

# A survey of the management of idiopathic thrombocytopenic purpura in South Africa: Do we need guidelines for developing countries?

D C Stefan, MMed (Ped), FCP (Paed), MD

G Wessels, MB ChB, MMed (Ped), MD

Department of Paediatrics and Child Health, Tygerberg Hospital and Stellenbosch University, Tygerberg, W Cape

**Introduction.** Idiopathic thrombocytopenic purpura (ITP) is the most common bleeding disorder of childhood.

**Aim.** To describe the management of ITP in South Africa.

**Methods.** A survey was sent to 410 doctors in the country, describing four different scenarios in children newly diagnosed with ITP and soliciting responses concerning the diagnosis and management.

**Results.** Steroids were the first line of choice in treating ITP. Anti-D immunoglobulin was not considered in the management, and most practitioners would perform a bone marrow aspiration even if no treatment with steroids would be given. The vast majority of the patients would be treated in hospital.

**Conclusions.** This is the first study done in South Africa (and in Africa), and it shows a great variation in the management of children with newly diagnosed ITP. Prospective studies in developing countries where various constraints to health care delivery exist are required to produce evidence-based recommendations for this patient group.

Idiopathic thrombocytopenic purpura (ITP) is the most common bleeding disorder of childhood. It consists of a persistent decrease in the platelet count to less than  $150 \times 10^9/L$ , caused by autoantibodies that bind to thrombocytes and thus trigger their premature destruction by the reticuloendothelial system, mainly in the spleen.<sup>1</sup> Its incidence has been estimated at 4/100 000 children per year.<sup>2</sup>

In childhood this is usually a self-limiting disease, but in 25 - 30% of cases it may become chronic, lasting more than 6 months and sometimes many years. While most patients will only present with petechiae and bruises, and occasionally epistaxis, digestive bleeding or menorrhagia may be troublesome. Traumatic or operative excessive bleeding is possible as well. The most serious complication of ITP, potentially fatal intracerebral haemorrhage, is however rare.

Owing to the high rate of spontaneous remission, expectant management is a definite option. Other therapeutic resources are corticosteroids, intravenous immunoglobulins or anti-D immunoglobulins, and platelet transfusion for life-threatening (including intracerebral) haemorrhage. For chronic ITP, after 1 - 2 years with severe lifestyle restrictions, crippling menorrhagia or other life-threatening haemorrhage, splenectomy may be recommended.<sup>1</sup>

There is, however, no uniform approach to the indications for or sequence of therapies for patients with newly diagnosed ITP. Controversies exist with regard to treating patients as opposed to observing them; if treatment is instituted, some specialists use immunoglobulins first and corticosteroids as second line, others start with steroids. There is no uniformity in the use of bone marrow aspiration or biopsy to exclude other diseases before deciding on the course of management. Further, there

is no agreement on the need to hospitalise these patients. The guidelines published so far, among which those of the British Society for Haematology<sup>1</sup> and of the American Society of Hematology<sup>3</sup> are the most widely quoted, are based mainly on expert opinions rather than evidence. These two guidelines are also vastly different: while in the UK expectant management is recommended in most cases without significant bleeding, in the USA the balance inclines towards therapy, based only on the platelet count.

The dearth of evidence on which to build up management guidelines is mainly due to the relative rarity of the disease, its self-limiting character which makes it suitable for treatment by doctors with various levels of specialisation, and the lack of co-operation between specialists from different geographical areas with regard to patient data recording and randomised studies.

This survey was addressed to medical officers, registrars, specialists and paediatric haematologists and asked questions related to the management of ITP, with the aim of identifying the most frequent therapeutic choices. The results of this study will help to determine the need for implementing South African guidelines for managing ITP.

## Materials and methods

A 2-page survey with 14 questions was sent in August 2006 to 410 paediatricians, medical officers and registrars in private, tertiary, regional and district hospitals in South Africa. The questionnaire was adapted from a published North American study.<sup>4</sup> A similar questionnaire had been used in Australia.<sup>5</sup> Doctors were asked to complete the survey and return it by fax, e-mail or post.

The survey presented four clinical scenarios of children with acute ITP, with a platelet count of  $3 \times 10^9/l$ , with or without mucosal bleeding (wet and dry purpura, respectively). Participants were invited to describe how they would treat each of the children described in the scenarios, and were asked to avoid giving a standard textbook answer.

The first case (scenario A) described a 5-year-old boy with bruising and petechiae that had developed within a short time, but no other significant history. There was no mucous membrane bleeding and with the exception of the low platelet count the rest of the full blood count was normal. All data were consistent with a diagnosis of ITP.

