

Insulin Initiation with Insulin Degludec/Insulin Aspart versus Insulin Glargine in Oral Antidiabetic Drugs Failure Patients with Type 2 Diabetes Mellitus: A Real-World Study from India

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ABSTRACT

Context: Oral antidiabetic drug (OAD) failure is an indication for starting insulin therapy, but there is still a dilemma as to whether basal insulin or a premixed/co-formulation analog should be the choice. **Aim:** To compare the safety and efficacy of once daily (OD) insulin degludec/insulin aspart (IDegAsp) to OD insulin glargine (IGlar U100) in insulin-naïve Indian subjects with type 2 diabetes mellitus (T2DM), inadequately controlled with OADs alone. **Setting and design:** Retrospective study. **Methods and material:** Data was retrieved from the author's clinic database of OAD failure patients (18-80 years), who were started either with (IGlar U100, n = 120) or IDegAsp (n = 89) OD over and above the standard of care. Data of fasting plasma glucose (FPG), postprandial plasma glucose (PPG) and glycated hemoglobin (HbA1c) from baseline and at last follow-up visits were collected. **Statistical analysis used:** Baseline characteristics and change in study parameters during the follow-up period were computed between two groups (IGlar U100 vs. IDegAsp) by unpaired *t*-test and paired *t*-test, respectively. ANCOVA test was used to compute percentage reduction in body weight, body mass index (BMI), FPG, PPG and HbA1c in between two groups (IGlar U100 vs. IDegAsp). **Results:** IDegAsp caused a significantly greater reduction in FPG, PPG and HbA1c as compared to the IGlar U100 arm. There was no significant difference in the proportion of patients with hypoglycemia between IDegAsp and IGlar U100 groups ($p = 0.208$). No episodes of severe hypoglycemia were reported. **Conclusion:** Comparison of IDegAsp and IGlar U100 OD in T2DM patients indicated that both were relatively safe but the former controlled FPG and PPG levels more effectively.

Keywords: Oral antidiabetic agent, insulin, hypoglycemia, type 2 diabetes mellitus, India

Currently, 573 million people are living with diabetes globally. There is a worldwide increase in the prevalence and incidence of diabetes which is predicted to rise to 643 million by 2030. In India, the number of adults with diabetes in 2021 was 74.2 million which is expected to exceed 124 million by 2045.¹ Several national and international guidelines on the treatment of type 2 diabetes mellitus (T2DM) exist.²⁻⁵ As per all the national and international guidelines, oral antidiabetic drug (OAD) failure is an indication for starting insulin therapy. It can be defined as a clinical

situation where glycated hemoglobin (HbA1c) remains above goal, despite concurrent use of an optimum dose of three or more glucose-lowering drugs of different classes, one of which should be metformin and the second, preferably a sulfonylurea, provided adequate diet and exercise have been followed, and comorbid conditions causing hyperglycemia have been ruled out.⁶ Nevertheless, there is still a dilemma as to whether basal insulin or a premixed/co-formulation analog should be the choice for initiation.

Insulin treatment is administered as an injection of basal insulin or a combination of bolus and basal insulins. Insulin degludec/insulin aspart (IDegAsp) is a soluble combination of insulin degludec (IDeg), an ultra-long-acting basal insulin and the rapid-acting insulin analog, insulin aspart (IAsp). Within the IDegAsp formulation and after subcutaneous injection, independent pharmacokinetic/pharmacodynamic characteristics of the components are

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maintained.⁷ IDeg has a flat and stable glucose-lowering effect that results in a much longer duration of action (>42 h), and four times lower pharmacodynamic variability than insulin glargine (IGlar U100) under steady-state conditions.⁸⁻¹⁰ This in turn results in a lower risk of hypoglycemia, particularly nocturnal hypoglycemia with IDeg, a distinct clinical advantage over other basal insulin.^{11,12}

