

# Chapter 15: Aspects of Anaemia Management in Children with Established Renal Failure

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## Summary

- Despite the universal availability of erythropoietin and intravenous iron, 14% of transplant patients and 30% of dialysis patients have a haemoglobin below 10.5 g/dl. Only 11% of anaemic transplant patients were receiving erythropoietin.
- There was a linear relationship between eGFR and haemoglobin with the risk of anaemia occurring at a much higher eGFR than would be expected in the CKD population.
- There was also a significant association between the use of Mycophenolate and anaemia. 95% of dialysis patients were receiving erythropoietin and 47% intravenous iron.
- It is speculated that raising the target haemoglobin for this population to 13 g/dl could shift the whole distribution curve to the left, reducing the proportion with anaemia. Doing this would require careful monitoring to steepen the distribution curve and limit the upper tail if complications of high haematocrits are to be avoided.

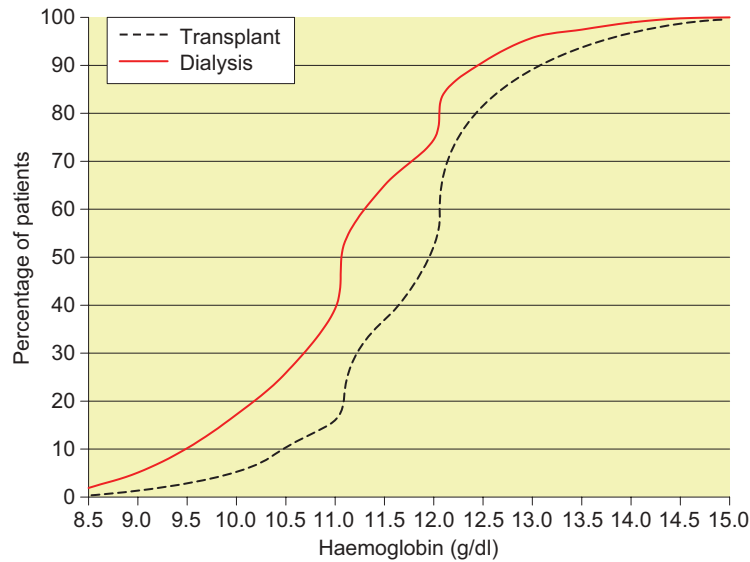
## Introduction

The control of anaemia is an important factor in the reduction of morbidity and mortality in the ERF population<sup>1</sup>. The Renal Association standards suggest that, outside of infancy, the haemoglobin of patients should be maintained at above 10.5 g/dl with a combination of erythropoietin and haematinics<sup>2</sup>. More recently the National Institute for Clinical Excellence suggested a higher target with the aim of maintaining the haemoglobin between 11 and 12 g/dl and taking action when the haemoglobin is outside of this range, or appeared to be moving

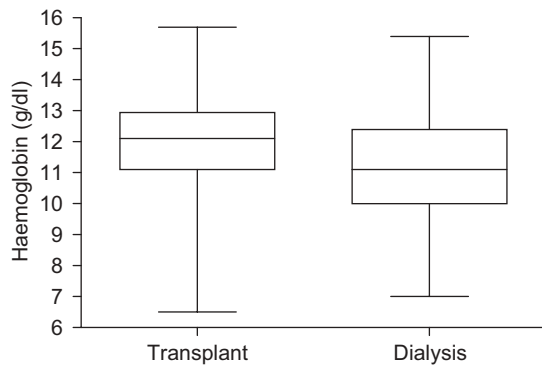
outside this range on trend analysis<sup>3</sup>. Whilst great attention is paid to this in the dialysis and CKD population, it is easy to overlook haemoglobin parameters in those with renal allografts as concentration within the clinic is usually on other factors such as eGFR and immunosuppression. However, the paediatric transplant population is the largest cohort of patients being reviewed regularly with CKD. Moreover, their reduced renal function, together with the effects of some immunosuppressants upon the bone marrow and the effects of antihypertensives such as ACE inhibitors and ARB's, make them prone to anaemia.

The cumulative frequency distribution of Hb levels for 135 dialysis patients with a full data set available and 386 transplant patients who had been grafted at least 12 months before the collection of the data set are shown in Figure 15.1. There is clearly a difference in the distributions with the transplanted patients doing better. However, 14% of transplant patients and 30% of dialysis patients had a Hb below the NICE guidelines of 10.5 g/dl. Using the European Best Practice guidelines of maintaining the Hb above 11 g/dl, 20% of transplant patients and 47% of dialysis patients were below this figure. For transplant patients, 47% had a Hb above the 12 g/dl whilst 33% of dialysis patients were above this level. This left just 33% of transplant patients and 20% of dialysis patients within the desired range. The difference between the distributions was significant ( $p < 0.0001$ ). The median Hb in transplant patients was 12.1 g/dl whilst the median in dialysis patients was 1 g/dl lower at 11.1 g/dl (Figure 15.2).

