Copper Levels in Patients with Unexplained Dysplastic Cytopenia
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Supplementary Materials

ESM1 Inclusion and exclusion criteria

| Inclusion criteria                                                                 | Exclusion criteria                                                                 |
|-----------------------------------------------------------------------------------|------------------------------------------------------------------------------------|
| Patient had one or more persistent cytopenia(s) or macrocytosis                    | Bone marrow blasts found to be increased in excess of >5%                           |
| Patient had had a bone marrow examination performed to investigate persistent and unexplained cytopenia(s) or macrocytosis, and a diagnosis of ICUS, IDUS or MDS was made | Patient found to have a clonal cytogenetic or molecular abnormality (with the exception of deletion of chromosome Y) |
| Patient was over 18 years of age.                                                 | Patient had been started on treatment for MDS (excluding transfusion, erythropoietin and/or steroid therapy). |
| Patient had given consent to participate.                                         | Patient unable or unwilling to give consent.                                        |
| Patient was under the care of haematology at Hammersmith Hospital.                | Patients who received copper replacement therapy in the past 12 months.            |
### Participant demographics

| Demographic | Frequency (%) |
|-------------|---------------|
| **Age**     |               |
| 50 to 59    | 2 (12%)       |
| 60 to 69    | 2 (12%)       |
| 70 to 79    | 6 (35%)       |
| 80 to 89    | 7 (41%)       |
| **Sex**     |               |
| Male        | 9 (53%)       |
| Female      | 8 (47%)       |
| **Ethnicity** |             |
| Black Caribbean | 4 (24%)     |
| Greek       | 1 (6%)        |
| Indian      | 1 (6%)        |
| Middle Eastern | 2 (12%)   |
| Moroccan    | 1 (6%)        |
| Turkish     | 1 (6%)        |
| White British | 5 (29%)    |
| White Irish | 2 (12%)       |
| **BMI**     |               |
| <18.5       | 2 (12%)       |
| 18.5 to 24.9| 6 (35%)       |
| 25.0 to 29.9| 6 (35%)       |
| >30.0       | 3 (18%)       |
ESM3 Full blood count results at time of inclusion. All participants had at least one cytopenia M – males; F – females

| Blood test            | Mean value (median) | Range               | (Reference Range)          |
|-----------------------|---------------------|---------------------|-----------------------------|
| **Red cell count**    | M: 4.17 (3.95)      | M: 2.85 to 6.05     | (M: 4.7 to 6.1 x10^12/L)    |
|                       | F: 3.38 (3.49)      | F: 2.32 to 4.61     | (F: 4.2 to 5.4 x10^12/L)    |
| **Haemoglobin**       | M: 115 (118.0)      | M: 95 to 127        | (M: 130 to 180 g/L)         |
|                       | F: 104.3 (107.5)    | F: 74 to 135        | (F: 114-165 g/L)            |
| **Mean Cell Volume**  | 92.6 (96.4)         | 58.9 to 109.9       | (83.5 to 99.5 fL)           |
| **Platelets**         | 127.2 (113.0)       | 34 to 387           | (130 to 370 x10^9/L)        |
| **White Cell Count**  | 4.6 (4.1)           | 2.2 to 8.1          | (4.2 to 10.6 x10^9/L)       |
| **Neutrophils**       | 2.2 (2.6)           | 0.6 to 6.0          | (2.0 to 7.1 x10^9/L)        |
**ESM4 Findings for each patient** BMI – Body Mass Index, Cu – serum copper level, Hb – haemoglobin, RCC – red cell count, MCV – mean cell volume, WCC – white cell count, Neut – neutrophils, Plts – platelets, CRP – C-reactive protein, PPI – proton pump inhibitor