In T2DM, IDegAsp once daily (OD) has been analyzed as initiation as well as intensification strategy. IDegAsp can be initiated in either OD or twice daily (BID) doses based on the clinical situation, as monotherapy or together with metformin. T2DM patients switching from OD basal or premix insulin therapy can be converted unit-to-unit to IDegAsp OD at an equivalent previous total daily insulin dose.^{13,14} IDegAsp has been shown to provide significant reductions in fasting plasma glucose (FPG), the total daily dose of insulin, and rate of overall and nocturnal hypoglycemia as compared to biphasic insulin.¹⁵

To suit Indian reality of diabetes management (such as high carbohydrate diet), guidelines and recommendations need to be adapted.^{16,17} Thus, consensus on initiation and intensification of premix insulin in the management of T2DM recommends premix insulin/co-formulation for effective and accessible glycemic control (predominantly postprandial hyperglycemia).¹⁸ This real-world study aimed at comparing the safety and efficacy of IDegAsp OD to that of IGLar U100 OD in insulin-naïve Indian subjects with T2DM insufficiently controlled with oral antidiabetic medicines alone.

SUBJECTS AND METHODS

Data was retrieved from the author's clinic database of OAD failure patients (18-80 years) who were started on basal insulin (IGlar U100, n = 120) or IDegAsp (n = 89) OD over and above the standard of care. The data of FPG, postprandial plasma glucose (PPG) and HbA1c from baseline and at last follow-up visit was collected for analysis.

Key eligibility criteria for study consisted of the following:

Inclusion Criteria

- Indian insulin naïve adults with T2DM.
- Age 18 to 80 years.
- On stable optimal dose of 3 OADs for last 90 days.
- HbA1c <11%.

Exclusion Criteria

- Type 1, gestational diabetes mellitus (GDM) and other types of diabetes.
- Pregnancy and lactation.
- Requiring insulin as rescue medication due to intercurrent illness in last 3 months.
- Incomplete dataset and irregular intake of history of insulin.
- Faulty injection technique.

All patients visiting the author's outdoor clinic from 1st January 2019 to 30th October 2019 were assessed for the type of diabetes therapy. Patients who had been on basal insulin (IGlar U100) or IDegAsp, OD for 35 weeks or more were included in the study. Informed consent was obtained from all subjects. Details were collected regarding basic demographics, dosage, frequency of insulin, body weight, blood pressure and glycemic control. Indications for the use of IGLar U100 and IDegAsp were recorded. Data is expressed using descriptive statistics as mean \pm SEM (standard error of the mean), wherever applicable. Data was analyzed using SPSS/Microsoft Excel software.

Baseline characteristics and changes in study parameters during the follow-up period were compared between two groups (IGlar U100 vs. IDegAsp) by unpaired *t*-test and paired *t*-test, respectively. Analysis of covariance (ANCOVA) test was used to compare the percentage change in body weight, body mass index (BMI), FPG, PPG and HbA1c between two groups (IGlar U100 vs. IDegAsp). Data at baseline, 35.56 \pm 25.97 weeks (IGlar U100 cohort), and 28.53 \pm 19.63 weeks (IDegAsp cohort) was used for analysis.

Assessment

Subjects were treated with either IDegAsp or IGLar U100 OD, using stratification (by previous OAD treatment). The IDegAsp dose was administered subcutaneously just before the largest meal of the day and IGLar U100 (Lantus®, SoloSTAR®, Sanofi-Aventis, Frankfurt, Germany) was administered according to the approved labeling (either before breakfast or at bedtime).

RESULTS

The baseline demographics and clinical parameters were found to be comparable, except for body weight that was nonsignificantly higher in the IGLar U100 arm and hence required a higher insulin dose. The mean (\pm SD) duration of follow-up was 35.56 \pm 25.97 weeks in IGLar U100 cohort and 28.53 \pm 19.63 weeks in IDegAsp

cohort and this difference was nonsignificant ($p = 0.104$). The glycemic triad, i.e., FPG, PPG and HbA1c was significantly reduced from baseline in both the arms (Table 1).

