A systematic review on materno-foetal outcomes in pregnant women with IgA nephropathy: a case of "late-maternal" preeclampsia?

Montersino Benedetta (1), Piccoli Giorgina Barbara (2), Kooij Isabelle (1), Attini Rossella (1), Cabiddu Gianfranca (3), Fassio Federica (1), Gerbino Martina (1), Biolcati Marilisa (4), Versino Elisabetta (4), Todros Tullia (1)

(1) Dipartimento di Scienze Chirurgiche, Unità Materno-fetale, Università di Torino, Torino, Italia
(2) Dipartimento di Scienze Cliniche e Biologiche, Università di Torino, Torino, Italia; Nephrologie, Centre Hospitalier Le Mans, Le Mans, France
(3) Nefrologia, Ospedale Brotzu, Cagliari, Italia
(4) Epidemiologia, Dipartimento di Scienze Cliniche e Biologiche, Università di Torino, Italia

OBJECTIVE

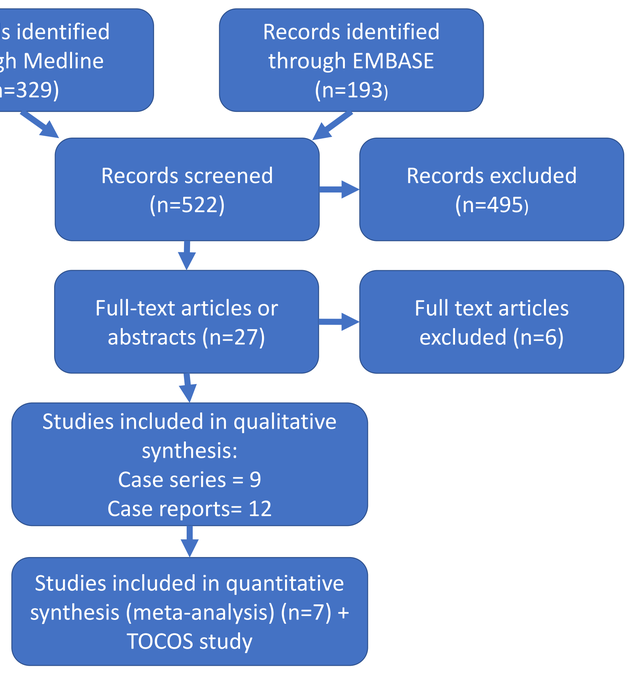
IgA nephropathy is the most common primary glomerulonephritis in pregnancy and shares with immunologic diseases and kidney diseases a relationship with adverse maternal outcomes, whose entity and pattern is only partially quantified. Recent studies and reviews provide information on progression of kidney disease, but no systematic review was addressed to pregnancy outcomes with respect to a low-risk reference cohort. Therefore, this review was aimed at analyzing pregnancy-related outcomes in IgA nephropathy, to perfect the estimation of the risks and to identify specific research needs.

METHODS

A search strategy on Medline, EMBASE and the Cochrane review for the period 2000-2016 included both series with at least 6 cases of IgA nephropathy, with or without control groups and case reports, to look into specific rare occurrences. The analysis was performed in comparison to the provided control group (194 non-pregnant controls available for kidney function). For pregnancy-related outcomes, we employed as a control group the low-risk population from the TOCOS database (Torino Cagliari Observational Study).

RESULTS

The search retrieved 522 papers, of which 21 were included (9 series and 12 case-reports). The series report on 403 women with 531 pregnancies.



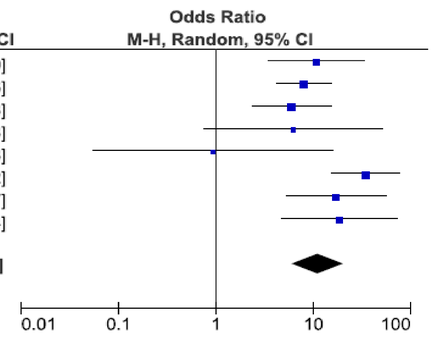
No significant difference in kidney function decline was found in any of the case series in women with and without pregnancy, possibly due to the overall preserved kidney function at baseline. Conversely, risk for adverse pregnancy-related outcomes was increased compared to low-risk controls: for preeclampsia (PE) (OR 11.21; CI: 6.14-20.48), PIH (OR 21.06; CI 5.66-78.31), and preterm birth (OR 2.63; CI 1.21-5.71), while the incidence of "low birth weight babies" and caesarean section was not statistically different (OR 1.81 IC: 0.89-3.69; OR 1.44 IC: 0.66-3.15). This pattern suggests the presence of "maternal", late PE that may affect less severely foetal growth.

