included the presenting full blood count, age at diagnosis, date of presentation and initial therapy instituted. Additional information on medications, co-existing medical problems with particular reference to preceding viral symptoms, presence of systemic lupus erythromatosus or other autoimmune disorder and co-morbidity with malignant disease was also collected.

Follow-up was to 30 June 2000 with median follow-up of 60 months (range 6–78 months). At first follow-up, details of presenting symptoms and signs, with particular reference to haemorrhagic symptoms and response to initial treatment, were recorded. The requirement for subsequent therapy, with a record of the response, and whether splenectomy was performed was also made. Whether the patients undergoing splenectomy had been registered on the Regional Asplenia Register (Spickett *et al*, 1999) was also audited.

For the purposes of this study, the current information on symptoms, details of subsequent treatment, date of last clinic attendance and most recent platelet count were collected at the final follow-up (date last seen nearest to 30 June 2000).

Treatment. Clinicians instituted the appropriate therapy according to their clinical judgement and not according to a set protocol.

Remission status. A normalization of the platelet count to $\geq 100 \times 10^9$/l was deemed complete remission (CR). Remission status was taken as the count on the date the patient was last seen in the clinic and/or platelet count was recorded (6–78 months disease duration). Partial remission was defined as platelet count above the count at presentation but $<100 \times 10^9$/l, with or without haemorrhagic symptoms or signs. However, if the platelet count failed to attain 30×10^9/l, this was considered not a remission.

Chronic ITP was defined as persistent thrombocytopenia ($< 50 \times 10^9$/l) for more than 6 months after diagnosis.

Mortality. The date and cause of death were documented if applicable.

Population statistics. Data were collated, managed and analysed using Microsoft EXCEL software. Age-specific population information was obtained from the UK 1991 Census from the Office of Population Censuses & Surveys (1995).

RESULTS

Study eligibility

Of the 343 patients registered, 98 were excluded from the study. There were therefore 245 evaluable patients.

Exclusions

The principle reasons for exclusion from the study are detailed below. The most common reasons were lack of bone marrow examination ($n = 40$) and drug-related thrombocytopenia ($n = 28$). Other reasons for exclusion were age <16 years ($n = 2$), platelet count $\geq 50 \times 10^9$/l ($n = 2$), relapse of previous ITP ($n = 3$), gestational ITP ($n = 2$), systemic lupus erythematosus ($n = 8$), no records available ($n = 7$) and other causes ($n = 6$).

Quinine was the commonest drug-related cause of thrombocytopenia ($n = 13/28$; 46·4%). The platelet count at diagnosis in these patients was within the range $1–27 \times 10^9$/l, with a median count of 4×10^9/l. There were four males and nine females, with a median age of 72 years (range 45–82 years); three of the 13 patients were asymptomatic. All responded to withdrawal of quinine and/or first-line treatment, with normalization of the platelet count.

In those patients taking drugs other than quinine (including gold, thiazide diuretics, antiepileptics, antischizophrenic drugs and cotrimoxazole), the median age was 50 years (range 17–76 years), with three males and 12 females in this category. In this cohort, the platelet count at diagnosis was in the range $2–32 \times 10^9$/l, with a median of 10×10^9/l. Five of the 15 patients in this group were asymptomatic. Six of the 14 patients who were treated in this group failed to respond to first-line therapy, with three proceeding to splenectomy.

Age and gender distribution

The age range of the patients presenting with confirmed ITP was 16–91 years, with a median age at diagnosis of 56 years of age. There was a female to male ratio of 1·2:1 (134 females to 111 males).

Annual incidence

The overall incidence of ITP in patients presenting with platelet count $< 50 \times 10^9$/l was $1{\cdot}6/10^5$/year. Figure 1 shows the incidence rates according to age and gender. The incidence was approximately equal for gender except for patients aged 45–59 years. The highest age-specific incidence was in those aged > 60 years.

Associated disorders

Within our cohort of 245 cases, 13 patients had a previous or concomitant history of solid tumours, and three patients had a previous history of haematological malignancies; bone marrow examination revealed no evidence of infiltration at the time of diagnosis of ITP in any of these patients. The three patients with previous haematological malignancy [one acute myeloid leukaemia, one Non-Hodgkin's lymphoma (NHL) and one Hodgkin lymphoma] attained CR from their ITP and have maintained this without relapse of either their primary disorder or their ITP.

