Investigation of the Incidence of CALR,MPL and JAK2 Gene Mutations in Essential Thrombocytosis Cases with Laboratory Findings and Complications

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TÜBİTAK

TABLE OF CONTENTS

INTRODUCTION

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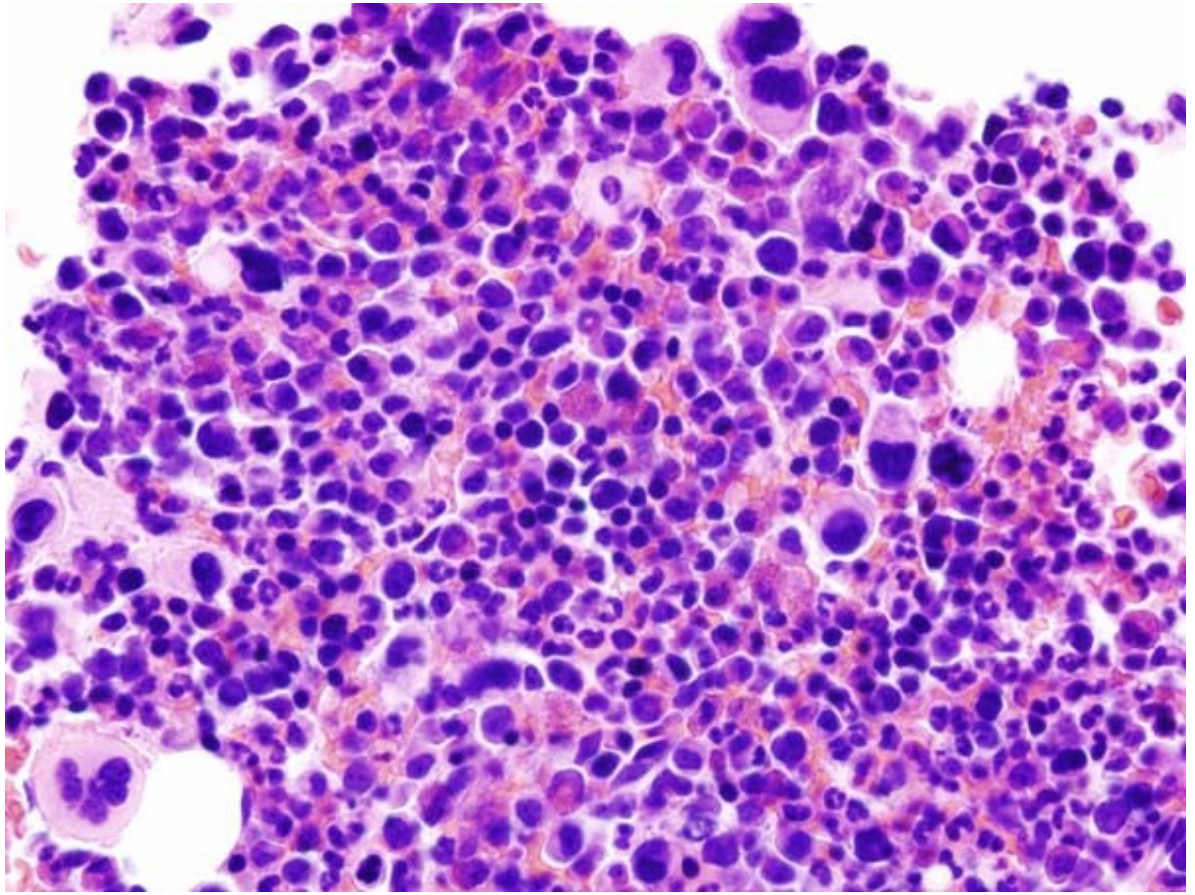
WHAT IS THIS DISEASE?



•Chronic myeloproliferative diseases (CMPDs) are clonal hematopoietic stem cell disorders characterized by proliferation of one or more myeloid cell lineages in the bone marrow and increased numbers of mature and immature cells in the peripheral blood. CMPDs include polycythemia vera (PV), essential thrombocythemia (ET), idiopathic myelofibrosis (IMF) and chronic myeloid leukemia.

•One of the most common of these diseases is essential thrombocytosis, a rare disease characterized by splenomegaly, increased risk of thrombosis and hyperplasia in megakaryocytes.

INTRODUCTION

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HOW CAN WE DIAGNOSE?