Odds ratio for PE (A), preterm delivery (B), low-birth weight (C) and caesarean section (D) in IgA nephropathy versus low risk controls (from the TOCOS study)

A)

Study or Subgroup	IgA Events	IgA Total	Low-risk Events	Low-risk Total	Weight	Odds Ratio M-H, Random, 95% CI
Donggyu 2010	4	25	25	1418	13.3%	10.61 [3.39, 33.19]
Limardo 2010	17	136	25	1418	19.6%	7.96 [4.18, 15.16]
Liu 2014	6	62	25	1418	15.8%	5.97 [2.36, 15.13]
Ronkainen 2006	1	10	25	1418	6.2%	6.19 [0.76, 50.73]
Shimizu 2010	0	29	25	1418	3.9%	0.93 [0.06, 15.58]
Suetsugu 2011	13	34	25	1418	17.5%	34.49 [15.55, 76.52]
TOCOS 2016	4	17	25	1418	12.7%	17.14 [5.22, 56.27]
Waness 2010	3	12	25	1418	11.0%	18.57 [4.74, 72.74]
Total (95% CI)		**325**		**11344**	**100.0%**	**11.21 [6.14, 20.48]**
Total events	48		200			

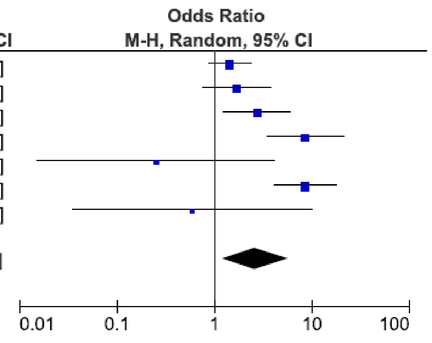
Heterogeneity: Tau² = 0.37; Chi² = 15.66, df = 7 (P = 0.03); I² = 55%
Test for overall effect: Z = 7.86 (P < 0.00001)



B)

Study or Subgroup	IgA Events	IgA Total	Low-risk Events	Low-risk Total	Weight	Odds Ratio M-H, Random, 95% CI
Limardo 2010	20	229	89	1418	19.6%	1.43 [0.86, 2.37]
Liu 2014	7	69	89	1418	17.3%	1.69 [0.75, 3.79]
Oh 2011	8	52	89	1418	17.5%	2.72 [1.24, 5.94]
Ronkainen 2006	8	22	89	1418	16.6%	8.53 [3.49, 20.88]
Shimizu 2010	0	29	89	1418	5.6%	0.25 [0.02, 4.15]
TOCOS 2016	12	33	89	1418	17.9%	8.53 [4.07, 17.90]
Waness 2010	0	12	89	1418	5.5%	0.59 [0.03, 10.12]
Total (95% CI)		**446**		**9926**	**100.0%**	**2.63 [1.21, 5.71]**
Total events	55		623			

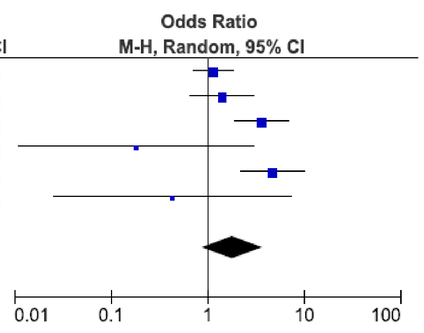
Heterogeneity: Tau² = 0.73; Chi² = 28.39, df = 6 (P < 0.0001); I² = 79%
Test for overall effect: Z = 2.45 (P = 0.01)



C)