Five patients had co-existing inflammatory bowel disease, but only one was receiving treatment for this complaint at the time of diagnosis with ITP. One patient presented with ITP at age 32 years, with a previous history of autoimmune haemolytic anaemia at 14 years old.

'Post-infection' thrombocytopenia

Twenty-two (16 females and six males) of the 245 patients had a history suggesting preceding infection, two of whom had proven infectious mononucleosis. A further patient was IgM positive for both cytomegalovirus and human parvovirus B19 at presentation. In all other cases, the clinical history was the only evidence of infectious illness. Thirteen of 22 patients presented with platelet count $< 10 \times 10^9$/l, although only one had frank bleeding.

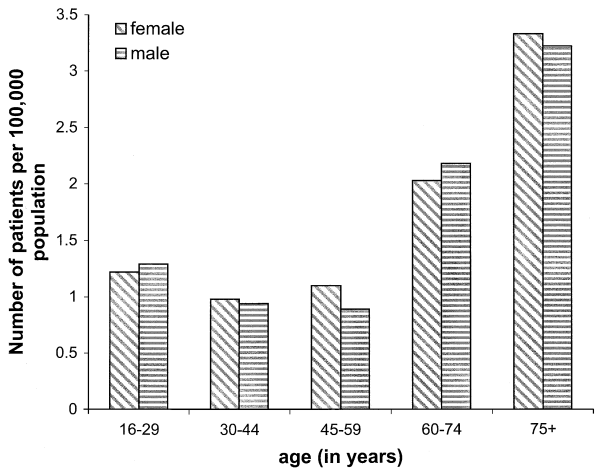

Fig 1. Age/gender-specific incidence per 100 000 population of newly presenting clinically significant autoimmune thrombocytopenia. Age/gender-specific incidence was greatest in patients aged > 60 years. There was no gender difference, except for the 45–59 age group.

Two patients achieved spontaneous remission. Seven of 19 patients who received steroids as initial treatment had no response to therapy and proceeded to treatment with immunoglobulin; three patients eventually underwent splenectomy.

Nineteen of 22 patients remain in continuous CR 6–76 months after diagnosis. Two patients are in partial remission with no symptoms (PRNS) requiring no therapy, with neither patient having received immunoglobulin or undergone splenectomy.

Seasonal variation

No evidence of seasonal variation of presentation was demonstrated in this study cohort (data not shown).

Haemorrhagic symptoms at presentation

Presenting symptoms by platelet count are summarized in Table I.

With lower platelet counts, most patients were symptomatic with frank bleeding as well as purpura; however, once the platelet count reached $> 30 \times 10^9$/l, frank bleeding became less problematic, and purpura predominated, although the majority of patients were asymptomatic. There was evidence of a difference in presenting haemorrhagic symptoms with age and gender (see Table II). Ten per cent of females presented with frank bleeding compared with 14% of males, but the difference between females and males did not achieve statistical significance ($P = 0{\cdot}3$, chi-squared test).

There was one acute haemorrhagic death in the study patients. Full details are given in the section on Deaths.

Spontaneous remissions

There were five patients who underwent spontaneous remission from their ITP; one of particular note attained spontaneous remission after *Herpes zoster* infection 5 years after diagnosis.

Response to therapy

Full details of response to therapy are summarized in Tables III and IV.

Of the 114 patients who presented with a platelet count $< 10 \times 10^9$/l, the majority (78%) eventually achieved CR, with 67% having first-line treatment only and 10% undergoing splenectomy. The prognosis was excellent; < 20% of cases developed chronic ITP that required ongoing treatment.

Fifty-one patients presented with a platelet count between 10 and 19×10^9/l, with 60% achieving CR. Fifty-one per cent of patients required first-line therapy only, 25% proceeded to splenectomy, while 33% were considered to have chronic ITP.

As the platelet count at presentation rose, fewer patients required therapy. Of the 26 patients with a presenting

Table I. Presenting symptoms by presenting platelet count and gender.