| Patient | Gender | Age | BMI  | Cu   | Hb   | RCC  | MCV  | WCC  | Neut | Plts | CRP | Dysplastic lineage(s) | Risk factors                      |
|---------|--------|-----|------|------|------|------|------|------|------|------|-----|----------------------|-----------------------------------|
| 1       | Male   | 79  | 21.30| 11.3 | 113  | 6.05 | 58.9 | 2.9  | 1.5  | 36   | 0.6 | Erythroid & Megakaryoblastic |                                   |
| 2       | Male   | 78  | 28.10| 13.3 | 119  | 5.74 | 62.4 | 3.6  | 1.4  | 133  | 1.0 | Erythroid             |                                   |
| 3       | Male   | 81  | 31.60| 14.7 | 127  | 4.47 | 82.7 | 4.1  | 0.7  | 116  | 0.3 | No CRP               | Dialysis, PPI                     |
| 4       | Female | 71  | 24.20| 15.3 | 114  | 3.44 | 104.9| 4.2  | 2.8  | 126  | 2.5 | Erythroid & Megakaryoblastic | Dialysis, PPI                     |
| 5       | Male   | 82  | 32.50| 16.8 | 124  | 4.15 | 101.0| 4.2  | 2.8  | 126  | 2.5 | Erythroid             | Dialysis, PPI                     |
| 6       | Female | 80  | 21.00| 17.1 | 95   | 3.04 | 97.0 | 8.1  | 5.0  | 387  | 2.0 | No CRP               | Dialysis                          |
| 7       | Male   | 67  | 27.40| 18.9 | 104  | 3.45 | 92.0 | 4.9  | 2.2  | 194  | 0.3 | Trilineage            | Low copper diet                    |
| 8       | Male   | 64  | 34.30| 19   | 110  | 3.60 | 96.4 | 7.7  | 6.0  | 82   | 9.8 | Erythroid             | PPI                               |
| 9       | Female | 76  | 17.90| 19.5 | 111  | 3.65 | 101.4| 2.3  | 1.6  | 87   | 1.1 | Trilineage            | PPI                               |
| 10      | Female | 74  | 17.90| 19.7 | 135  | 4.61 | 89.2 | 6.0  | 3.4  | 111  | 0.4 | Megakaryoblastic      | PPI, low copper diet               |
| 11      | Male   | 83  | 21.10| 19.7 | 118  | 3.25 | 107.7| 3.2  | 2.2  | 151  | 2.9 | Erythroid             |                                   |
| 12      | Female | 55  | 27.18| 20.6 | 81   | 2.32 | 109.9| 4.0  | 2.0  | 34   | 1.4 | Erythroid & Megakaryoblastic |                                   |
| 13      | Male   | 83  | 27.40| 20.9 | 125  | 3.95 | 95.9 | 5.7  | 2.8  | 113  | 0.3 | Myeloid              | PPI, multivitamins                 |
| 14      | Male   | 84  | 28.30| 21.8 | 95   | 2.85 | 103.5| 2.3  | 0.9  | 76   | 32.5 | Myeloid & Megakaryoblastic | Multivitamin, neuropathy          |
| 15      | Female | 75  | 28.60| 22.0 | 74   | 2.52 | 82.5 | 2.2  | 0.6  | 49   | 58.8 | Trilineage            | PPI                               |
| 16      | Female | 59  | 20.10| 22.8 | 104  | 3.88 | 83.0 | 8.0  | 4.6  | 200  | 3.9 | Trilineage            |                                   |
| 17      | Female | 72  | 20.80| 23.6 | 121  | 3.54 | 105.4| 5.3  | 3.7  | 199  | 2.4 | Megakaryoblastic      |                                   |
## Risk factors for copper deficiency in our population

