

1. Introduction

- Chronic Granulomatous Disease (CGD) is a rare disorder of white blood cells leading to serious infection and inflammation.
- 70% of cases are due to an X-linked (XL) mutation.
- There is increasing evidence that female carriers of XL-CGD experience a range of inflammatory symptoms.^[1]
- Many XL-CGD carriers also report excessive fatigue^[2] which may be due to inflammatory processes mediated by cytokines.
- To date, there has been no investigation of the possible mechanism of this fatigue in XL-CGD carriers.

2. Aim

- To investigate whether XL carriers of CGD have raised serum levels of inflammatory cytokines which are associated with fatigue.

3. Methods

- Design:** Serum from 52 XL-CGD carriers was compared with inflammatory disease control groups of 10 high and 10 low fatigue Sjogren's disease patients and 15 healthy controls.
- Data collection:** Cytometric Bead Array (CBA) immunoassay assessed levels of IL-1 α , IL-5, IL-8, IL-10, IL-17, IFN α and IFN γ using BD Biosciences LSRFortessa™ cell analyser (Figure 1).
- Data analysis:** FACSDiva, BD Biosciences; FCAP Array, Soft Flow Inc.; SPSS, IBM (Mann-Whitney U Tests).

4. Results

- 25/52 (48%) of XL-CGD carriers reported fatigue on a validated questionnaire.^[3]
- IL-8 concentration (mean 1459u/ml) was significantly higher in XL-CGD carriers than in healthy controls (mean 72u/ml) ($p=0.015$) and Sjogren's disease controls (mean 203u/ml) ($p=0.031$) as a whole (high and low fatigue grouped).
- IL-8 concentration was significantly higher in the subgroup of XL-CGD carriers who reported fatigue (mean 2405u/ml) than in those who did not (mean 400u/ml) ($p=0.005$).
- Other investigated cytokines were not significantly raised.

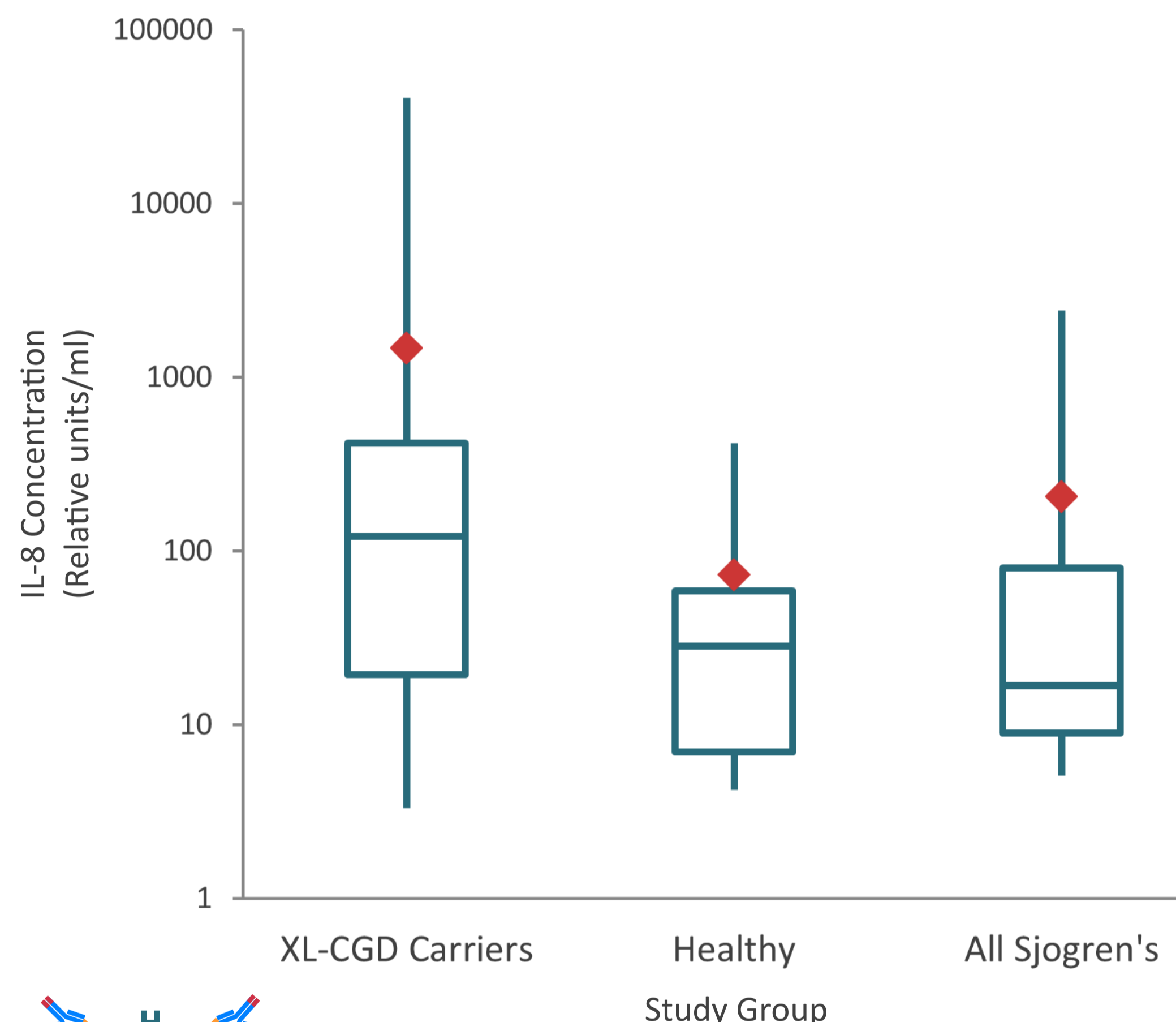


Figure 2: Log box plot of IL-8 concentration in each group.

