

# ***TRIAL OF HYDROXYUREA IN THALASSEMIA INTERMEDIA***

**PROF. JOVARIA MANNAN  
DR. FOUZIA HASNAIN**

# INTRODUCTION

- Thalassemia is the commonest inherited hematological disorder as a result of genetic defects in beta-globin gene expression<sup>1</sup>.
- It is estimated that around 60 – 80 million people in the world carry the thalassemia gene .
- The prevalence rate of thalassemia carrier in Pakistan is 5.6%.

# INTRODUCTION

- Chemotherapeutic approach involves increased production of gamma chain to definitively correct or modulate the underlying pathology in beta thalasseмииs.
- This ameliorates the severity of beta-thalasseμία intermedia.
- Recent research is on in Thalassaemia major as well .

# INTRODUCTION

- Hydroxyurea has been used to induce production of fetal hemoglobin resulting in less globin imbalance and less severe anemia rendering some transfusion independent<sup>2</sup>.

# OBJECTIVE

- The purpose of this study was to determine the clinical response of Hydroxyurea in Thalassemia Intermedia and its relation to beta-globin gene mutations if any.

# STUDY DESIGN

- Non Randomized Experimental Study.

# STUDY PLACE & DURATION

- Thalassemia Center, Sir Ganga Ram Hospital, Lahore.
- Feb, 2007 – Dec, 2009 (2 Years 9 mo).

# PATIENTS & METHODS

- 40 patients clinically diagnosed as thalassemia intermedia.
- Hydroxyurea  
Dose= 15 mg/kg/d once orally  
Folic acid was given to every patient.

# PATIENTS & METHODS

## RESPONSE CRITERIA

- Good Response: Transfusion Independence or Hb rise of  $> 2\text{gm/dl}$
- Partial Response: Rise in Hb of 1- 2 gm/dl or reduction in transfusion frequency by 50%.
- No Response: No rise in Hb or remained at the same level of transfusion dependency.

# PATIENTS & METHODS

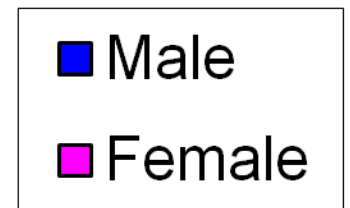
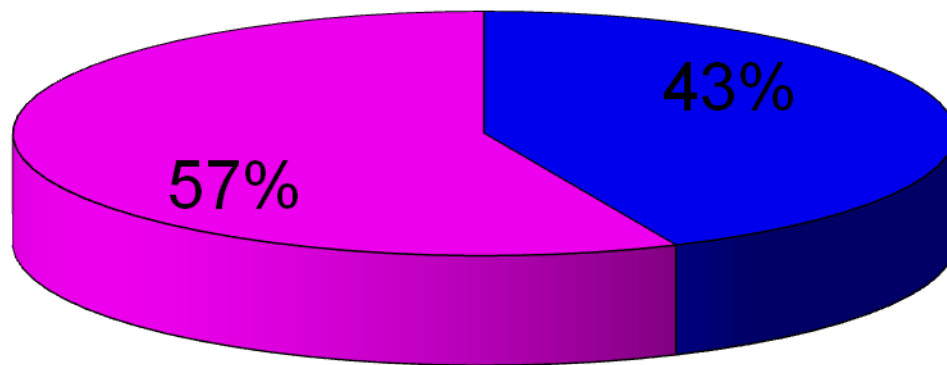
- Molecular Genetic Testing –  
By Amplification Refractory Mutation  
Specific (ARMS) PCR for common beta-  
thalassemia mutation.

The background is a solid teal color with a subtle, repeating pattern of small, light-colored spheres connected by thin lines, creating a grid-like structure that recedes into the distance. The word "RESULTS" is centered in a bold, yellow, serif font.