Platelet count ($\times 10^9$/l)	Patient gender	Haemorrhage		Purpura		Asymptomatic	
		M	F	M	F	M	F
0–9 ($n = 114$)	56M:58F	12 (21%)	6 (10%)	39 (70%)	36 (62%)	5 (9%)	16 (28%)
10–19 ($n = 51$)	21M:30F	1 (5%)	5 (16%)	15 (71%)	19 (64%)	5 (24%)	6 (20%)
20–29 ($n = 26$)	5M:21F	2 (40%)	2 (10%)	1 (20%)	11 (52%)	2 (40%)	8 (38%)
30–49 ($n = 54$)	29M:25F	1 (4%)	1 (4%)	10 (34%)	13 (52%)	18 (62%)	11 (44%)
Total 245	111M:134F	(14%)	(10%)	(58%)	(59%)	(27%)	(31%)

Men were more likely than women to present with frank bleeding, although this did not reach statistical significance.

Table II. Frank bleeding at presentation (%) by age and gender.

Age range (years)	Male	Female
16–29 ($n = 53$)	1/27 (4%)	4/26 (15%)
30–44 ($n = 43$)	3/21 (14%)	3/22 (14%)
45–59 ($n = 36$)	3/16 (19%)	0/20 (0%)
60–74 ($n = 67$)	7/32 (22%)	5/35 (14%)
75+ ($n = 46$)	2/15 (13%)	2/31 (6%)
Total (all ages) ($n = 245$)	16/111 (14%)	14/134 (10%)

Females showed an increased incidence of haemorrhage only in the 16–29 age group.

platelet count of 20–29 $\times 10^9$/l, 69% achieved CR and 50% of patients required first-line therapy only. The majority of the 54 patients (57%) presenting with a platelet count $> 30 \times 10^9$/l did not receive therapy. Of those patients who required therapy, 33% achieved CR. Most of this cohort continued to have platelet counts between 30 and 100×10^9/l. There were no haemorrhagic deaths recorded.

Splenectomy

Thirty patients (12%) proceeded to splenectomy. Treatment before splenectomy and post-operative response is detailed in Table V. The three patients with platelet counts $> 30 \times 10^9$/l at presentation subsequently became symptomatic as a result of falling platelet counts, and therefore had a splenectomy. Seven of the 30 patients did not achieve CR but are currently asymptomatic. One patient (patient 18) died in the post-operative period on d 15 as a consequence of sepsis.

All patients who underwent splenectomy were registered on the Regional Asplenia Register (Spickett *et al*, 1999).

Table III. Number of treatment modalities given according to presenting platelet count.

Platelet count	No therapy	First line only	Second line	Third line or more	Total proceeding to splenectomy
$< 10 \times 10^9$/l ($n = 114$)	2 (2%)	77 (68%)	26 (23%)	9 (8%)	11 (10%)
10–19 $\times 10^9$/l ($n = 51$)	6 (12%)	26 (51%)	11 (22%)	8 (16%)	13 (25%)
20–29 $\times 10^9$/l ($n = 26$)	7 (27%)	13 (50%)	6 (23%)	0 (0%)	4 (15%)
$\geq 30 \times 10^9$/l ($n = 54$)	31 (57%)	19 (35%)	3 (6%)	1 (2%)	2 (4%)
Total 245	46 (19%)	135 (55%)	46 (19%)	18 (7%)	30 (12%)

The majority of patients responded to first-line therapy. Only 12% of the patient cohort underwent splenectomy during the course of their disease.

Table IV. Clinical outcome by presenting platelet count.

Platelet count	CR	PRNS	PR	M/NR	Lost to follow-up	Haemorrhagic death
$< 10 \times 10^9$/l ($n = 114$)	89 (78%)	15 (13%)	3 (2%)	4 (3%)	1	1
$10–19 \times 10^9$/l ($n = 51$)	31 (60%)	14 (27%)	1 (2%)	2 (4%)	1	2
$20–29 \times 10^9$/l ($n = 26$)	18 (69%)	7 (27%)	0 (0%)	1 (4%)	0	0
$\geq 30 \times 10^9$/l ($n = 54$)	17 (33%)	23 (45%)	1 (2%)	10 (5%)	0	0
Total (245)	155 (63%)	59 (24%)	5 (2%)	17 (7%)	2	3

CR, complete remission; PRNS, partial remission with no symptoms; PR, partial remission; M/NR, minimal/no response.

