***Significance of Neutrophil Gelatinase-associated Lipocalin as a Biomarker for the Diagnosis of Diabetic Kidney Disease: A Systematic Review and Meta-analysis***

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***Supplementary data***

**Item S1 Retrieval strategy of the meta-analysis**

*PUBMED*

(((((((((("Diabetic Nephropathies"[Mesh]) OR Diabetic Nephropathies) OR Diabetic Nephropathy) OR Diabetic Kidney Disease) OR Diabetic Glomerulosclerosis) OR Kimmelstiel Wilson Syndrome) OR Kimmelstiel Wilson Disease) OR Nodular Glomerulosclerosis) OR Intracapillary Glomerulosclerosis)) AND (((((("Lipocalin-2"[Mesh]) OR NGAL) OR Lipocalin 2) OR Oncogene 24p3 Protein) OR Siderocalin Protein) OR Neutrophil Gelatinase Associated Lipocalin)

*EMBASE*

No. Query Results Results Date

#11. #7 AND #10 439 13 Apr 2019

#10. #8 OR #9 68,662 13 Apr 2019

#9. diabetes AND nephropathy OR (diabetic AND 68,662 13 Apr 2019

 glomerulopathy) OR (diabetic AND

 glomerulosclerosis) OR (diabetic AND

 intercapillary AND glomerulosclerosis) OR

 (diabetic AND kidney AND disease) OR (diabetic

 AND nephropathies) OR (diabetic AND

 nephrosclerosis) OR (glomerulonecrosis, AND

 intercapillary) OR (glomerulosclerosis, AND

 diabetic) OR (glomerulosclerosis, AND

 intercapillary) OR (intercapillary AND

 glomerulosclerosis) OR (kimmelstiehl AND wilson

 AND syndrome) OR (kimmelstiel AND wilson AND

 disease) OR (kimmelstiel AND wilson AND

 nephropathy) OR (kimmelstiel AND wilson AND

 syndrome) OR (nephropathy, AND diabetic)

#8. 'diabetic nephropathy'/exp 39,442 13 Apr 2019

#7. #2 OR #6 11,395 13 Apr 2019

#6. #3 OR #5 11,395 13 Apr 2019

#5. neutrophil AND gelatinase AND associated AND 8,166 13 Apr 2019

 lipocalin

#3. ngal OR (24p3 AND protein) OR (lcn2 AND protein) 11,275 13 Apr 2019

 OR (lipocalin AND 2) OR (lipocalin AND 24p3) OR

 'lipocalin 2' OR (ngal AND protein) OR (protein

 AND 24p3) OR (protein AND lcn2) OR (protein AND

 ngal) OR (protein AND sip24) OR siderochalin OR

 sip24 OR (sip24 AND protein) OR (superinducible

 AND protein AND 24) OR uterocalin

#2. 'neutrophil gelatinase associated lipocalin'/exp 7,781 13 Apr 2019

*Cochrane Library*

ID Search

#1 MeSH descriptor: [Lipocalin-2] explode all trees

#2 (NGAL) (Word variations have been searched)

#3 (neutrophil gelatinase-associated lipocalin) (Word variations have been searched)

#4 (lipocalin 2) (Word variations have been searched)

#5 MeSH descriptor: [Diabetic Nephropathies] explode all trees

#6 (diabetic nephropathy) (Word variations have been searched)

#7 diabetic nephropathies

#8 diabetic kidney disease

#9 #1 or #2

#10 #9 or #3

#11 #10 or #4

#12 #5 or #6

#13 #12 or #7

#14 #13 or #8

#15 #11 and #14



**Figure S2 Methodological quality assessment of included studies using** **QUADAS-2**

Abbreviation: QUADAS-2,Quality Assessment of Diagnostic Accuracy Studies 2.

**Table S3 Diagnostic value of NGAL for normoalbuminuric diabetes in individual studies**

|  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Study** | **Cutoff value****(ng/ml)** | **Sensitivity****(%)** | **Specificity****(%)** | **TP****（n）** | **FP****（n）** | **FN****（n）** | **TN****（n）** | **AUC** |
| **Serum NGAL** |  |  |  |  |  |  |  |  |
| Shen 2016 [36] | 225.5 | 93 | 91 | 25 | 3 | 2 | 32 | 0.960 |
| Lacquaniti 2013 [37] | 77.4 | 88 | 100 | 44 | 0 | 6 | 35 | 0.970 |
| Bolignano 2009 [8] | 88 | 94 | 100 | 15 | 0 | 1 | 18 | 0.969 |
| **Urine NGAL** |  |  |  |  |  |  |  |  |
| Hosny 2018 [35] | 3.38 | 95 | 100 | 19 | 0 | 1 | 20 | 0.990 |
| Lacquaniti 2013 [37] | 9.3 | 100 | 80 | 50 | 7 | 0 | 28 | 0.956  |
| Bolignano 2009 [8] | 22 | 75 | 100 | 12 | 0 | 4 | 18 | 0.780  |

Abbreviations: AUC, area under the curve; FP, false-positive; FN, false-negative; NGAL, neutrophil gelatinase-associated lipocalin; NR, not reported; TP, true-positive; TN, true-negative.

**Figure S4 The sensitivity, specificity and SROC of Serum and urine NGAL for normoalbuminuric diabetes diagnosis**

*Serum NGAL*

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*Urine NGAL*

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**Table S5 Summary of the excluded studies due to insufficient data**

|  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Reference** | **Location** | **Desigh** | **Total** | **Case/control** | **Target group** | **Specimen** | **NGAL assay** | **AUC** |
| Siddiqui 2019 [38] | Saudi Arabia | Cross-sectional | 92 | 46/46 | DKD/non-DKD | Urine | ELISA | 0.659 |
| Siddiqi 2017 [41] | India | Cross-sectional | 180 | 90/90 | MI/NO | Serum | ELISA | 0.789 |
|  |  |  |  |  |  | Urine | ELISA | 1.000 |
| Su 2018 [39] | China | Cross-sectional | 67 | 32/35 | MI/NO | Serum | TIIA | 0.858 |
| Dai 2018 [40] | China | Cross-sectional | 64 | 26+20/18 | MA+MI/NO | Serum | ELISA | 0.813 |
| Luo 2017 [42] | China | Cross-sectional | 158 | 58+48/52 | MA+MI/NO | Serum | ELISA | 0812 |
| Hao 2016 [43] | China | Cross-sectional | 60 | 40/20 | MA+MI/NO | Urine | ELISA | 0.821 |
| Wang 2015 [44] | China | Cross-sectional | 76 | 50/26 | MA+MI/NO | Serum | TIIA | 0.862 |

Abbreviations: DKD, diabetic kidney disease; ELISA, electrochemiluminescence immunoassay; MA, macroalbuminuria; MI, microalbuminuria; NGAL, neutrophil gelatinase-associated lipocalin; NO, normoalbuminuria; NR, not reported; TIIA, turbidimetric inhibition immuno assay.