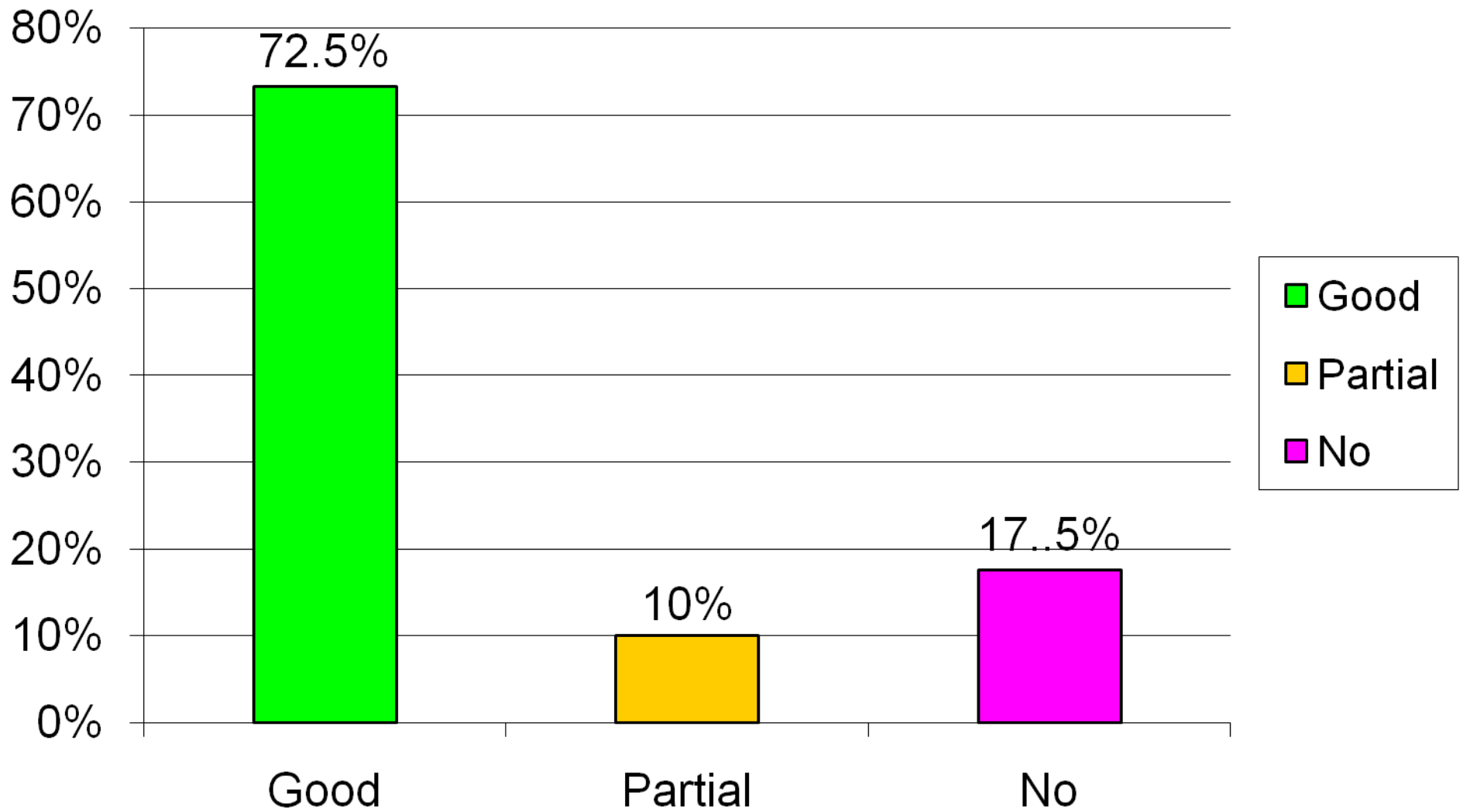
# RESULTS

# Sex Distribution

n=40



# Response to HU in TI Patients



# Response of HU with Frequency of Blood Transfusions

n=40

Prior to HU	Response to HU		
	GOOD	PARTIAL	POOR
Transfusion Dependent n=17	11 (65%)	3(18%)	3 (17%)
Received 1-2 Transfusions n= 19	14 (73%)	1(5%)	4 (21%)
No Transfusion n=4	4 (100%)	—	—