Platelet count at diagnosis did not predict outcome.

Table V. Clinical details of patients who underwent splenectomy.

Patient no.	Age (years)	Sex	Platelet count ($\times 10^9$/l)	First-line treatment	Second-line treatment	Third-line treatment	Fourth-line treatment	Current status
1	27	F	4	S	IgG + SPL			CR
2	37	F	10	S	SPL			PRNS
3	35	M	13	S	SPL			CR
4	25	M	6	S + IgG	SPL			CR
5	16	F	22	N	SPL			CR
6	17	M	10	S	SPL			PRNS
7	42	F	20	S	SPL			CR
8	38	F	20	S	SPL			CR
9	46	M	37	N	SPL			CR
10	79	F	24	N	SPL			CR
11	28	F	3	S	IgG	SPL		CR
12	38	F	15	S	IgG	SPL		CR
13	66	F	11	S	IgG	SPL		CR
14	63	F	4	S	IgG	SPL		CR
15	27	M	18	S	IgG + S	SPL		PRNS
16	32	M	18	S	IgG	SPL		PRNS
17	65	M	48	S	S + IgG	SPL		Died (MI)
18	80	F	10	S	S	SPL		Died (Post-op sepsis)
19	22	F	4	S	S	SPL		CR
20	51	F	14	S	S	SPL		CR
21	75	F	6	S	IgG	SPL		CR
22	43	M	3	S	S + AZA	SPL		PRNS
23	38	M	8	S	IgG	SPL		CR
24	22	F	4	S	IVIG	SPL		CR
25	19	F	12	S	IgG	SPL		CR
26	48	M	2	S	IgG	SPL		CR
27	25	F	10	S + AZA	IgG	SPL		CR
28	69	M	11	S + IgG	AZA	DAN	SPL	PRNS
29	66	F	13	S	AZA	IgG	SPL	PRNS
30	77	M	5	S	IgG	IFN	SPL	CR

S, steroids; IgG, immunoglobulin; N, none; AZA, azathiaprine; SPL, splenectomy; DAN, danazol; IFN, interferon; CR, complete remission; PRNS, partial remission with no symptoms; MI, myocardial infarction.

No patients underwent splenectomy as first-line treatment. The majority of patients attained complete remission after splenectomy.

Follow-up to date has identified no late post-splenectomy infective deaths in this study cohort of patients.

Deaths

Twenty-seven patients died within the study period. The details are analysed according to platelet count at diagnosis (see Table VI). Three deaths were considered to be directly attributable to ITP, but only one of these three died at presentation.

One patient died in the acute phase of the disease, on d 5. This patient was a 19-year-old-male, who had concomitant acute autoimmune haemolytic anaemia, and died of gastrointestinal haemorrhage while receiving steroid therapy. A further two patients died later in the course of their disease, one of a gastrointestinal bleed having developed low-grade NHL and another while on warfarin. One patient died as a consequence of sepsis on the 15th day after splenectomy.

DISCUSSION

The authors of the American Society for Haematology practice guidelines for ITP identified priorities for future research following their evidence-based literature review (George *et al*, 1996). We have attempted to address aspects of three of their priorities in the current study:

1 The need for a prospective study of the clinical course of untreated ITP in patients presenting with mild or moderate thrombocytopenia and no clinically important bleeding, including long-term follow-up and the outcomes of bleeding and mortality.
2 The need to obtain data on the clinical course of chronic refractory ITP, especially in those untreated patients without clinically important bleeding.
3 The need to assess the prognostic relation of the platelet count to bleeding and mortality.

In relation to point 1, we have considered only patients who have moderate thrombocytopenia.

It is likely that our study will be the last to contain bone marrow confirmation of diagnosis as it has been recommended (George *et al*, 1996) that performing a bone marrow biopsy is unnecessary in patients under the age of 60 years with otherwise normal blood films.