However, IDegAsp caused statistically significant greater reduction in FPG, PPG and HbA1c as compared to the IGlax U100 arm. Three patients of IGlax U100 complained of injection site burning but no such adverse events were reported in the IDegAsp arm. There were overall 18 episodes of hypoglycemia in the IGlax U100 group and 10 episodes in the IDegAsp group. Though the proportion of patients with hypoglycemia was higher in IGlax U100 group as compared to IDegAsp group, the difference failed to reach any statistical significance ($p = 0.208$; Chi-square test). Severe hypoglycemia episodes were not reported.

Eighty-nine subjects (53 men and 36 women; mean age 59.49 ± 3.31 years) received IDegAsp and, 120 subjects (71 men and 49 women; mean age 61.88 ± 10.87 years) who received IGlax U100 treatment had completed the duration of 26 weeks or more. Fall in HbA1c from baseline to follow-up visit was $9.61 \pm 0.78\%$ to $8.56 \pm 0.18\%$ in the IGlax U100 cohort, and from $9.61 \pm 2.12\%$ to $8.02 \pm 1.02\%$ in the IDegAsp cohort. Mean percentage

reduction in the IDegAsp cohort was found to be -16.55 ± 4.07 and was statistically significant ($p = 0.044$) compared -9.88 ± 2.22 in the IGlax U100 cohort.

FPG decreased from 230.69 ± 7.49 mg/dL to 154.78 ± 7.59 mg/dL (IGlax U100 cohort), from 236.08 ± 86.31 to 134.31 ± 51.40 (IDegAsp cohort) and was found statistically significant ($p < 0.001$). Mean percentage reduction was -33.04 ± 8.61 (IGlax U100 cohort) and -34.63 ± 9.12 (IDegAsp cohort) with p -value 0.041.

Mean percentage reduction in PPG was -20.34 ± 2.89 (IGlax U100 cohort) and -41.53 ± 4.76 (IDegAsp cohort) with p -value 0.036. PPG decreased from 295.18 ± 11.75 mg/dL to 236.37 ± 10.58 mg/dL (IGlax U100 cohort) and from 309.06 ± 106.76 to 180.76 ± 55.09 (IDegAsp cohort) and was found statistically significant ($p < 0.001$). Mean insulin dose/kg body weight at the end of 26 weeks was significantly lower for patients treated with IDegAsp (0.23 ± 0.22) than IGlax U100 (0.42 ± 0.57), ($p = 0.010$).

DISCUSSION

In this Indian real-world evidence study of 26 weeks, IDegAsp administered OD significantly improved HbA1c levels as compared to IGlax U100 OD. While this

Table 1. Baseline Characteristics of the Patients

| | IGlax U100 (n = 120) | IDegAsp (n = 89) | P (t-test) |
|---|----------------------|---------------------|------------|
| Male, n (%) | 71 (59.17) | 53 (59.55) | 0.629 |
| Female, n (%) | 49 (40.83) | 36 (40.45) | |
| Age (years), Mean \pm SEM | 61.88 ± 10.87 | 59.49 ± 3.31 | 0.816 |
| Body weight (kg), Mean \pm SEM | 69.65 ± 2.13 | 68.51 ± 11.88 | 0.716 |
| SBP (mmHg), Mean \pm SEM | 132.22 ± 2.21 | 130.65 ± 2.28 | 0.487 |
| DBP (mmHg), Mean \pm SEM | 80.56 ± 1.31 | 78.97 ± 1.73 | 0.943 |
| BMI (kg/m ²), Mean \pm SEM | 26.78 ± 3.22 | 26.97 ± 2.19 | 0.865 |
| FPG (mg/dL), Mean \pm SEM | 230.69 ± 7.49 | 236.08 ± 86.31 | 0.206 |
| PPG (mg/dL), Mean \pm SEM | 295.18 ± 11.75 | 309.06 ± 106.76 | 0.578 |
| HbA1c (%), Mean \pm SEM | 9.61 ± 0.78 | 9.61 ± 2.12 | 0.385 |
| Insulin dose (IU), Mean \pm SEM | 13.44 ± 0.41 | 10.23 ± 1.41 | 0.001 |
| Insulin dose/kg body wt. (IU), Mean \pm SEM | 0.20 ± 0.18 | 0.14 ± 0.09 | 0.032 |
| LDL cholesterol (mg/dL), Mean \pm SEM | 90.01 ± 3.99 | 81.31 ± 4.86 | 0.039 |
| Serum creatinine (mg/dL), Mean \pm SEM | 0.95 ± 0.03 | 1.01 ± 0.33 | 0.701 |