For the transplanted patients, erythropoietin was recorded as being utilised in just 14 patients, eight of whom had a satisfactory Hb and six of whom were amongst the 55 patients with a Hb  $<10.5$  g/dl. Intravenous iron was only recorded as having been given to 1 patient



**Figure 15.1: Cumulative frequency distribution of haemoglobin values in dialysis and transplant patients**

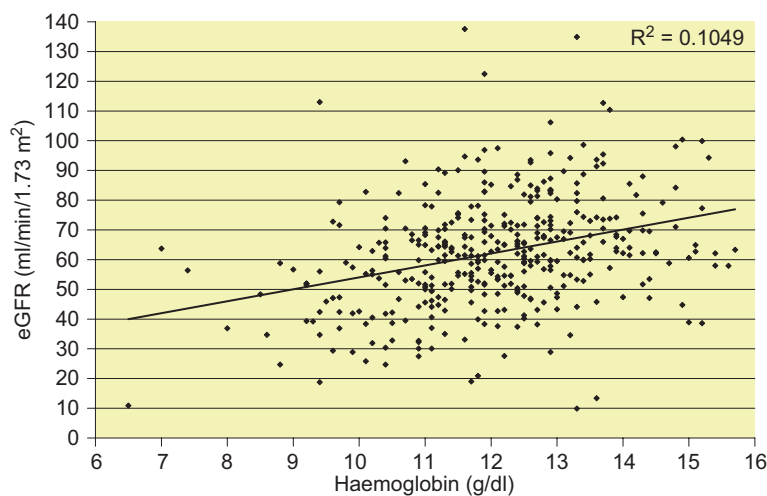


**Figure 15.2: Median, quartiles and range of haemoglobin in paediatric RRT patients**

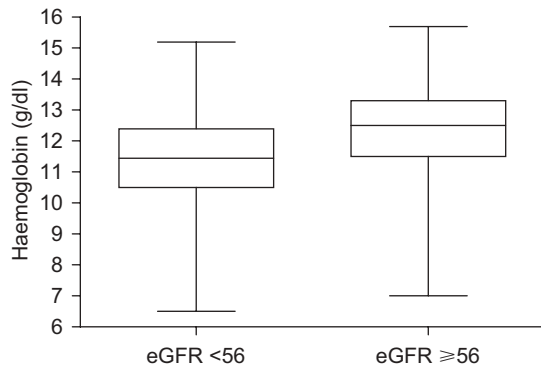
and that patient did have a low haemoglobin. Four patients were recorded as having had transfusions in the previous 12 months of whom two were in the low Hb group. This of

course, may not be a true marker for anaemia as transfusions may have been given following surgical or other procedures.

There was a significant linear correlation between eGFR as calculated by the Schwartz formula ( $40 \times \text{height \{cm\}/creatinine \{\mu\text{mol/L}\}}$ ) and Hb ( $r^2 = 0.10$ ,  $p < 0.0001$ , Figure 15.3). It is noteworthy that the regression line crosses a Hb of 10.5 g/dl at an eGFR of 56 ml/min/1.73 m<sup>2</sup>. This is a much higher eGFR figure than might be expected for the potential development of anaemia, particularly as a low value has been used for the constant for eGFR calculation, based upon the findings in previous reports. Comparing the Hb distributions of those with an eGFR below and above 56 ml/min/1.73 m<sup>2</sup>, they are significantly different