Study or Subgroup	Pregnant IgA Events	Pregnant IgA Total	Non-pregnant IgA Events	Non-pregnant IgA Total	Weight	Odds Ratio M-H, Random, 95% CI
Limardo 2010	22	229	120	1418	24.8%	1.15 [0.71, 1.85]
Liu 2014	8	69	120	1418	21.2%	1.42 [0.66, 3.03]
Oh 2011	13	52	120	1418	22.6%	3.61 [1.87, 6.94]
Shimizu 2010	0	29	120	1418	5.3%	0.18 [0.01, 3.01]
TOCOS 2016	10	33	120	1418	21.1%	4.70 [2.19, 10.11]
Waness 2010	0	12	120	1418	5.2%	0.43 [0.03, 7.33]
Total (95% CI)		**424**		**8508**	**100.0%**	**1.81 [0.89, 3.69]**
Total events	53		720			

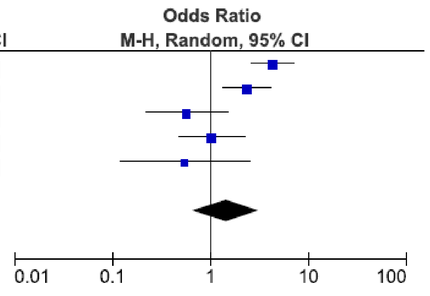
Heterogeneity: Tau² = 0.48; Chi² = 18.62, df = 5 (P = 0.002); I² = 73%
Test for overall effect: Z = 1.63 (P = 0.10)



D)

Study or Subgroup	IgA Events	IgA Total	Low-risk Events	Low-risk Total	Weight	Odds Ratio M-H, Random, 95% CI
Liu 2014	42	69	379	1418	23.8%	4.26 [2.59, 7.01]
Oh 2011	24	52	379	1418	23.3%	2.35 [1.35, 4.10]
Shimizu 2010	5	29	379	1418	18.8%	0.57 [0.22, 1.51]
TOCOS 2016	9	33	379	1418	21.0%	1.03 [0.47, 2.23]
Waness 2010	2	12	379	1418	13.2%	0.55 [0.12, 2.51]
Total (95% CI)		**195**		**7090**	**100.0%**	**1.44 [0.66, 3.15]**
Total events	82		1895			

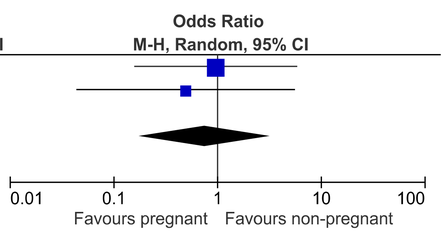
Heterogeneity: Tau² = 0.60; Chi² = 21.30, df = 4 (P = 0.0003); I² = 81%
Test for overall effect: Z = 0.92 (P = 0.36)



Odds ratio of worsening of the kidney function in IgA nephropathy in women with or without pregnancy (end stage renal disease)

Study or Subgroup	Pregnant IgA Events	Pregnant IgA Total	Non-pregnant IgA Events	Non-pregnant IgA Total	Weight	Odds Ratio M-H, Random, 95% CI
Limardo 2010	3	136	2	87	64.3%	0.96 [0.16, 5.86]
Liu 2014	1	62	2	62	35.7%	0.49 [0.04, 5.57]
Total (95% CI)		**198**		**149**	**100.0%**	**0.76 [0.18, 3.22]**
Total events	4		4			

Heterogeneity: Tau² = 0.00; Chi² = 0.19, df = 1 (P = 0.67); I² = 0%
Test for overall effect: Z = 0.38 (P = 0.70)



CONCLUSIONS

This is the largest number of papers narratively discussed and/or meta-analyzed on IgA nephropathy in pregnancy. The main findings of the review regard progression of kidney disease and pregnancy-related risks compared to the overall population. IgA nephropathy is not associated with an increased progression of kidney disease progression, at least in cases with well-preserved baseline function; the case reports may underline that positive pregnancy outcomes are possible, even in severe advanced chronic kidney disease. Furthermore, a strongly increased risk of PIH and PE, and of late preterm delivery, suggest the occurrence of "late" "maternal" PE, thought to affect foetal growth less severely than "placental" early PE. For clinicians working in obstetrics ad in nephrology, this finding may be of help in defining control policies. Further research is needed to guide clinical management.

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Glomerulonephritis II
Benedetta Montersino
DOI: 10.3252/pso.eu.54ERA.2017
ePosters supported by F. Hoffmann- La Roche Ltd.
54th ERA-EDTA CONGRESS Madrid, Spain June 3rd-6th 2017
PosterSessionOnline.com