SEM = Standard error mean; SBP = Systolic blood pressure; DBP = Diastolic blood pressure; BMI = Body mass index; FPG = Fasting plasma glucose; PPG = Postprandial plasma glucose; HbA1c = Glycated hemoglobin; LDL = Low-density lipoprotein.

$P < 0.05$ considered as statistically significant, p computed by unpaired t -test.

analysis is retrospective, not controlled, and is limited by the fact that dropouts were not studied, it does add value to existing literature. It must be noted that this study was performed in a nonreimbursed environment, where patients have to pay from their pocket for insulin and other supplies.

A multicenter, prospective, noninterventional, preference study was conducted with T2DM patients (n = 505) in India, with biphasic insulin aspart 30/70 (BIAsp 30). After 12 weeks of treatment, 96.4% of patients were willing to pay for BIAsp 30. Significantly improved mean treatment and device satisfaction was reported from baseline as well (p < 0.0001).¹⁹

As IDegAsp comprises rapid-acting insulin aspart and ultra-long-acting IDeg, it allows control over both FPG and PPG levels. IDegAsp provides advantages in dose titration, dose timing flexibility, treatment intensification (from OD to BID dose adjustments), lower injection burden, easy switching and lower hypoglycemia risk. IDegAsp and other antihyperglycemic drugs can be co-administered; however, sulfonylureas need to be stopped or their dose reduced. On the other hand, dose of IDegAsp may need to be lowered upon the addition of glucagon-like peptide-1 receptor agonists or sodium-glucose co-transporter-2 inhibitors.^{13,14} In a 12-week follow-up study with treatment-naïve, recently diagnosed T2DM Indian patients (n = 41), Chaudhuri

et al observed a significant improvement in FPG, PPG and HbA1c over the study period with 85.4% of patients receiving OD IDegAsp (10 units) + metformin extended-release (1 g/day).²⁰ Only 2 patients were reported for symptomatic hypoglycemia and none for severe or nocturnal hypoglycemia. Weight changes were nonsignificant. Conclusively, IDegAsp (OD or BID) was safe and effective for treatment-naïve Indian patients.

In a 16-week long exploratory study, it was found that IDegAsp was able to achieve target HbA1c <7.0%, without confirmed hypoglycemia in 67% of subjects (who were poorly controlled on metformin). The daily dose requirement of IDegAsp was 0.57 ± 0.23 U/kg and was 13% lower than that of BIAsp 30. In this study, significantly lower FPG and lower rate of confirmed hypoglycemia were noted with IDegAsp.²¹ Another 26-week long Asian study observed a lower dose requirement of IDegAsp OD (0.79 U/kg), as compared to BIAsp 30, in controlling HbA1c, with lower FPG and similar (low) risk of severe hypoglycemia.²²

Effective glycemic control was achieved including achievement of target HbA1c levels (8.02 ± 1.02%) with IDegAsp, after 26 weeks of treatment, with a percentage reduction -16.55 ± 4.07 in the IDegAsp cohort compared to -9.88 ± 2.22 in the IGlax U100 cohort (p = 0.044) (Table 2). Superior reduction in HbA1c was seen with OD IDegAsp as compared to OD IGlax U100 in a

