

## INTRODUCTION:

Gonadal insufficiency is a common long-term endocrinological complication of Bone Marrow Transplantation (BMT) and is mainly associated with the chemotherapy protocol. Gonadal insufficiency is reported as 66-80% in women and 35-60% in men after BMT

## AIM:

The aim of this cross-sectional study was to investigate the frequency and the factors affecting gonadal insufficiency in cases with BMT due to non-malignant indications in children or adolescence.

## METHODS:

- Between 2006 and 2016, non-malignant indications were evaluated in Pediatric Endocrinology Department after BMT,
- The effect of the primary diagnosis, age at BMT and treatment protocols used before and during BMT on gonadal insufficiency was investigated.
- Gonadal insufficiency was defined as
  - prepubertal stage in girls > 13 yrs and boys >14 years,
  - no progression of puberty stage for more than 12 months and/or
  - LH and FSH above the upper limit of the interval according to pubertal stage.
- Patients with known gonadal insufficiency prior to BMT, or who received any treatment that could cause gonadal insufficiency and chromosomal disorders were excluded

## RESULTS:

39 patients → 20 female (51.3%)  
19 male (49.3%)

Age at admission (median): 10.73 years (2.82-18.75)  
Age of BMT (median): 8.16 years (0.57-17.01)  
Gonadal insufficiency after BMT: 13 patients (33%)  
→ 4 male (21%)    9 female (45%)

- Gonadal insufficiency developed in all the patients who received at least two of the Fludarabine, Cyclophosphamide, or Busulfan regimens
- Gonadal insufficiency developed in 4 (80%) out of 5 patients who received Fludarabine-Busulfan-Cyclophosphamide of the BMT regimens.
- Gonadal insufficiency did not develop in the 5 patients who received cyclophosphamide alone.

## Age of BMT :

- Gonadal insufficiency (+): 11.23 years (5.56-16.11),
- Gonadal insufficiency (-): 6.88 years (0.57-17.01) (p=0.03)
- BMT – puberty– gonadal insufficiency (figure 3-4):**
  - Prepubertal → 46% (12/26) gonadal insufficiency (+)
  - Puberty stage 2 → 33% (1/3) gonadal insufficiency (+)
  - Puberty stage 3-5 → gonadal insufficiency ∅
- Gonadal insufficiency(+):**
  - Prepubertal stage BMT: 92%
  - Pubertal stage BMT: 52% (p=0.012)