The following scenario (B), on the same patient, added cutaneous bleeding, ongoing epistaxis, haemorrhagic bullae on the buccal mucosa, gingival oozing and a haemoglobin concentration of 9.8 g/dl.

The remaining two scenarios (C and D) were constructed on the same basis as scenario B, but changed the age of the child to a 9-month-old in C and a 12-year-old in D.

The description of each case was followed by questions related to initial therapy, doses of initial medication, need for hospitalisation or referral and opinion about bone marrow procedures. The same questions were asked after every scenario. Out of 4 - 5 possible answers, only one had to be chosen.

## Results

One hundred and one completed questionnaires were received, 78 from general paediatricians and subspecialists (we will refer to both categories as 'specialists' in the study), 10 from registrars and 11 from medical officers working in paediatrics. Two respondents did not state their level of training. Most of the specialists were working in tertiary or private hospitals (31 and 34, respectively), 3 were in regional hospitals and 2 were in district hospitals. Nine specialists did not specify their workplace. While the registrars were active mainly in tertiary hospitals, the medical officers were distributed between tertiary (3), regional (1) and district hospitals (2); 5 medical officers did not specify their employer.

Most patients were managed in academic hospitals. About two-thirds of the private practice respondents saw between 1 and 5 patients with ITP per year, while the other third of private practitioners rarely managed a case. A few children were managed in regional or district hospitals. Nineteen participants did not answer either the question about workplace or the one about the number of patients seen per year (Fig. 1).

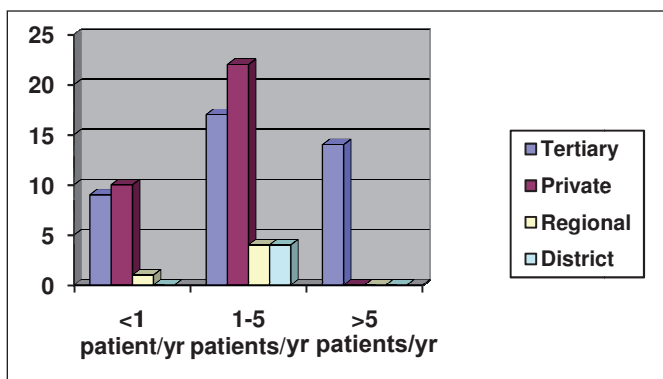


Fig. 1. Number of patients seen annually in various types of practices. The vertical axis represents numbers of respondents.

The responses to the question 'How would you usually treat such cases?' are depicted in Fig. 2. For the milder presentation described in scenario A, almost 1 in 4 respondents would choose expectant management but most would treat, mainly with steroids or - in a smaller number - with steroids combined with immunoglobulins. The more severe clinical picture in the remaining scenarios represented an indication to treat for most respondents; however, between 2 and 5 doctors per scenario would still wait for a spontaneous improvement. The tendency to use steroids with immunoglobulins in these cases was more substantial than in scenario A, but the number of respondents who would prescribe either steroids or immunoglobulins alone was larger than the number of those who would use both combined. Only one doctor would treat with anti-D immunoglobulins.

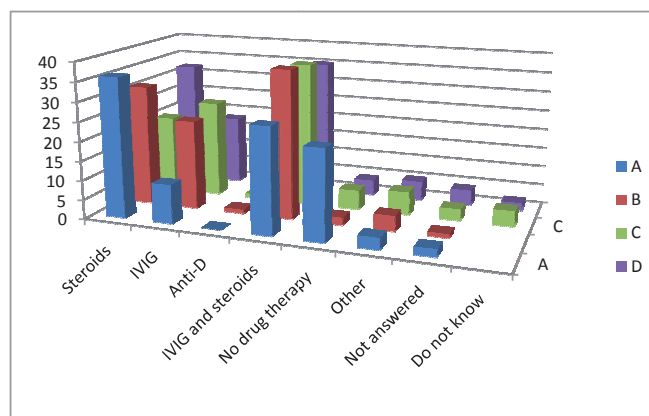


Fig. 2. Choice of therapeutic modality in each scenario. The vertical axis represents numbers of respondents.

The answers to the question 'What dosage of immunoglobulins would you use?' are summarised in Fig. 3. When intravenous immunoglobulins would be used, the dosage chosen varies substantially, but around 40% of responders who use this therapy would give 1 g/kg daily for 2 days. Between 13 and 19 respondents per scenario did not answer, because they would not consider using immunotherapy.