- The diagnosis of the disease is generally made according to WHO diagnostic criteria.
- However, complete blood test, bone marrow biopsy and genetic tests are also elements that must be considered in the diagnosis.
- It is diagnosed by the presence of platelet number of 450,000 and above, with the increase in the number of megakaryocytic cell lines and mature megakaryocytes in bone marrow biopsy, and the presence of a number of genetic mutations.

INTRODUCTION

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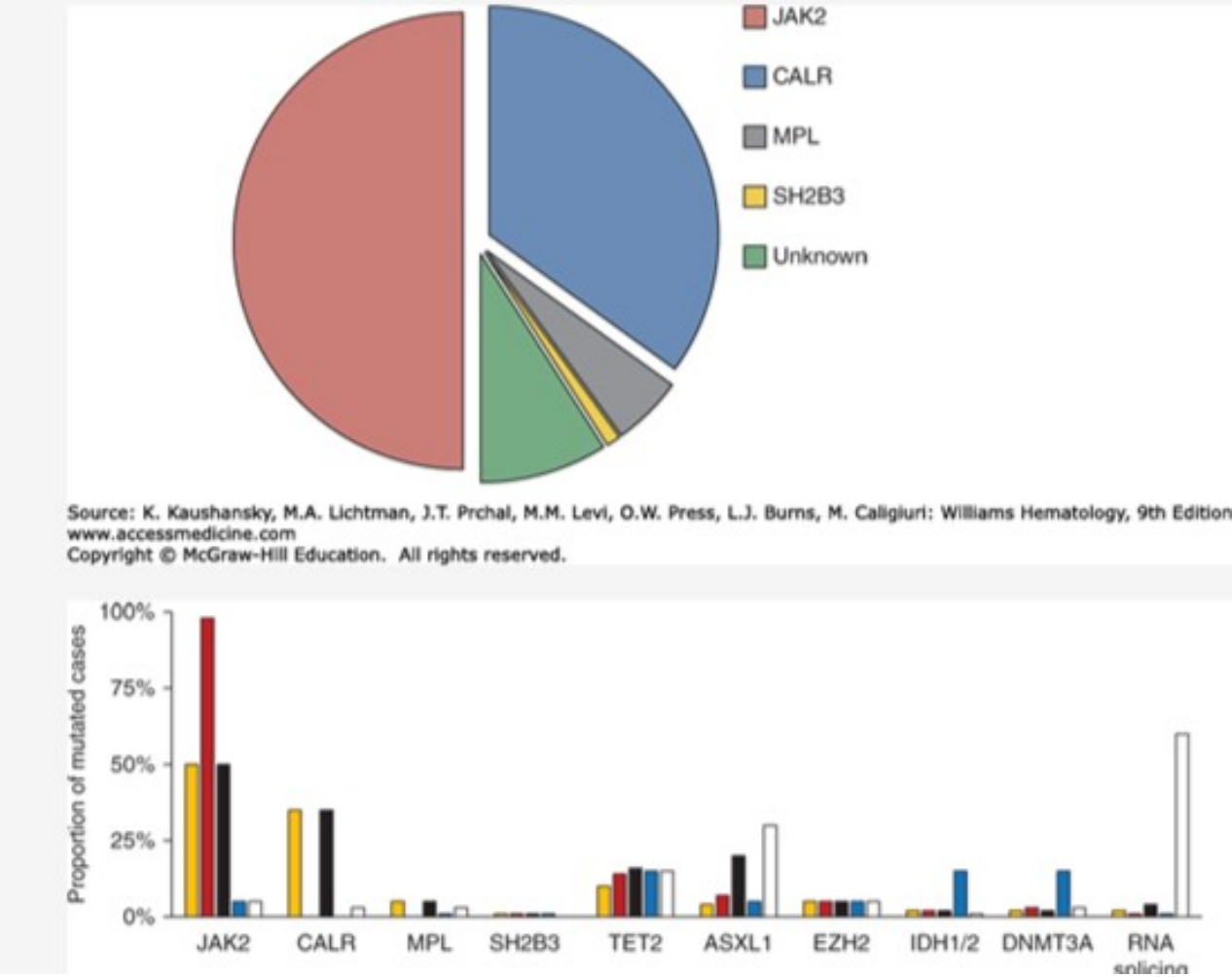
Which Mutations are Associated with the Essential Thrombocytosis Today?

- It has been proven by researchers that some mutations are directly related to the disease,like Jak2 mutation.
- However, there are some other gene mutations whose existence has been relatively recently proven and whose relationship with diseases is not well known.



AIM and SCOPE

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WHAT WE WANTED TO INVESTIGATE?