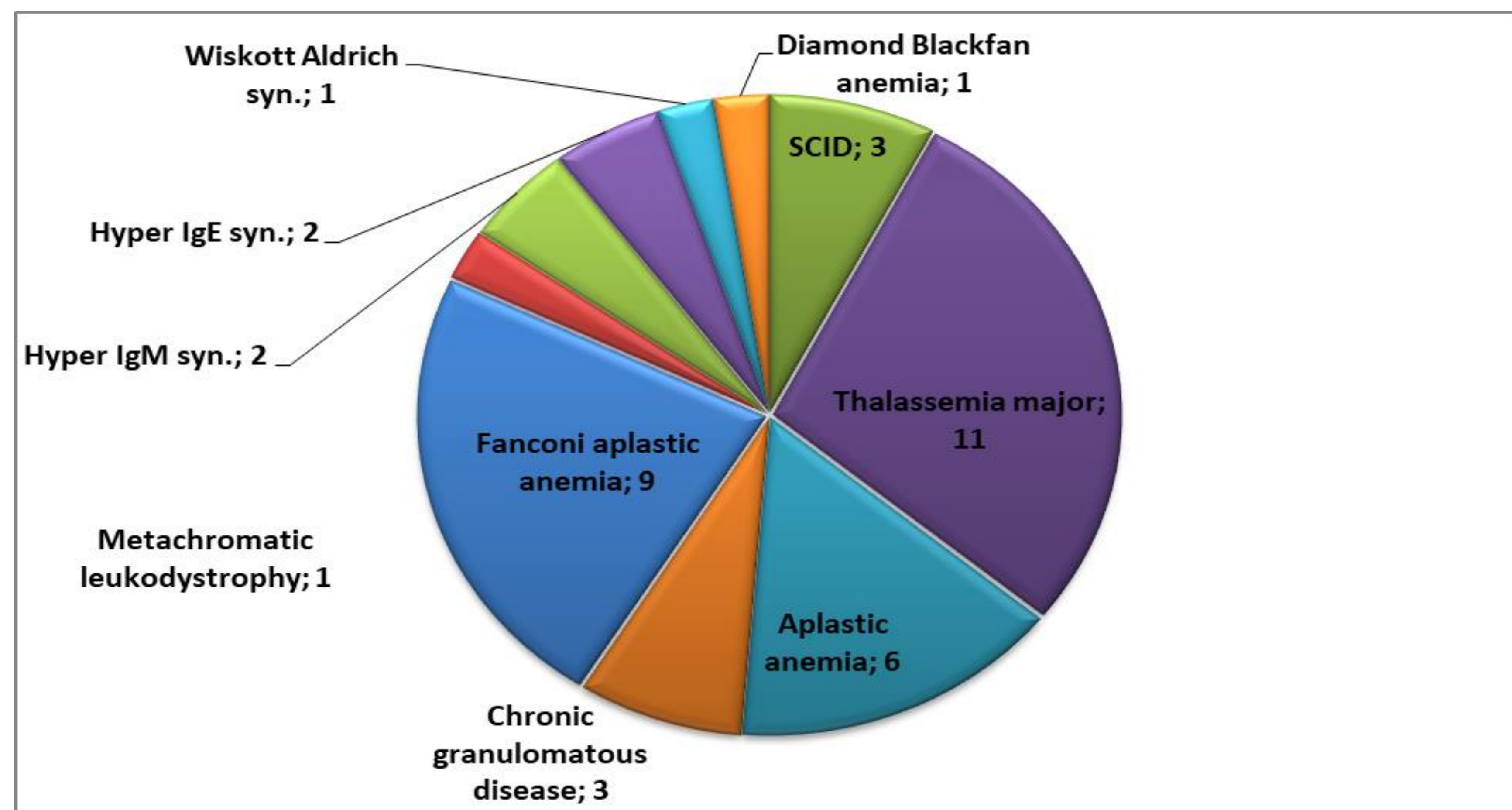


Figure 1: Distribution of patients according to the causes of BMT

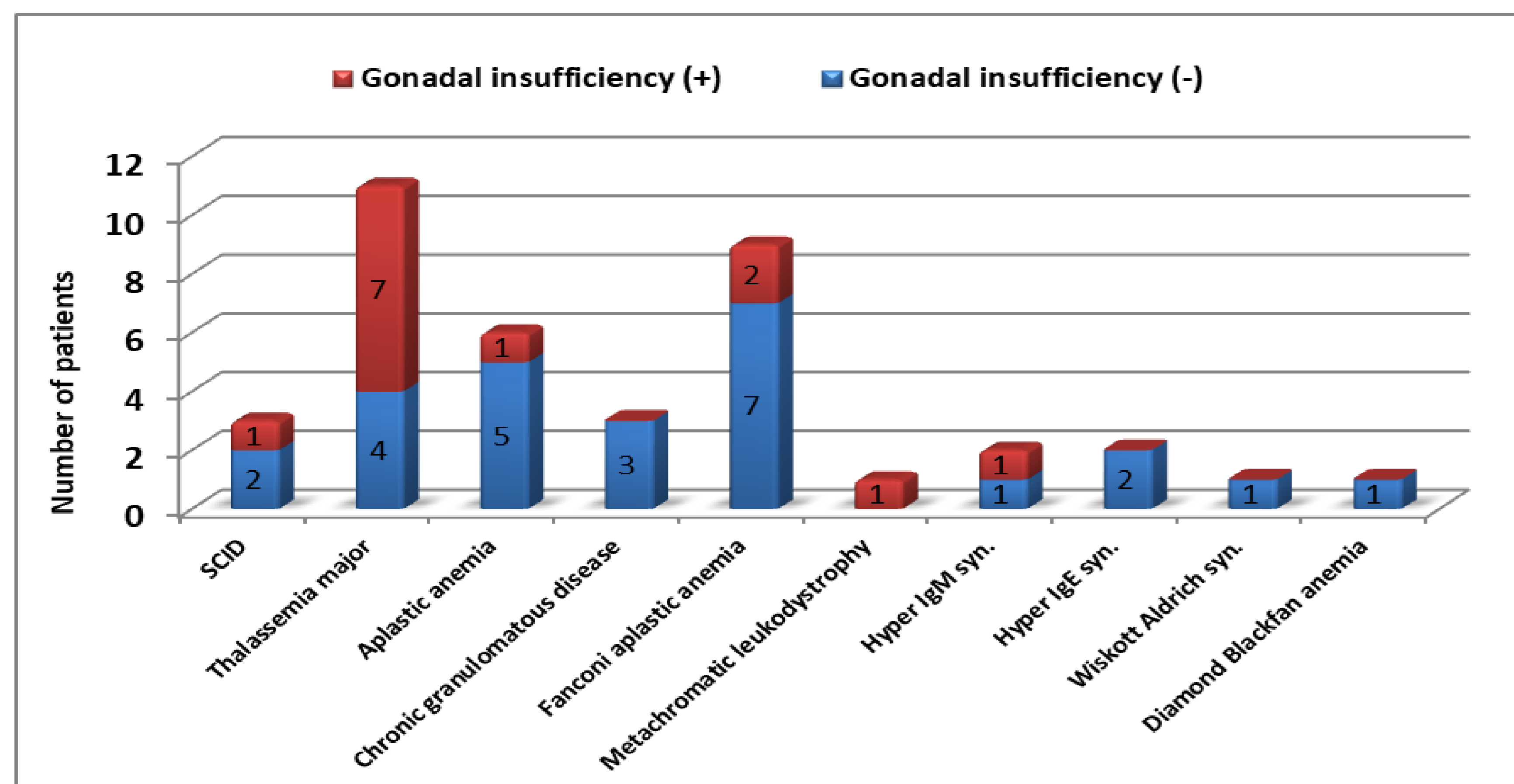


Figure 2: Number of patients with gonadal insufficiency due to BMT

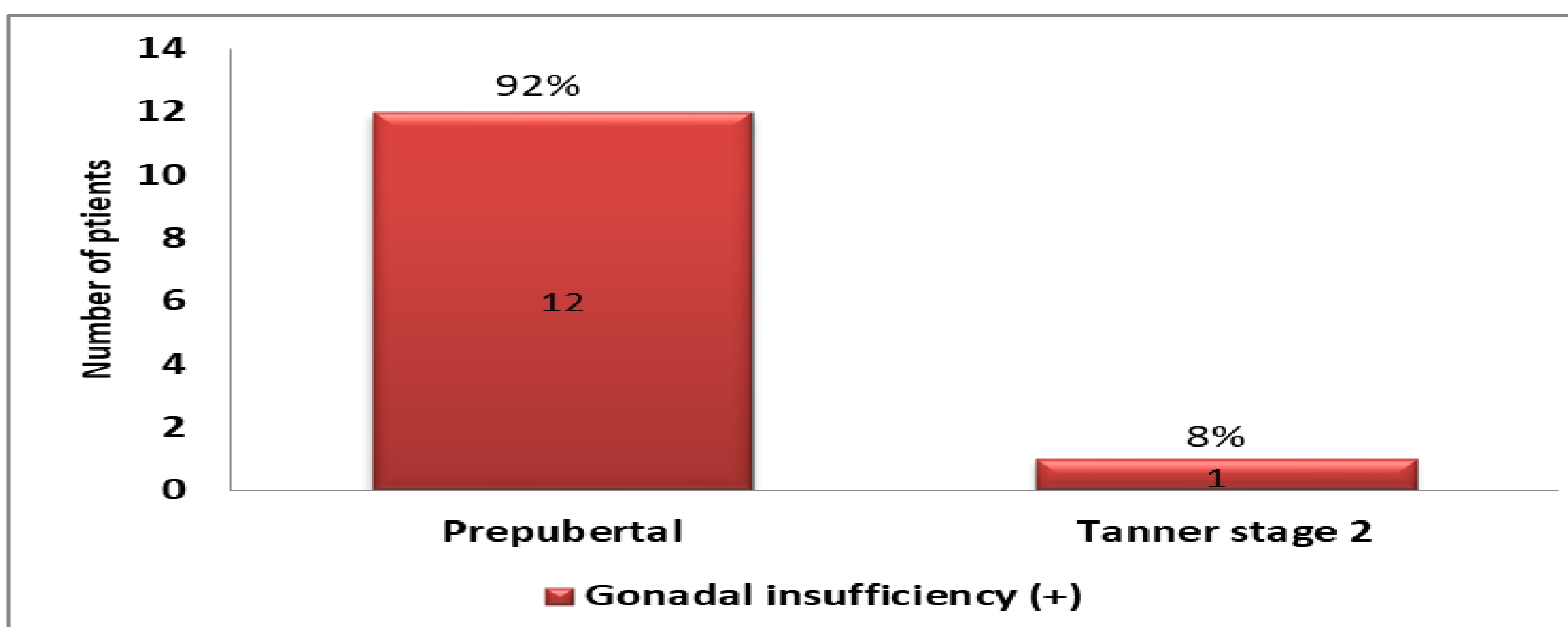