ITP is generally reported to be commoner in women than in men, and this is supported by numerous reports in the literature (Watson-Williams *et al*, 1958; Doan & Bouroncle, 1960; Thompson *et al*, 1972; DiFino *et al*, 1980; Pizzuto & Ambriz, 1984; Jacobs & Wood, 1986; Cortelazzo *et al*, 1991; Kaufman *et al*, 1993; George *et al*, 1995; Portielje *et al*, 2001; Godeau *et al*, 2002) (see Table VII). The present study, which is population based, found that, although the absolute majority of patients presenting with ITP are women, when the population at risk is taken into account, the age/gender-specific incidence is similar (see Fig 1). The actual incidence shows a biphasic distribution with most patients presenting during the seventh and eighth decades (Fig 1). This contrasts with the incidence of ITP in adults extrapolated from the incidence in children, which has been estimated to be 6·6 per 100 000 (George *et al*, 1995). However, our study was restricted to patients with platelet counts of $\leq 50 \times 10^9$/l. A higher threshold would have produced a greater incidence than 1·6 per 100 000 per year as found in the present study.

The median age at presentation in the five studies in which this information is available (Jacobs & Wood, 1986; Cortelazzo *et al*, 1991; Kaufman *et al*, 1993; Portielje *et al*, 2001; Godeau *et al*, 2002) was 38–49 years, whereas in the current study, it is 56 years. It is possible that a degree of selection in previous studies (e.g. reports from tertiary referral centres) may account for this difference in incidence. The median age of the general population has increased significantly over the last three decades, and this may have further influenced the age incidence patterns. Also, many of our patients (27·8%) were asymptomatic and only diagnosed incidentally after a routine full blood count. These patients would probably not have been identified before the automated full blood count analysis introduced over the last three decades, as platelet counts would not have been performed routinely.

Another characteristic of our patient cohort that differs from previously published observations is the pattern of incidence of haemorrhagic manifestations. As shown in

Table VI. Cause of death by presenting platelet count.

Platelet count at presentation ($\times 10^9$/l)	Cause of death
< 10	Bleeding
	Pneumonia
	Carcinoma of bronchus
	Carcinoma of colon ($n = 2$)
	Refractory anaemia with excess blasts
	Myocardial infarction ($n = 2$)
	Non-Hodgkin's lymphoma
10–19	'Old age'
	Alcoholism
	Bleeding ($n = 2$)
	Carcinoma of ovary
	Chronic lymphocytic leukaemia
	Cerebral vascular accident (NB. platelet count normal)
	Post-splenectomy complications
20–29	Post-operative bowel resection (ulcerative colitis)
	Carcinoma of breast
≥ 30	'Old age'
	Adenocarcinoma
	Carcinoma of bronchus
	Carcinoma of breast ($n = 2$)
	Myocardial infarction
	Chronic obstructive airways disease ($n = 2$)
	Ruptured aortic aneurysm

Only four patients died of bleeding and/or therapy that was directly attributable to their ITP.

Table VII. Summary of previous studies of ITP.

Study	No. of patients	Median age (range)	Ratio M:F	Platelet counts ($\times 10^9$/l) included in study	BM confirmation	At study entry % with chronic ITP	Bleeding at presentation-line therapy	Response to first-line treatment	% having splenectomy	(%) Death rate
Watson-Williams *et al* (1958)	58	NA	1:2·6	< 100	N	21%	NA	75%	39	0·1
Doan & Bouroncle (1960)	271	(0–80)	1:2·1	< 50	Y	NA	33%	NA	62	1·4
Thompson *et al* (1972)	66	(14–80)	1:2·1	< 100	Y	NA	NA	49% CR 26% PR	54	0·1
Jiji *et al* (1973)	54	NA	NA	'Significant reduction'	Y	100%	NA	24%	88	0·1
DiFino *et al* (1980)	62	NA	1:2	< 30	Y	71%	63%	43%	60	0·1
Picozzi *et al* (1980)	38	(0–70)	NA	NA	NA	100%	5%	3% CR 39% PR	68%	0·1
Pizzuto & Ambriz (1984)	934	(20–65)	1:3·3	NA	NA	NA	NA	65%	43%	5·0
Jacobs & Wood (1986)	148	38 (13–38)	1:3·2	10–180	Y	NA	1%	19%	69%	NA
Cortelazzo *et al* (1991)	117	43 (16–84)	1:2·9	< 100	NA	100%	7%	NA	28%	0·1
Kaufman *et al* (1993)	255	49	1:1·8	< 30	Y	NA	NA	NA	NA	NA
Portielje *et al* (2001)	152	38 (15–86)	1:1·7	< 100	Y	0%	82%	59%	57%	2·6%
Godeau *et al* (2002)*	122	38 (24–59)	1:1·9	< 20	Y	0%	Excluded from study	40%	N/A	N/A
Present study	245	56 (16–91)	1:1·2	< 50	Y	0%	12%	68%	12%	1·6%

*Randomized trial.