- To increase the prognostic significance of mpl,calr and jak2 genes,
- To investigate the effect of Jak2 gene relationship with other gene mutations on the complications of the disease,
- To ensure that clinicians and patients are alert to how serious this disease and its complications are.

WHAT WE DID?

- The files of the follow-up patients who applied to the Bezmialem University Faculty of Medicine, Department of Internal Medicine, Hematology Department between January 2012 and September 2023,and whose MPL,CALR gene mutations,especially JAK 2,were examined,they were evaluated retrospectively.
- In the study,age gender,laboratory findings obtained from the archive.Until November 2023,there have been 101 patients whose MPL, CALR and JAK2 genes were examined together.

MATERIALS & METHODS

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- The files of the patients who applied to Bezmialem University Faculty of Medicine, Department of Internal Medicine, Department of Hematology, between January 2012 and May 2023, and followed up for MPL, CALR gene mutations, especially JAK 2, will be evaluated retrospectively.

	A	B	C	D	E	F	G	H	I	J	K	L	M
1	Name/Surname	Age	Gender	Date of the Diagnosis	Alive/Dead	JAK2 Existence	MPL Existence	CALR Existence	Leukocytosis	Thrombosis	Hepatomegaly	Splenomegaly	Hemorrhage
2													
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RESULTS

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- In the statistical analysis made with the data collected from 101 patients in whom these three genes were examined together, 63.4% (n=64) were female, 36.6% (n=37) male aging from 19 to 90.
- No significant difference was found between the three mutation genes we examined gender, age, smoke consumption,hepatomegaly and hemorrhage.
- A significant difference was found between the incidence of splenomegaly with jak2 and mpl mutations (p=0,05 ; p=0,01).

- Low hemoglobine count, extremely high platelet count were found to be significantly different in Jak2 negative patients compared to positive patients. But the situation was the opposite for splenomegaly.
- A significant difference was found between the absence of the jak2 mutation gene and low hemoglobine count and platelet count over 1 million (p=0,004 ;p=0,01).”

RESULTS

			CALR GENE 0	CALR GENE 1	p
MPL GENE	0	Count	63	10	<0,001
		% within calr	88,7%	33,3%	
	1	Count	8	20	
		% within calr	11,3%	66,7%	
Total		Count	71	30	101
		% within calr	100,0%	100,0%	100,0%

Kappa Value =0,565

			JAK2 GENE 0	JAK2 GENE 1	p
Platelet Count Over 1M. on the Diagnosis	0	Count	36	42	0,019
		% within jak	67,9%	87,5%	
	1	Count	17	6	
		% within jak	32,1%	12,5%	
Total		Count	53	48	101
		% within jak	100,0%	100,0%	100,0%

			JAK2 GENE 0	JAK2 GENE 1	p
CALR GENE	0	Count	42	29	0,050
		% within jak	79,2%	60,4%	
	1	Count	11	19	
		% within jak	20,8%	39,6%	
Total		Count	53	48	101
		% within jak	100,0%	100,0%	100,0%

Kappa Value =0,192

			JAK2 GENE 0	JAK2 GENE 1	p
SPLENOMEGALİ	0	Count	37	25	0,050
		% within jak	69,8%	52,1%	
	1	Count	16	23	
		% within jak	30,2%	47,9%	

			MPL GENE 0	MPL GENE 1	p
SPLENOMEGALİ	0	Count	50	12	0,018
		% within mpl	68,5%	42,9%	
	1	Count	23	16	
		% within mpl	31,5%	57,1%	

			JAK2 GENE 0	JAK2 GENE 1	p
MPL GENE	0	Count	45	28	0,004
		% within jak	84,9%	58,3%	
	1	Count	8	20	
		% within jak	15,1%	41,7%	
Total		Count	53	48	101
		% within jak	100,0%	100,0%	100,0%

Kappa Value =0,271

			JAK2 GENE 0	JAK2 GENE 1	p
Hemoglobine	0	Count	13	25	0,004
		% within jak	24,5%	52,1%	
	2	Count	40	23	
		% within jak	75,5%	47,9%	
Total		Count	53	48	101
		% within jak	100,0%	100,0%	100,0%