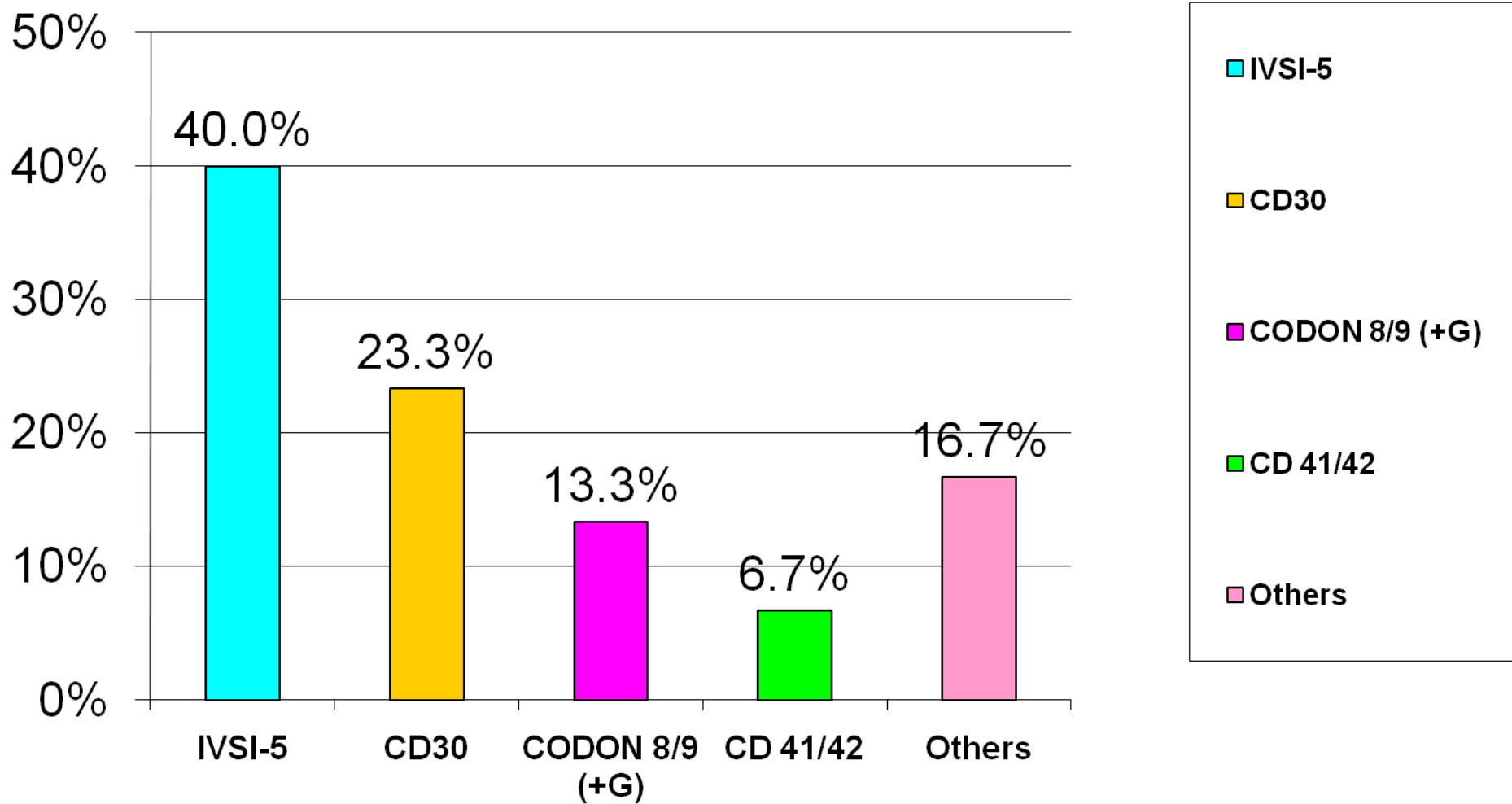
## Correlation of Age with response to Hydroxyurea n=40

	Response to HU		
	Good	Partial	No
Age < 2 year n=12	4 (33.3%)	2 (16.6%)	6(50%)
Age > 2 year n=28	25 (89.1%)	2 (7.4%)	1(3.5%)

## Spectrum of Clinical Response in Good Responders n=29

Rise in Hb > 2 gm/dl	13 (45%)
Reduced Spleen size	11 (38%)
Blood Transfusion Free	5 (17%)

# Spectrum of Beta Globin Gene Mutation in TI Patients



## Correlation of 4 Common beta-globin Mutations with HU Treatment in TI Patients

4 Common Beta-globin gene mutations n=25	Response to HU		
	Good	Partial	No
IVS 1-5 (G → C) n=12	9	-	3
CD30 (G → C) n=7	5	-	2
CODON8/9 (+G) n=4	3	1	-
CD41/42 n=2	2	-	-

## Comparison of Current Study with Other Published Studies on Efficacy of HU in TI

Study	No. of Patients	Response of Hydroxyurea		
		Good	Partial	Over all response
Dixit A et al <sup>3</sup>	37	17	9	26(70.2%)
Marwaha et al <sup>4</sup>	73	43	13	56(76.7%)
Current study	40	29	4	33(82.5%)

# CONCLUSION

- Hydroxyurea is safe, well tolerated and affordable drug in TI patient with minimal side effects.
- Patient clinically diagnosed as TI, receiving regular blood transfusions can also be given trial of HU to minimize or even eliminate the need for regular transfusion and concomitant iron overload.

# CONCLUSION

- Clinical trial of HU is worthwhile in TI above 2 year of age.
- Codon 8/9 (+G) ,CD41/42 may be a modulating factor predicting good response to Hydroxyurea in TI, although need confirmation in large size study along with Xmn-1 study.

- Hydroxyurea seems a promising drug in the treatment of TI patients in our set up.
- Multicentre studies should be carried out to try this drug in our country

# REFERENCES

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2. Cappellini MD, Cohen A, Eleftheriou A, Piga A, Porter J, Taher A. Alternative Approaches to the treatment of Thalassemia: Guidelines for the clinical management of thalassemia 2<sup>nd</sup> ed. Thalassemia International Federation; pp136 – 138
3. Dixit A, Chatterjee T.C, Mishra P, Choudhry DR, Mahapatra M, Tyagi S, Kabra M, Saxena R, Choudhry V.P, Hydroxyurea in thalassemia intermedia – a Promising therapy. Ann Hematol (2005)84 : 441 – 446

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4. Marwaha RK, Narange K, Panigrahi I and Das R. Hydroxyurea in children with Beta Thalassemia Intermedia. 5<sup>th</sup> ASH Annual Meeting and Exposition Dec 6, 2008

THANK YOU