Seasonal variation and Kidney Transplant rejection – First clinical study

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Introduction:

- In organ transplantation, rejection considered a major incident that affects graft outcome
- Stronger pro-inflammatory state and higher autoimmune diseases incidence is observed during cold season¹.
- This variation might affect transplant immunology.
- No reports to suggest the effect of seasonal variation on transplant rejection

Methods:

- A retrospective review included all kidney transplants at Sheffield Kidney unit from 2008 to 2012.
- Patients follow-up was 46 ± 25 months (Mean $\pm$ SD).
- December, January and February were considered Winter (cold season).
- Rejection was considered if proven by biopsy. Recurrence was defined as another rejection 90 days after biopsy.
- IBM SPSS 9Ver 20) was used for statistical analysis.

Results:

- 435 transplants were included with 79 rejection episodes in 43 grafts (10%)
- According to month of rejection, rejection episodes were classified into Winter/non winter.
- There was no major difference between both groups in different immunological factors as in table
- All winter rejections group received triple maintenance immunosuppression in comparison to non winter rejection (p 0.01, Chi², SPSS)
- The graft survival of grafts had rejection at winter was inferior to non winter rejections although did not reach statistical significance. Winter Vs non Winter rejections survival 48% Vs 58% at 7 years, p 0.19, Kaplan-Meier.
- **More rejection episodes in Winter required more than steroid pulse to treat in comparison to rejection at the rest of the year (60% vs 45%, p 0.03, Chi²)**

- There was no difference in rejection recurrence rate between both groups

Conclusion:

Despite stronger maintenance immunosuppression, graft rejections at winter (cold season in UK) is more difficult to treat and usually requires more than steroid pulse to control.

Discussion:

- Molecular basis behind immune system response is dynamic
- Even genetics controlling the process undergoes different modulations to affect its expression (Epigenetics)
- Many review articles has suggested these modulations can be translated to control immune response of transplant recipients.²
- Seasonal variations might affect immune system response and genetics expressions as suggested by recent reports
- So far, no clinical trials to take into account or suggest relation between different epigenetic and environmental factors and transplant immunology
- We report the first clinical study to suggest such relation
- Limitations for our study is the small study group, single center and the retrospective nature. Larger clinical trials should follow to support or decline such hypothesis

Rejection group characteristics	Winter Rejection(n 15)	Non winter Rejection(n 64)	P value
Recipient age (Mean $\pm$ SD) years	47 $\pm$ 16	46 $\pm$ 16	0.93
Type (Antibody/Cell mediated)	7/8	24/40	0.53
Recurrent rejection	2 (13%)	7 (11%)	0.79
First/Previous Transplant	10/5	48/16	0.51
Donor Type (Cadaveric/living)	8/7	42/22	0.37
Immunosuppression(double/3 agents)	0/15	20/44	0.01*
Induction (Basilix-standard/High risk)	11/4	49/15	0.79
HLA match (No mismatch/ 1 or more)	2/13	10/54	0.82

References:

- 1-Dopico XC, Evangelou M, Ferreira RC, Guo H, Pekalski ML, Smyth DJ, Cooper N, Burren OS, Fulford AJ, Hennig BJ, Prentice AM, Ziegler AG, Bonifacio E, Wallace C, Todd JA. [Widespread seasonal gene expression reveals annual differences in human immunity and physiology](#). Nat Commun. 2015 May 12;6:7000
- 2 - Schildberg FA, Hagmann CA, Böhnert V, Tolba RH. [Improved transplantation outcome by epigenetic changes](#). Transpl Immunol. 2010 Jul;23(3):104-10