**Figure 15.3: Correlation of haemoglobin against eGFR in paediatric allograft recipients**

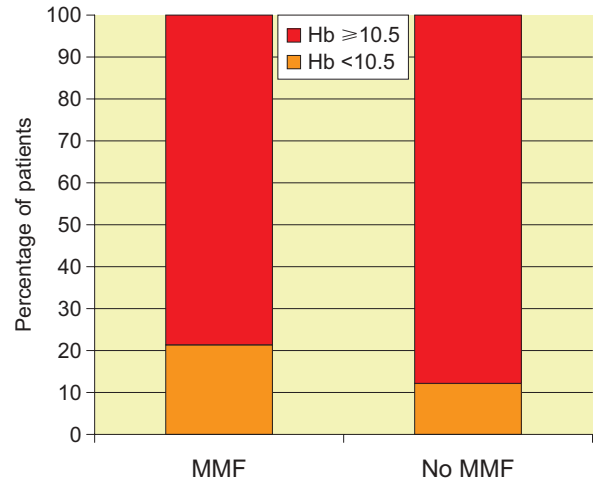


**Figure 15.4: Median, quartiles and range of haemoglobin by eGFR**

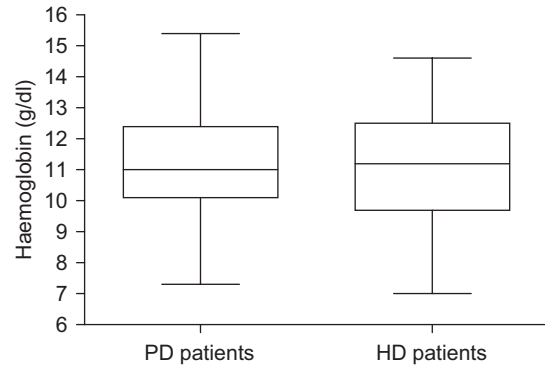
( $p=0.0001$ , Figure 15.4). Thus, special attention needs to be paid to the Hb of patients with renal allografts at a level at which problems would not be expected in the ordinary childhood CKD population.

In addition to the poor agreement between eGFR and true GFR in transplant patients, this phenomenon will be related to the use of drugs such as ACE inhibitors and immunosuppressive drugs. One recent change in practice has been a move to using Mycophenolate rather than Azathioprine. To investigate the effect of this upon anaemia, the distributions of the Hb values in 89 of the above cohort who were receiving Mycophenolate were compared with the 297 who were not. As all these patients were at least one year post engraftment, post surgical anaemia should not have played a part. Some of the patients may have been changed onto Mycophenolate because of chronic allograft nephropathy and will also have had lower eGFR's as a consequence. For others however, the use of Mycophenolate would simply have been in line with updated immunosuppressive protocols. The use of Mycophenolate was associated with a significantly greater proportion of patients with a Hb below 10.5 g/dl ( $p=0.0374$ , Figure 15.5).

For patients on dialysis, the use of erythropoietin was recorded in 127 of the 135 patients on this modality. Intravenous iron was used in 63 patients (47%). The usage of intravenous iron appeared to be less in those with a low Hb ( $<10.5$  g/dl) though this difference failed to reach statistical significance. Twelve patients were recorded as having received transfusions (9%), 6 of these had a Hb  $<10.5$  g/dl. Despite the potential for blood loss there was no difference in the



**Figure 15.5: Haemoglobin achievement and the use of Mycophenolate (MMF)**



**Figure 15.6: Median, quartiles and range of haemoglobin for PD and HD paediatric patients**

Hb distribution of those on haemodialysis to those on peritoneal dialysis (Figure 15.6).

## Conclusions

These data suggest that whilst the majority of paediatric ERF patients have an acceptable haemoglobin, a significant minority do not. Within the transplant population there needs to be a greater awareness of the risk of anaemia at a relatively high GFR. Screening and treatment with haematinics and erythropoietin need to be part of routine patient assessment. For the dialysis population there may be potential for a greater use of intravenous iron. There are however, other factors, such as control of renal osteodystrophy, that play a major role in the control of anaemia.

These data were collected at a time when the Renal Association Standards were available but

before the publication of the NICE guidelines. It remains to be seen whether changing to these recommendations improves the distribution of haemoglobin in the paediatric ERF population. It may transpire that the range quoted by NICE is too narrow.

Movement of the whole distribution curve to give a median haemoglobin for the population of 13 g/dl would potentially leave 9% of transplant patients and 18% of dialysis patients with a haemoglobin above 15 g/dl. This is potentially undesirable with the reported morbidity associated with higher haemoglobin values<sup>4,5,6,7</sup>, though all this data relates to adult studies and there is as yet, no reported morbidity from having a haemoglobin at the high end of the normal range in children. Careful monitoring could limit the numbers in this bracket by creating a steeper distribution curve with a smaller upper tail whilst the movement of the population towards having a higher median haemoglobin would have a major effect on the proportion of significantly anaemic patients. The answer to this question will come from further Registry analyses after the NICE guidelines have been implemented for a period of time.

## References

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This report was reviewed, revised and approved by the UK Paediatric Renal Registry subcommittee comprising:

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This report is presented on behalf of the BAPN.