Table 2. Change in Study Parameters During the Follow-up Period

| | IGlar U100 Cohort (n = 120) | | | IDegAsp Cohort (n = 89) | | |
|---|-----------------------------|----------------------|--------|-------------------------|----------------------|--------|
| | Baseline, Mean ± SEM | Follow-up Mean ± SEM | P | Baseline, Mean ± SEM | Follow-up Mean ± SEM | P |
| Body weight (kg) | 69.65 ± 2.13 | 69.58 ± 2.13 | 0.714 | 68.51 ± 11.88 | 69.04 ± 1.19 | 0.873 |
| BMI (kg/m ²) | 26.78 ± 3.22 | 27.05 ± 0.69 | 0.830 | 26.97 ± 2.19 | 27.19 ± 3.42 | 0.812 |
| SBP (mmHg) | 132.22 ± 2.21 | 130.61 ± 1.59 | 0.736 | 130.65 ± 2.28 | 130.44 ± 1.64 | 0.907 |
| DBP (mmHg) | 80.56 ± 1.31 | 81.36 ± 1.07 | 0.782 | 78.97 ± 1.73 | 77.21 ± 1.71 | 0.901 |
| FPG (mg/dL) | 230.69 ± 7.49 | 154.78 ± 7.59 | <0.001 | 236.08 ± 86.31 | 134.31 ± 51.40 | <0.001 |
| PPG (mg/dL) | 295.18 ± 11.75 | 236.37 ± 10.58 | <0.001 | 309.06 ± 106.76 | 180.76 ± 55.09 | <0.001 |
| HbA1c (%) | 9.61 ± 0.78 | 8.56 ± 0.18 | <0.001 | 9.61 ± 2.12 | 8.02 ± 1.02 | <0.001 |
| Serum creatinine (mg/dL) | 0.95 ± 0.03 | 0.99 ± 0.03 | 0.901 | 1.01 ± 0.33 | 1.03 ± 0.39 | 0.897 |
| Insulin dose (IU) | 13.44 ± 0.41 | 24.1 ± 1.45 | <0.001 | 10.23 ± 1.41 | 16.31 ± 3.78 | 0.768 |
| Insulin dose/kg body wt. (IU), Mean ± SEM | 0.20 ± 0.18 | 0.42 ± 0.57 | <0.001 | 0.14 ± 0.09 | 0.23 ± 0.22 | 0.010 |

SEM = Standard error mean; SBP = Systolic blood pressure; DBP = Diastolic blood pressure; BMI = Body mass index; FPG = Fasting plasma glucose; PPG = Postprandial plasma glucose; HbA1c = Glycated hemoglobin.

P < 0.05 considered as statistically significant, p computed by paired t-test.

Table 3. Percentage Reduction in Study Variables

| | IGlar U100 | IDegAsp | P (ANCOVA) |
|---|-------------------|--------------------|------------|
| Percent change in body weight, Mean \pm SEM | -0.11 \pm 0.02 | 0.72 \pm 0.66 | 0.102 |
| Percent change in BMI, Mean \pm SEM | -0.93 \pm 0.08 | 0.85 \pm 0.52 | 0.712 |
| Percent change in FPG, Mean \pm SEM | -33.04 \pm 8.61 | -34.63 \pm 9.12* | 0.041 |
| Percent change in PPG, Mean \pm SEM | -20.34 \pm 2.89 | -41.53 \pm 4.76* | 0.036 |
| Percent change in HbA1c, Mean \pm SEM | -9.88 \pm 2.22 | -16.55 \pm 4.07* | 0.044 |

SEM = Standard error mean; BMI = Body mass index; FPG = Fasting plasma glucose; PPG = Postprandial plasma glucose; HbA1c = Glycated hemoglobin.
P < 0.05 considered as statistically significant, p computed by ANCOVA test adjusted for baseline values.