RESULTS

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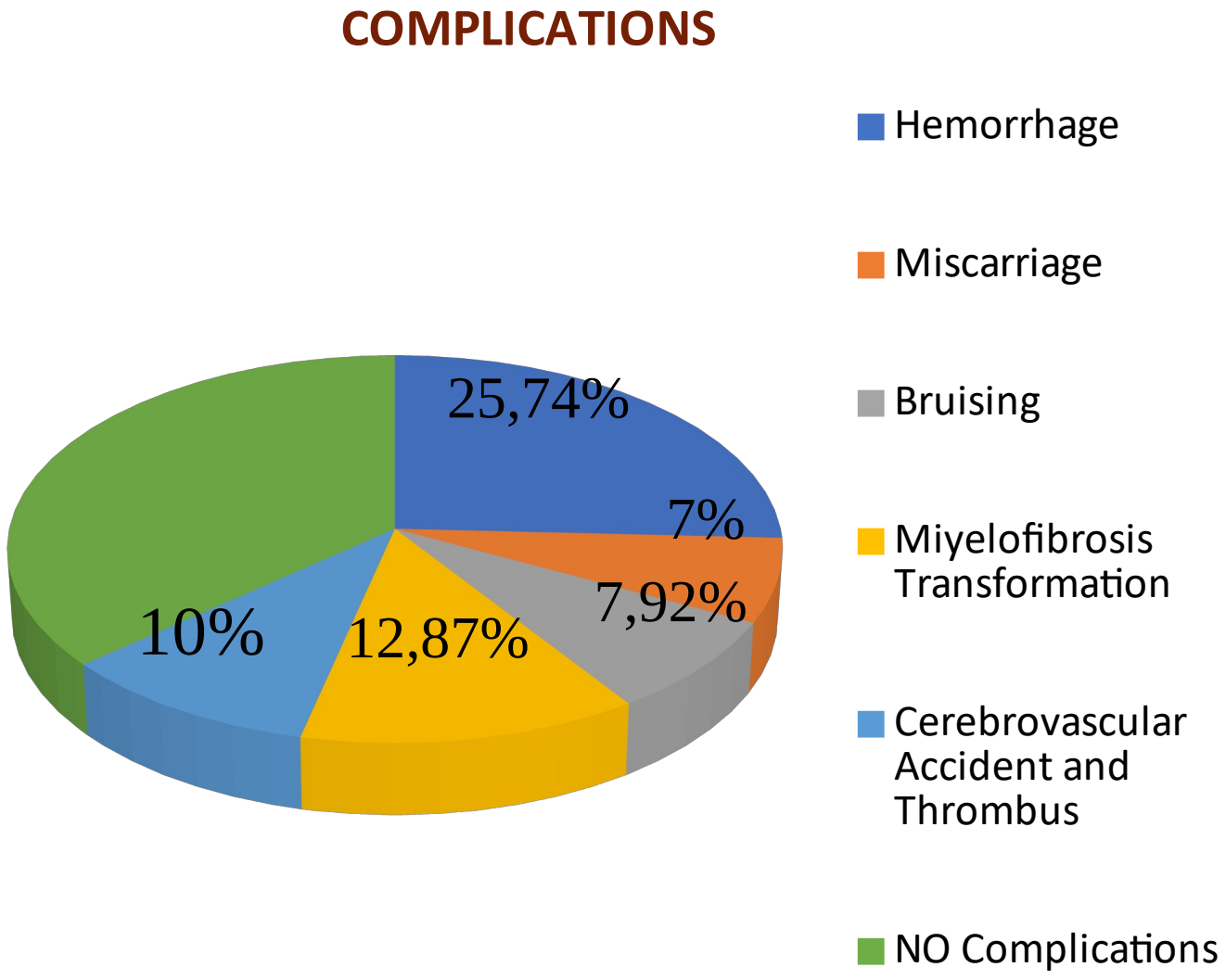
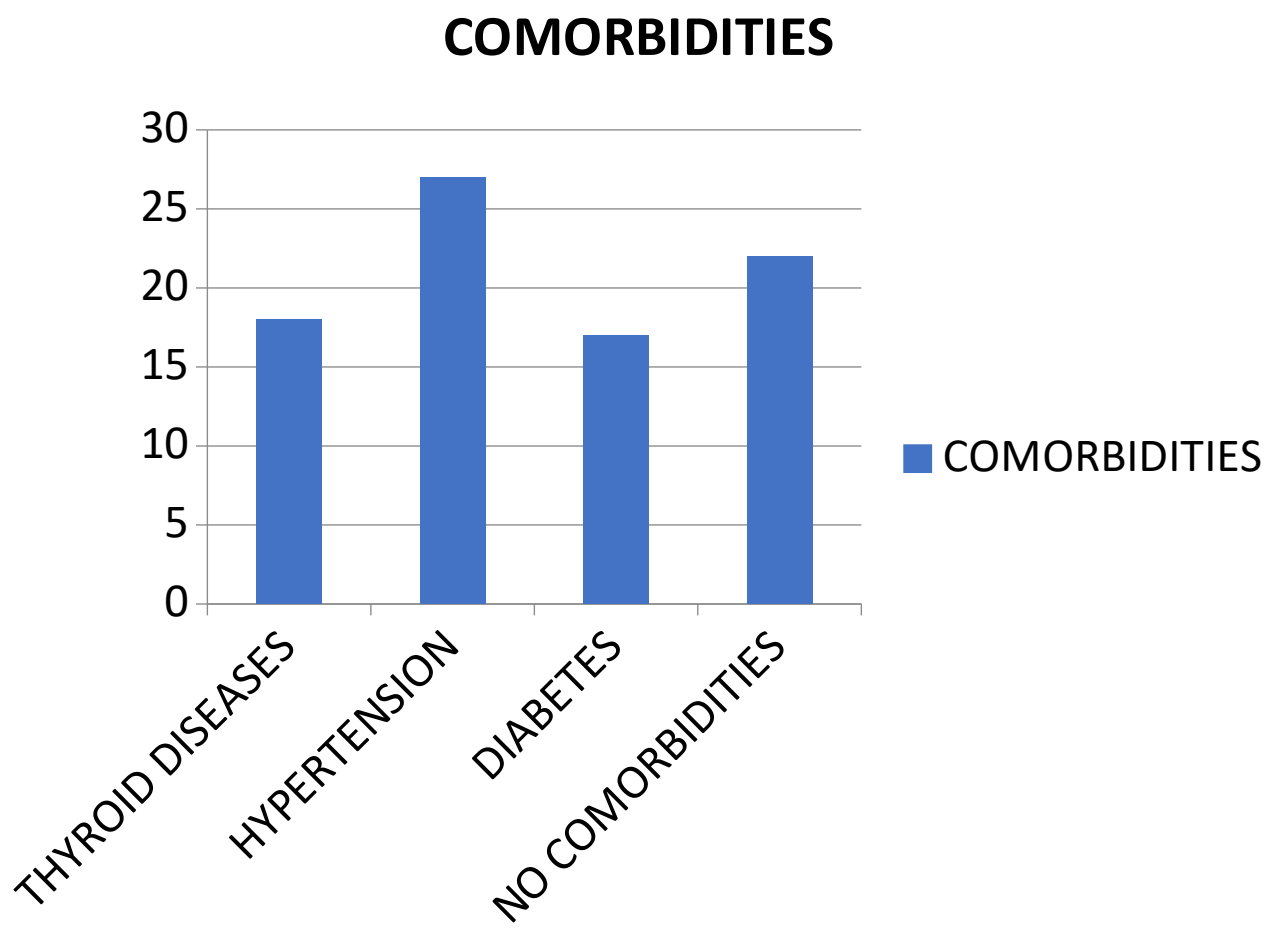
- We noted that some vital complications and comorbidities that encountered on our patients.
- Lots of patients complained bruising their knee,legs and arms.
- Some of them experienced hemorrhoidal and gingival bleeding at least one time.
- 7% of women had a history of miscarriage in the presence of diagnosis.
- 10% patients had previous cerebrovascular accident, as well as thrombus in organs such as the kidney, spleen, and the portal vein and aorta.
- One patient was noted to have avascular necrosis on femur.
- Prefibrotic phase myelofibrosis transformation was noticed in 13 patients.



RESULTS

- The most surprising result in our study was that 18 patients had thyroid disease.
- However, 27 patients had hypertension and 17 were diabetic.
- Finally, one patient had Budd Chiari syndrome and 2 patients had Hashimoto's with hypothyroidism.
- There was no comorbidities in 22 patients.



LIMITATIONS & DISCUSSION

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- Single centered study
- Decrease number of patient due to genetic test expensiveness
- Difficulty in accessing complications noted by other clinicians in patients‘ medical histories
- Past comorbidities of the patients

FUTURE DIRECTIONS

- This study should be repeated with more patients and gene data.

Conclusions

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- The results of the present study show that there is no co-relation between CALR, MPL and clinical prognostic parameters. However, it has been shown that patients carrying the jak2 gene are at higher risk for complications and we confirmed its diagnostic importance. Our results should be confirmed with further experimental and clinical studies.

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Thank you for listening