NA, not available; N/A, not applicable.

The majority of studies described patients who were diagnosed before the era of readily available automated blood counts. There has been only one recent randomized study of treatment in this disorder.

Table I, this unselected cohort showed a non-statistically significant trend for males to be more likely to present with frank bleeding, whereas in females, the presenting symptoms were more likely to be purpura.

In the present study, the death rate from causes directly related to ITP or its treatment was 1·6% with only one patient dying at presentation. This would be in keeping with the experience of others (Watson-Williams *et al*, 1958; Doan & Bouroncle, 1960; Thompson *et al*, 1972; JiJi *et al*, 1973; DiFino *et al*, 1980; Picozzi *et al*, 1980; Pizzuto & Ambriz, 1984; Cortelazzo *et al*, 1991; Portielje *et al*, 2001) where the reported incidence was 0–5%.

Although not strictly ITP, but a drug-related thrombocytopenia, it was interesting to note that quinine was the commonest drug identified as causing thrombocytopenia (46·4%). In two of these patients, this diagnosis was made only when 'relapse' occurred and a more detailed history was taken; the consequence of patients being unaware that tonic water may contain the drug quinine. We feel that quinine should be specifically enquired about when obtaining a drug ingestion history in patients with ITP, particularly as these are older patients presenting with a low platelet count who are mostly symptomatic. Withdrawal of the drug resulted in a good response.

The most frequently used form of first-line treatment for our cohort was steroid therapy. Although not completely comparable, the response rate was similar to that reported in the most recent studies (Portielje *et al*, 2001; Godeau *et al*, 2002). The total number of patients progressing to splenectomy was 12% (see Table III). This is lower than in the literature (28–88%, see Table VII) (Watson-Williams *et al*, 1958; Doan & Bouroncle, 1960; Thompson *et al*, 1972; JiJi *et al*, 1973; DiFino *et al*, 1980; Picozzi *et al*, 1980; Pizzuto & Ambriz, 1984; Jacobs & Wood, 1986; Cortelazzo *et al*, 1991; Portielje *et al*, 2001) and may reflect a more selected group of patients in other studies.

In this study cohort, presenting platelet count was not a predictor of likelihood of progression to splenectomy. Table III shows that the majority of patients became clinically stable or achieved remission after treatment with steroids. A small number required further effective second-line treatment. The prognosis was excellent: only 81 (33%) had chronic ITP (with a platelet count $< 50 \times 10^9$/l). The majority of these patients were asymptomatic, not requiring therapy (and 19 never received any treatment at all for their ITP).

In conclusion, this population-based study of clinically significant ITP showed that, contrary to previously published studies, the age/gender-specific incidence was approximately equal for males and females, and the maximum age-specific incidence was in the eighth decade. This is in contradiction to the generally accepted epidemiological data found in textbooks (George *et al*, 1995), and may reflect the changing age profile of the population, the referral patterns of patients in previous studies and the introduction of automated cell counters. The platelet count at presentation was not found to be a prognostic indicator for splenectomy; interestingly, it was the cohort with a presenting platelet count of $10–19 \times 10^9$/l who were more likely to proceed to splenectomy. Patients with a platelet count $> 30 \times 10^9$/l were mostly asymptomatic and required no treatment. Response to first-line therapy was good, with only 32·2% of patients proceeding to further therapy. Generally, our treatment approach relied less on splenectomy as a first- or second-line therapy compared with other studies. The death rate for ITP was low, with three out of 245 patients dying of bleeding, and only one of the three was in the initial phase of the disease. It is interesting to note that only a minority of patients required further intervention after steroid therapy, with relatively few progressing to chronic ITP.

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