P-0972 – Is metformin in first trimester of pregnancy safe for the mother and fetus in gestational diabetes mellitus?
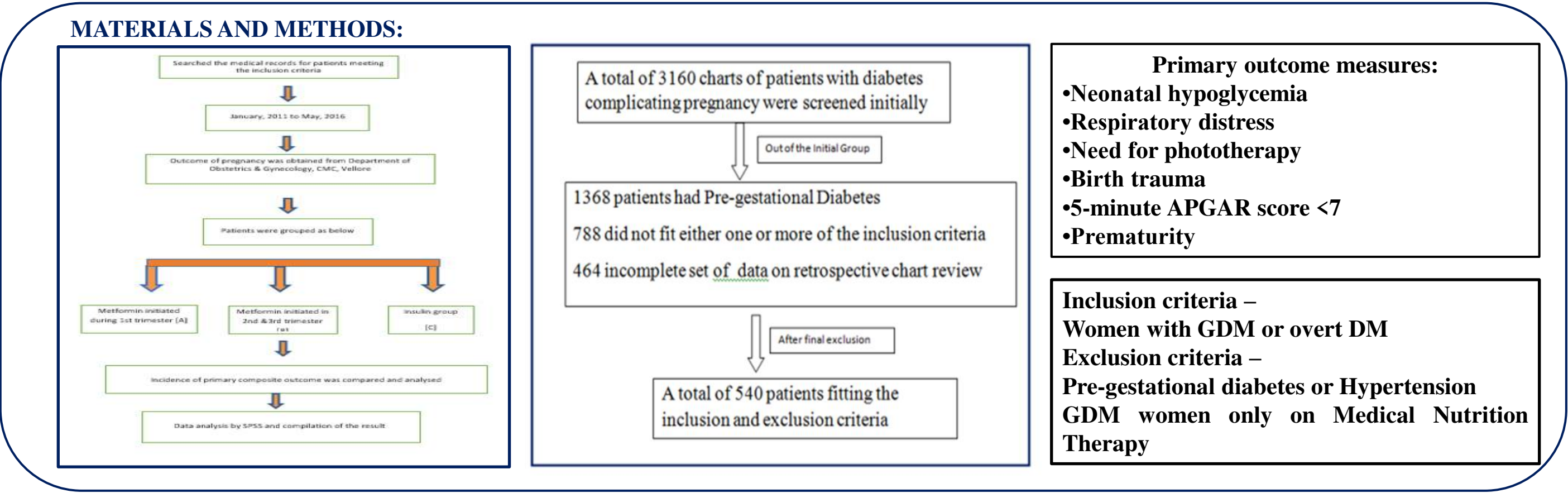
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AIMS AND OBJECTIVES :

- **In women with Gestational Diabetes Mellitus(GDM):**

  ➢ Assess the maternal and fetal outcomes with use of metformin in the first trimester of pregnancy

  ➢ Compare these outcomes with initiation of metformin after the first trimester of pregnancy or initiation of insulin alone during any trimester

MATERIALS AND METHODS:

Flowchart: Searched the medical records for patients meeting the inclusion criteria → January, 2011 to May, 2016 → Outcome of pregnancy was obtained from Department of Obstetrics & Gynecology, CMC, Vellore → Patients were grouped as below → [Metformin initiated during 1st trimester [A] | Metformin initiated in 2nd & 3rd trimester [B] | Insulin group [C]] → Incidence of primary composite outcome was compared and analysed → Data analysis by SPSS and compilation of the result

A total of 3160 charts of patients with diabetes complicating pregnancy were screened initially

Out of the Initial Group

1368 patients had Pre-gestational Diabetes
788 did not fit either one or more of the inclusion criteria
464 incomplete set of data on retrospective chart review

After final exclusion

A total of 540 patients fitting the inclusion and exclusion criteria

Primary outcome measures:
- Neonatal hypoglycemia
- Respiratory distress
- Need for phototherapy
- Birth trauma
- 5-minute APGAR score <7
- Prematurity

Inclusion criteria –
Women with GDM or overt DM
Exclusion criteria –
Pre-gestational diabetes or Hypertension
GDM women only on Medical Nutrition Therapy

