



Is the absence of *JAK2*^{V617F} mutation a risk factor for bleeding in Philadelphia Chromosome Negative Myeloproliferative Neoplasms?

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Background

Thromboembolic events and bleeding episodes are the main complications of myeloproliferative neoplasms (MPNs). *JAK2*^{V617F} mutation proved as a thrombotic risk factor in MPNs while few data correlate *JAK2*^{V617F} with bleeding risk. So, a thrombosis / hemorrhage risk reassessment in MPNs patients should be reappraised.

Objective

The aim of our study is to evaluate the impact of *JAK2*^{V617F} mutation positivity on bleeding complications in MPNs.

Methodology

- A cross-sectional study in two tertiary centers in upper Egypt; Assiut and Qena University Hospitals from January 2019 to December 2020
- Newly diagnosed MPNs patients went through history taking, physical examination, basic laboratory work and molecular assessment of both *JAK2*^{V617F} and Philadelphia chromosome.

Results

The cohort included 78 Philadelphia negative MPNs patients with 55% females and the median age was 57 (range 40-85). Half of the patients were polycythemia rubra vera (PRV; n=40, 51%) while one third were primary myelofibrosis (PMF; n=28, 36%) and only 13% were essential thrombocytosis (ET; n=10). The median of total leucocytic count (TLC) was 9.6 (range:0.3-190) x 10⁹/L, hemoglobin level (HB) 15 (range:4-21) g/dl, and the platelets median was 359 (range: 3-2960) x 10⁹/L. Almost half of the patients (n=35;45%) harbor *JAK2*^{V617F}.

The main observation was that thrombosis occurred significantly higher in *JAK2*^{V617F} positive group (49% *vs.* 16%; *P*=0.0003) on the contrary there was no significant difference in bleeding between *JAK2*^{V617F} positive (23%) and *JAK2*^{V617F} negative groups (28%); *P*=0.6.

Multivariate model was done for the significant independent variables that leads to bleeding showed that only platelet (odd ratio =1) and, splenomegaly (odds ratio=8.5) had significant effects.

Table 1: Patients characteristics.

	<i>JAK</i> positive N=35	<i>JAK</i> negative N=43	<i>P</i> value
Clinical Characteristics n (%)			
Itching	2 (6)	4 (9)	0.6
Erythema	12 (34)	6 (14)	0.0008
Splenomegaly	25 (71)	29(67)	0.8
Bleeding tendency	8 (23)	12 (28)	0.6
Thrombosis	17 (49)	7 (16)	0.0003
Laboratory Finding mean ± SD			
WBC (10 ⁹ /L)	18±38	10±11	0.2
HB (g/dl)	15±5	14±10	0.5
Platelet (10 ⁹ /L)	494±337	444±627	0.7

Table 2 : Multivarait model of independent factors that leads to bleeding

Variable	Odds ratio (OR)	95% confidence interval (CI)
Female gender	2.3	0.8 – 6.9
Age in years	0.95	0.9 – 1.01
ET <i>vs.</i> MF	0.3	0.05 – 1.6
PRV <i>vs.</i> MF	0.2	0.05 – 0.5
WBC	0.9	0.7 – 0.9
HB	0.8	0.7 – 0.9
Platelet count	0.99	0.9 - 1
Splenomegaly	8.5	1.1 - 68
<i>JAK2</i> ^{V617F} mutation	0.7	0.3 – 2.1

Conclusions

Data confirmed that *JAK2*^{V617F} associated with increased risk of thrombosis in MPNs, but it does not have a role on increased bleeding risk in MPNs. Large prospective studies are needed to confirm the role of *JAK2*^{V617F} in bleeding during the course of MPNs and its relation to different lines of treatment.