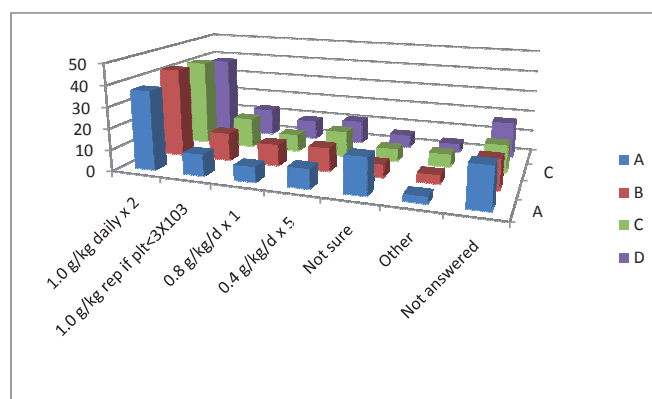


Fig. 3. Dosages of immunoglobulins reported. The vertical axis represents numbers of respondents.

In response to the question 'What dosage of corticosteroids would you use?', over 40% of those surveyed would use prednisone 2 mg/kg/day for 7 days minimum (Fig. 4). There was also a strong trend to give 4 mg/kg/day for a minimum of 4 days, probably because of the convenience of a shorter duration of therapy. Other dosages are rarely used.

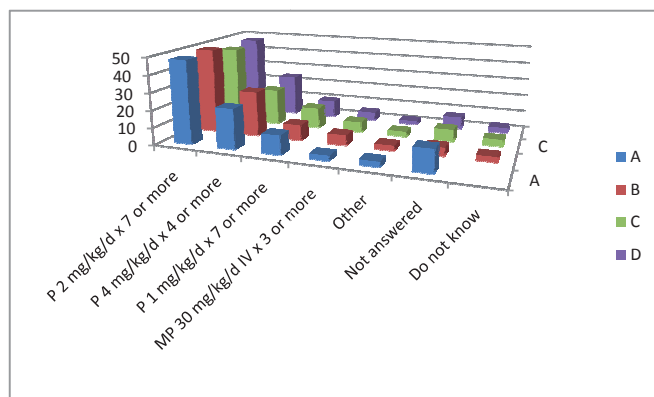


Fig. 4. Dosages of corticosteroids reported (P = prednisone, MP = methylprednisolone). The vertical axis represents numbers of respondents.

The replies to the question ‘Do you hospitalize such patients?’ indicated a trend to admit the more severe cases to hospital, while for the milder scenario A, hospital referral was not seen as essential. The distribution of the various responses is shown in Fig. 5.

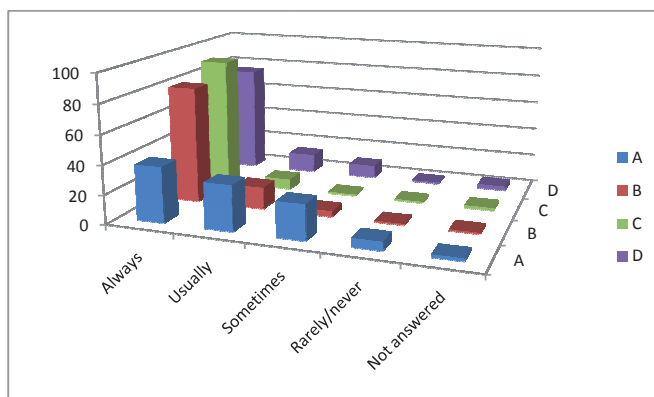


Fig. 5. Decisions on admission to hospital per scenario. The vertical axis represents numbers of respondents.

The answers to the question ‘Would you perform a bone marrow aspirate before starting corticosteroid treatment?’ are summarised in Fig. 6. This approach is far from being standard, although this survey showed a strong trend to perform bone marrow aspiration or biopsy.

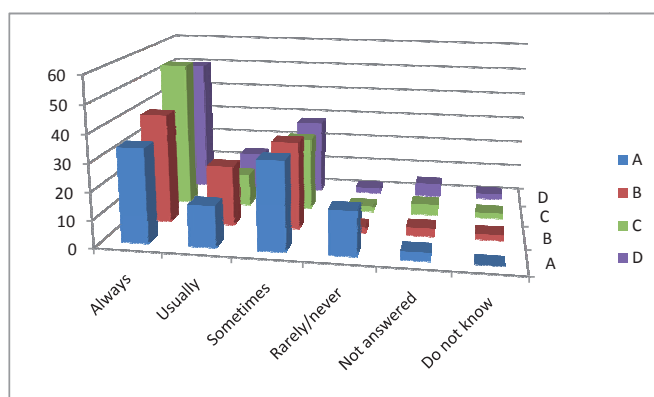


Fig. 6. Frequency of performing bone marrow aspirate before giving corticosteroids. The vertical axis represents numbers of respondents.

