MORTALITY RATES ARE INCREASED IN PATIENTS WITH Systemic JUVENILE IDIOPATHIC ARTHRITIS (SJIA).

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Juvenile idiopathic arthritis (JIA) represents the most common chronic inflammatory musculoskeletal disease in children. It is characterised by the onset of inflammatory arthritis prior to the 16th birthday and can follow many patterns ranging from oligoarthritis to polyarthritis to the most severe subtype, systemic juvenile idiopathic arthritis (sJIA). ([1](#_ENREF_1))The disease course can be variable with many children achieving drug-free remission. It is estimated at least 60% of children will require systemic drug therapy with methotrexate, primarily but not limited to those with polyarthritis and systemic arthritis, and of these, at least 20% will go on to require additional treatment with a biologic. (2)

Mortality rates in JIA are reported to be increased when compared to the general population, but likely vary by subtype and disease severity. (3-5) It is important however to understand the potential mortality risk of this disease, to ensure children with JIA are referred early to specialist care. To this end, we investigated the mortality rates of children with systemic and non-systemic JIA requiring immunosuppressant treatment with methotrexate and/or biologic therapy.

1556 patients with JIA (196 with sJIA) recruited at the point of starting methotrexate (n=542) or biologics (n=1014) in the British Society for Paediatric and Adolescent Rheumatology Etanercept Cohort Study (BSPAR-ETN) or the Biologics for Children with Rheumatic Disease study (BCRD), were included. Patients were followed until death, or 31.11.2014, whichever came first. Deaths were identified through regular study follow-up and linkage to the National Death Register. Standardised mortality rates (SMR) were calculated using population rates per 1,000 of the population of England and Wales, taken from the Office of National Statistics website from 2001 to 2013 as a comparator. (6)

Ten deaths were reported, 5 in patients with sJIA and 5 in non-systemic patients. Median age at death was 11 years, 6 patients were female, and 3 had received stem cell transplants. Causes of death were varied and included infection (5 patients including one septicaemia post stem-cell transplant for RF(+) JIA), other complications post stem-cell transplant (2 patients with sJIA), macrophage activation syndrome, asthma and an accidental overdose.

The overall mortality rate was 1.1 per 1,000 person-years (pyears) with an SMR of 2.8 (95% CI 2.2, 11.2) (Table 1). Patients with sJIA had a higher mortality rate at 3.9/1,000 pyears compared to 0.6/1,000 pyears in those with non-systemic disease. The SMR was highest in sJIA patients (8.3 (95% CI 2.7, 19.4)). For children without systemic JIA, the SMR was also increased (1.7 (95% CI 0.5, 4.0)) but did not reach statistical significance. Unfortunately given the low number of deaths, this analysis was not powered to confirm increased mortality in this group.

In summary, although death was a very rare outcome, mortality rates in this cohort of children with JIA requiring treatment with methotrexate and/or biologics, were high overall and very high among children with sJIA. Although the data cannot be used to draw any specific conclusions on a causal relationship with disease or its treatments, the elevated mortality rates within our cohort serve to highlight the severity of JIA, especially sJIA, as a disease to clinicians who assess and treat children, even within this era of modern therapies.

**References**

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**Table 1. Mortality Incidence Rates and Standardised Mortality Rates compared to the general population.**

|  |  |  |  |
| --- | --- | --- | --- |
|  | **Total cohort** | **Systemic JIA** | **Non-systemic JIA** |
| **Death** |  |  |  |
| Subjects, n | 1556 | 196 | 1360 |
| Male, n  | 503 | 80 | 423 |
| Female, n | 1053 | 116 | 937 |
| Follow-up time (pyrs)  | 8983 | 1272 | 7711 |
| Overall observed deaths, n  | 10  | 5  | 5 |
| Overall expected deaths, n | 3.5 | 0.6 | 2.9 |
| Overall mortality incidence rate/1,000 pyrs (95% CI) | 1.1 (0.5, 2.0) | 3.9 (1.3, 9.2) | 0.6 (0.2, 1.5) |
| Overall SMR (95% CI) | 2.8 (1.4, 5.2) | 8.3 (2.7, 19.4) | 1.7 (0.5, 4.0) |

\*pyrs = person-years of follow-up; 95% CI=95% confidence interval