RESULTS AND ANALYSIS :

BASELINE CHARACTERISTICS	Subjects (N=540)
Age of subject (years)	29.06 ± 4.64
Gestational age at diagnosis (weeks + days)	21.8 ± 8.6
0 hour plasma glucose(OGTT, in mg%)	122.36 ± 43.05
2 hours plasma glucose(OGTT, in mg%)	202.44 ± 108.98
History of GDM (%)	121 ±22.4
Family history of diabetes mellitus (%)	311±61.29
Duration of hospital stay during delivery (days)	5.54 ± 2.76
Pregnancy loss (%)	14±2.59
Pre eclampsia (%)	12 ±2.22
Birth length (cm)	47.90 ± 2.61
Gestational age at delivery (weeks + days)	38.49 ± 5.60

Individual outcome comparison : Group A&B and Group A&C

Variables	Total subjects= 389		P-value	Group C (N-151)	P-value
	Group A (N=186) (%)	GroupB (N=203) (%)			
Neonatal hypoglycemia	3 (1.61%)	0	0.203	2(1.32%)	0.204
Respiratory distress	1 (0.53%)	0	0.377	0	0.368
Need for phototherapy	1 (0.53%)	2 (0.98%)	0.876	1 (0.66%)	0.886
Birth trauma	1 (0.53%)	0	0.534	1 (0.66%)	0.530
5 minutes APGAR <7	0	2 (0.98%)	0.193	0	0.197
Premature birth	18 (9.67%)	14 (6.89%)	0.540	14 (9.27%)	0.537
Gestational HTN	158 (84.94%)	181 (89.16%)	0.101	140(92%)	0.104
PPGT##	10 (12.98%)	14 (18.8 %)	0.227	14 (9.3%)	0.232
Optimal Maternal glycemic control **	149 (92.5%)	144 (90%)	0.661	110(92%)	0.659
Birth weight <4 kgs	183 (90.14%)	198 (97.53%)	0.462	146(96%)	0.465
Birth length <50cms^^	106 (87.6%)	129 (92.8%)	0.273	45(36.5%)	0.277

Composite outcome (Group A & B)	Value	Lower CI (95%)	Upper CI (95%)
Primary outcome (OR)	1.738	0.657	4.597
Primary outcome yes	1.633	0.685	3.891
Primary outcome no	0.939	0.843	1.046
Secondary outcome (OR)	1.617	0.618	4.115
Secondary outcome- yes	1.702	0.689	3.651
Secondary outcome- no	0.840	0.850	1.00

Composite outcome (Group A & C)	Value	Lower CI (95%)	Upper CI (95%)
Primary outcome (OR)	1.717	0.715	4.119
Primary outcome yes	1.614	0.742	3.510
Primary outcome no	0.940	0.849	1.040
Secondary outcome (OR)	1.720	0.619	4.117
Secondary outcome- yes	1.612	0.733	3.540
Secondary outcome- no	0.955	0.852	1.006

N= 14 (2.59%)					
PREGNANCY LOSS COMPARISON			Group A(N=11)	Group B(N=1)	Group C(N=2)
Spontaneous abortion			1 (9.1%)	0	0
MTP	IUD	Still birth	6 (54.5%)	1 (100%)	0
	Anomaly	CVS	1 (9.1%)	0	1 (50%)
		NS	2 (18.2%)	0	1 (50%)
		Rhizomelia	1 (9.1%)	0	0
Total			11	1	2

Key Findings:
➢ Premature birth numerically higher (9.9%) in Group A compared to Group B (6.9%) patients and Group C (9.3%) (P-Value 0.540, 0.537)- similar to MiG Trial (12.1%)

➢ No other primary or secondary composite outcome comparison showed statistically significant difference

CONCLUSIONS:
➢ Our findings strongly suggest that metformin use in the first[t] trimester has no significant maternal or fetal adverse outcomes
➢ Prematurity and fetal loss are two outcomes that warrant further critical evaluation in future studies in larger cohorts of GDM.
➢ Metformin can prove to be a safe, effective and cheaper modality of treatment in the first trimester of gestation in GDM mothers .