In reply to the question ‘Would you perform a bone marrow aspirate even if you are not going to administer corticosteroids?’, from 36 to 47 responders per scenario would always do a bone marrow study even if they did not plan to give prednisone. This question was only asked for scenarios B, C and D. The answers are shown in Fig. 7.

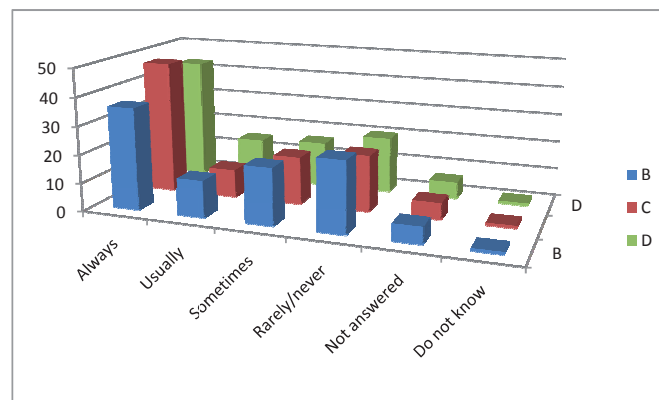


Fig. 7. Frequency of performing bone marrow aspirate when no corticosteroid therapy was planned. The vertical axis represents numbers of respondents.

## Discussion

The survey describes some differences of approach to the child with ITP among our 101 responders. Most cases are treated in academic centres, indicating a high rate of referrals. Two-thirds of the private paediatricians would treat the patients themselves; the remaining third rarely saw any cases and would rather refer them to tertiary hospitals.

Even in the mild scenario A, the vast majority of doctors would prescribe steroids or immunoglobulins and only a limited number of practitioners would adopt the conservative approach. On analysing these data further, it appeared that those responders who would opt for conservative management were working in the government health care system, while private practitioners would always treat such cases. Prednisone dosages of 2 mg/kg/day for 7 days or 4 mg/kg/day for 4 days were the most common regimens used. In the severe cases the tendency was to use steroids or immunoglobulins, while about one-third of respondents would use combinations of the two therapies. Only 1 respondent would use anti-D. This may be due to the high cost of this therapy.

Most responders would do a bone marrow aspirate before prescribing steroid therapy. This investigation would rule out the rare but possible leukaemia, which sometimes manifests with haemorrhagic features and thrombocytopenia. As steroids would delay the institution of appropriate therapy and even worsen the prognosis in cases of leukaemia,<sup>6</sup> many

*This survey showed a strong trend to perform bone marrow aspiration or biopsy.*



authors recommend a marrow aspirate before corticosteroid therapy is started.

Many of the respondents would also perform a bone marrow examination even when they were not intending to prescribe steroids. However, this approach is controversial and many experts incline not to test the bone marrow in such cases, except when there is doubt about the diagnosis.<sup>1,7</sup>

Most respondents would admit the child with ITP to hospital, probably owing to the frequent use of medications to speed up the increase in the platelet count. However, there were no questions related to the social circumstances of the child's family, the availability of transport or the distance to the hospital, although these factors might have been considered when rejecting an expectant approach combined with outpatient follow-ups.

This survey indicates that controversy over the diagnosis and management of childhood idiopathic purpura exists in South Africa and is similar to that highlighted in published overseas studies.<sup>3,8-10</sup> The *Standard Treatment Guidelines and Essential Drug List, Hospital Level, Paediatrics*, published by the Department of Health in 2006,<sup>11</sup> contains guidelines for the treatment of ITP at district and regional hospital level. These are presumably either not known or not accepted at the tertiary or private health care level where most patients with ITP are treated, and a wide diversity in treatment strategies for this disease therefore still exists.

Several limitations to this study are acknowledged. Firstly, the response rate was low (25%). Secondly, the respondents do not constitute a representative sample of the practitioners who treat childhood ITP in South Africa, because of small numbers and disproportional representation of specialists. Thirdly, a small bias might result from the fact that several doctors working in the same institution might follow the same protocols.

However, this first and only survey on ITP, which is the most common bleeding disorder in children in South Africa,

provides substantial evidence of the multitude of management approaches in childhood ITP. The data presented highlight the need for the implementation of a common practice guideline.

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