| Risk factor                                                                 | Frequency (%) |
|---------------------------------------------------------------------------|---------------|
| Dialysis                                                                  | 2 (12%)       |
| Proton pump inhibitor use                                                 | 7 (41%)       |
| **Nutrition & Metabolic**                                                 |               |
| Low copper intake                                                         | 2 (12%)       |
| Alcohol excess                                                            | 0 (0%)        |
| Zinc-containing supplements                                               | 0 (0%)        |
| Enteral nutrition, Total parenteral nutrition                              | 0 (0%)        |
| Copper metabolism defects e.g. Menkes, Wilson’s                           | 0 (0%)        |
| **Gastrointestinal**                                                      |               |
| Upper bowel resection, Bariatric surgery                                   | 0 (0%)        |
| Short bowel syndrome                                                      | 0 (0%)        |
| Chronic diarrhoea                                                         | 0 (0%)        |
| Inflammatory bowel disease                                                | 0 (0%)        |
| **Neurology**                                                             |               |
| Optic neuropathy                                                          | 1 (6%)        |
| Peripheral neuropathy                                                     | 1 (6%)        |
Health Questionnaire

For the participants of the study: Reviewing the prevalence of copper deficiency in patients with suspect myelodysplastic syndromes

Please answer as many questions as you wish. The information you provide will only be available to researchers in this study, who will anonymise this information when it is entered into a password-protected document on an Imperial College Healthcare NHS Trust computer. This form will be disposed of in a confidential waste bin.

Full name: _______________________________________

Date of birth: _____________________________________

Gender: ___________________________________________

Occupation: _________________________________________

Are you exposed to any hazardous chemicals at work? Yes/No. If yes, please specify:

____________________________________________________

Ethnic Origin:

This is not about nationality, place of birth or citizenship. It is about the group to which you perceive you belong. Please circle the appropriate answer.

Prefer not to say

White: English/Welsh/Scottish/Northern Irish/Irish/British/Other, please specify: ________________________________

Mixed/multiple ethnic groups: White and Black Caribbean/White and Black African/White and Asian/Other mixed background, please specify:

____________________________________________________

Asian: Indian/Pakistani/Bangladeshi/Chinese/Asian British/Other, please specify: ________________________________
Black: Black/African/Caribbean/Black British/Other, please specify:

Any other ethnic group, please specify:

Height: ______________________  Weight: ______________________

Current medications:

______________________________________________________________

______________________________________________________________

______________________________________________________________

Are you currently undergoing any form of dialysis? Yes/No. If yes, please give details and the length of time you have been on dialysis:

______________________________________________________________

Are you currently involved in any other research studies? Yes/No. If yes, please give details of the other study/studies:

______________________________________________________________

Diet:

Are you vegetarian/vegan (please delete as appropriate)? Yes/No.

Do you follow a specific diet plan? Yes/No. If yes, please give details of your diet:

______________________________________________________________

______________________________________________________________

______________________________________________________________

Do you take any vitamins or supplements e.g. zinc supplements? Yes/No. If yes, please specify:

______________________________________________________________

______________________________________________________________

______________________________________________________________
Have you received enteral nutrition (i.e. received food through a tube that is attached directly to your intestinal tract) or intravenous nutrition in the past 3 months? Yes/No. Please specify why you had this type of nutrition and for how long:

________________________________________________________________________
________________________________________________________________________

How much alcohol do you drink in a typical week?

None (please circle if appropriate)

Beer _____ pints

Cider _____ pints

Wine _____ bottles

Spirits _____ bottles

For how many years has this level of drinking been typical?

________________________________________________________________________

Medical History:

Have you ever had gastrointestinal surgery e.g. bowel resection, bariatric surgery? Yes/No. If yes, please specify:

________________________________________________________________________

Do you suffer from any of the following?

Coeliac Disease. Yes/No.

Cystic Fibrosis. Yes/No.

Short Bowel Syndrome. Yes/No.

Chronic Diarrhoea. Yes/No
Any other digestive or malabsorption condition (please specify):



Peripheral neuropathy. Yes/No.

Myeloneuropathy. Yes/No.

Spasticity. Yes/No.

Any other neurological condition (please specify):



Any visual impairment (please specify):



Wilson’s Disease. Yes/No.

Menkes Disease. Yes/No.

Have you ever been diagnosed with any other conditions of copper metabolism? Yes/No. If yes, please specify:



Many thanks for any information you have provided and for your participation in our study.