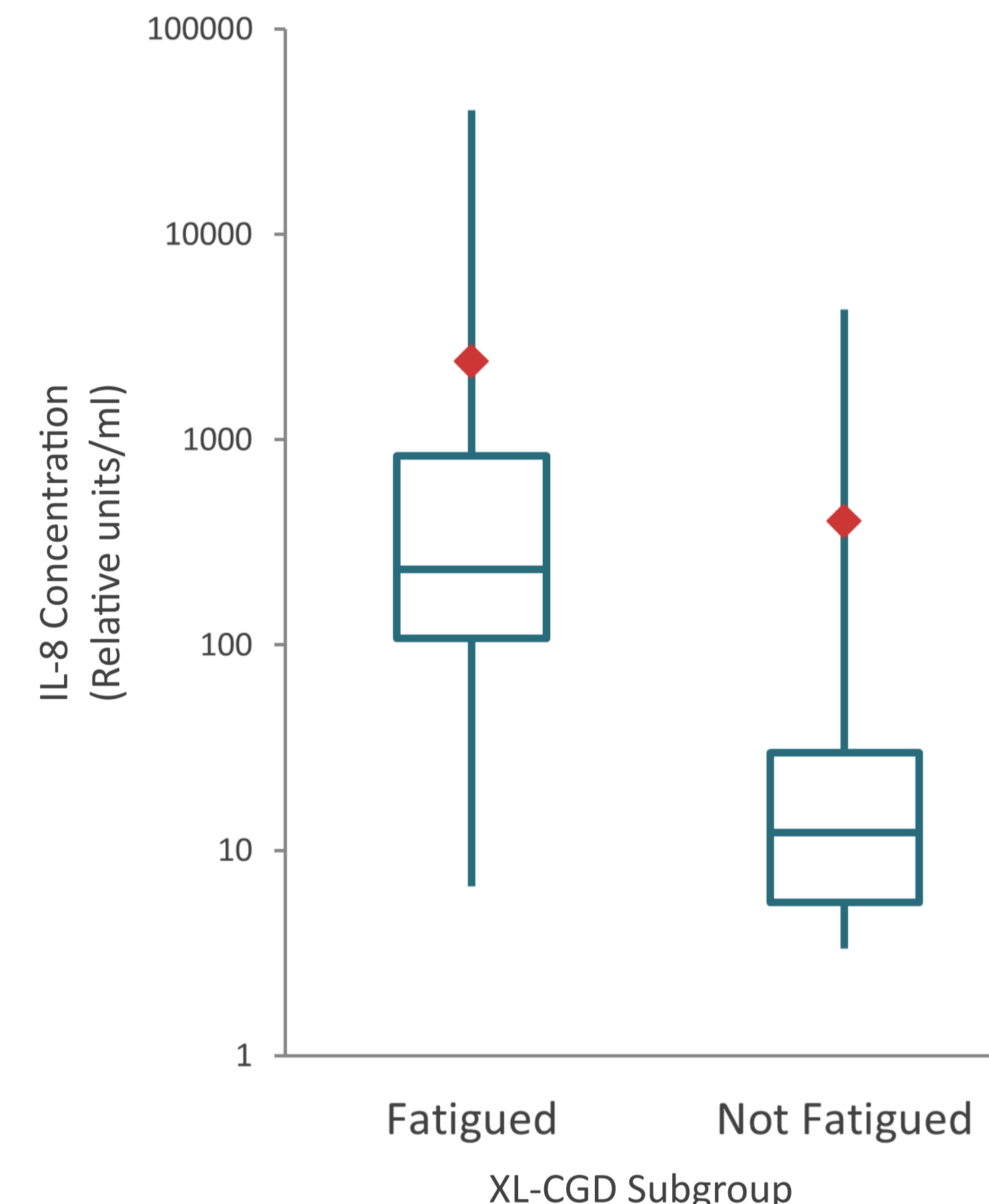


Figure 3: Log box plot of IL-8 concentration in each XL-CGD sub-group.

5. Conclusions

- Serum IL-8 is significantly higher in XL-CGD carriers than in healthy and Sjogren's disease control groups.
- Higher serum IL-8 levels are significantly correlated with higher levels of fatigue in XL-CGD carriers.
- IL-8, which has been associated with fatigue,^[4] may be a driver of fatigue in this group via an inflammatory process.
- It is hoped that this initial finding will stimulate further research into how IL-8 influences fatigue in XL-CGD carriers and how its effects can be managed to improve the quality of life for these women.

6. Citations & Acknowledgements

- ^[1] Battersby AC, Cale AM, Goldblatt D, Gennery AR. *Clinical manifestations of disease in X-linked carriers of chronic granulomatous disease*. Journal of Clinical Immunology 2013;33(8):1276-84
- ^[2] Cale CM, Morton L, Goldblatt D. *Cutaneous and other lupus-like symptoms in carriers of X-linked chronic granulomatous disease: incidence and autoimmune serology*. Clinical & Experimental Immunology 2007;148(1):79-84
- ^[3] Multidimensional Fatigue Symptom Inventory Short Form (MFSI-SF)
- ^[4] Sorenson M, Jason L, Lerch A et al. *The Production of Interleukin-8 Is Increased in Plasma and Peripheral Blood Mononuclear Cells of Patients with Fatigue*. Neuroscience and Medicine 2012; 3, 47-53.
- This research was supported by a scholarship grant from the Faculty of Medical Sciences, Newcastle University and The Bubble Foundation.
- a: Institute of Cellular Medicine, Newcastle University. b: Clinical Immunology, Great Ormond Street Hospital, London. c: Institute of Child Health, University College London, London.

Figure 1: Preparation and analysis of samples