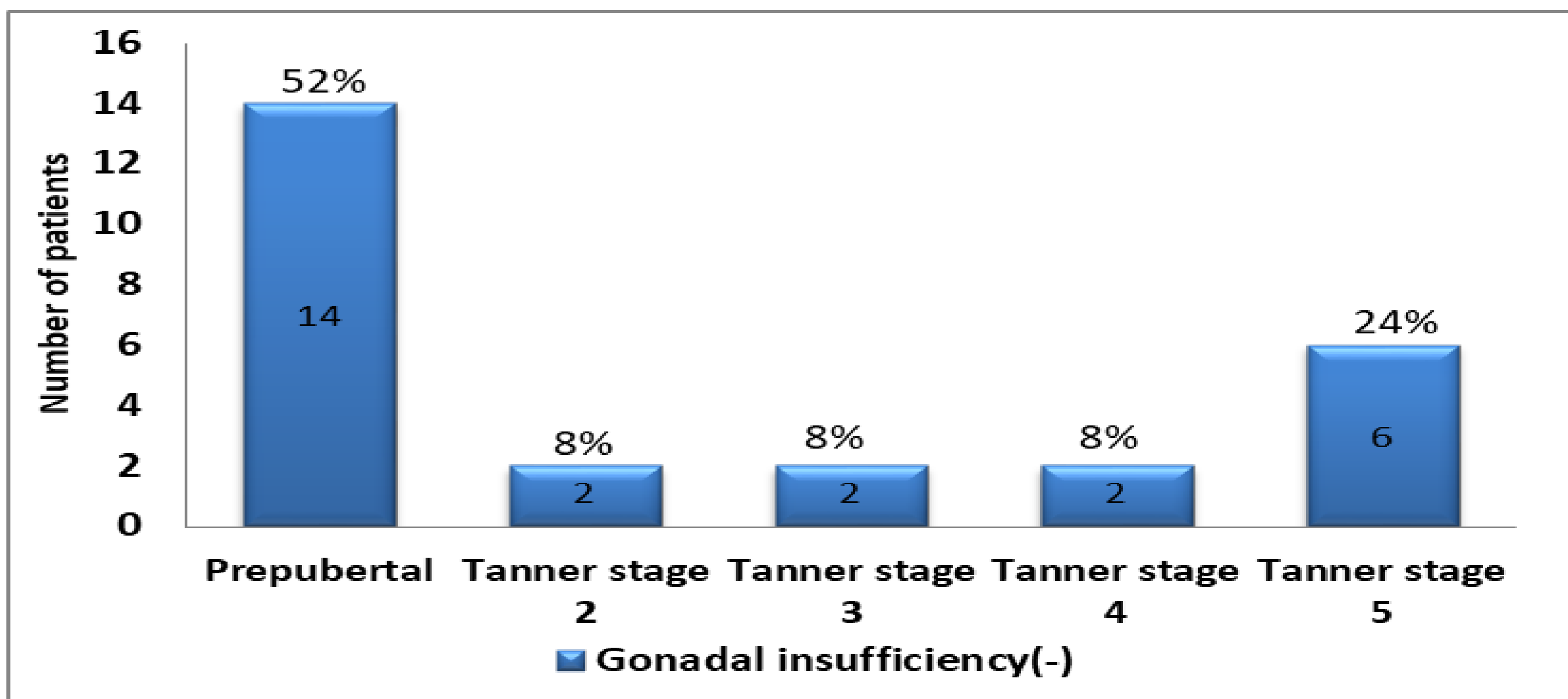


Figure 3-4: Puberty stage at the time of BMT in patients with and without gonadal insufficiency

## CONCLUSION:

- Within the BMT indications, non-malignant causes are increasing and treatment protocols are changing within the years.
- Gonadal insufficiency was seen at a higher rate in patients who underwent BMT due to thalassaemia major.
- Older age and prepubertal stage during BMT and the combination of at least two Fludarabine, Cyclophosphamide or Busulfan regimens in pre-BMT regimens increases gonadal insufficiency risk.