26 weeks randomized controlled trial wherein patients in the OD IDegAsp arm took it before the major meal.²³ In this study, participants on IDegAsp received relatively lower mean total insulin dose compared with those on IGLar U100. Patients receiving IDegAsp were able to reduce their FPG levels (134.31 \pm 51.40) to a greater extent than with IGLar U100 (154.78 \pm 7.59) p < 0.001, while receiving lower insulin dose (Table 2), suggesting that the glucose-lowering effects of IDeg are preserved in IDegAsp. A nonsignificant increase in mean body weight was observed in patients at 26 weeks associated with IDegAsp. IDegAsp provided significant control as compared to IGLar U100 in reducing the PPG increment. Monnier et al²⁴ had reported that reduction of PPG excursions has profound effects on long-term glycemic control once FPG has reached the target. The results of this real-world study support this observation as we find a larger reduction in HbA1c with IDegAsp while, the reduction in FPG was similar in both treatment groups after 26 weeks (Table 3).

Both treatments had similar safety profiles. Findings demonstrate that IDegAsp results in a lower rate of hypoglycemia compared with IGLar U100 when using this threshold in the Indian population.²³ The BOOST study data also supports this finding. As hypoglycemia is of particular concern in the elderly, the results of this post hoc analysis are reassuring. The low rates of hypoglycemia are suggest that there is no need for special precautions when using IDegAsp in the elderly.¹³ A different approach was selected by Monnier and co-authors²⁴ to estimate the relative contribution of FPG and PPG to the overall glycemia. It was stated that PPG plays a major role in patients suffering from mild or moderate hyperglycemia. In Asian T2DM patients, PPG at 4 and 24 hours after meals was a predominant contributor to excess hyperglycemia in well-controlled patients and was equally important as FPG or PPG in moderately to poorly controlled patients

with mean HbA1c up to 10%.²⁵ The data on the Indian population from this study indicates that PPG strongly correlates with HbA1c or contributes significantly to overall glycemic control. Hence, PPG monitoring will be more conducive for optimal glycemic control and prevent long-term diabetes complications than FPG alone in the absence of HbA1c, especially in developing countries.

The STARCH study on the Indian population showed that T2DM patients from across India consume higher carbohydrates (CHO) in their diet (such as rice, idli and so on), more than the dietary recommendations.^{14,25} Around 64.1 \pm 8.3% (95% confidence interval [CI] 63.27-64.93) of total calories came from total CHO in the T2DM group. This reflects that CHO consumption by Indian T2DM patients is higher (Δ 4.1% above the upper limit of 60%) than that recommended by the guidelines and within the recommended limits as per the WHO expert consensus. In addition to dietary and lifestyle modifications, multiple therapeutic strategies like insulin may benefit T2DM patients. This approach may have a leading role in an Indian setting where the role of α -glucosidase inhibitors (AGIs) is more significant because of CHO-rich meal, as seen in this study.¹⁴ The choice of insulin for initiation has been a matter of debate, with evidence slightly being in favor of basal insulin as recommended by various western guidelines. Nonetheless, insulin initiation was considered at HbA1c levels as high as 8.5% or 9%, where the contribution of FPG was found to be substantially higher in the western population. On the contrary, a study done by Wang et al has conclusively revealed contribution of PPG at all quintiles of HbA1c in the South-East Asian population.²⁵ While premixed analogs were a part of the International Diabetes Federation (IDF) guidelines to initiate insulin, studies revealed greater reduction of HbA1c at the cost of increased hypoglycemia. Availability of IDegAsp with data of reduced overall and nocturnal hypoglycemia

versus premixed analogs as well as IGlax U100 made us ponder about its utility as a choice of once daily insulin in OAD failure subjects. IDegAsp demonstrated greater reduction in FPG, PPG and HbA1c as compared to IGlax U100. On the safety front, no statistically significant difference in hypoglycemia was noted between the two arms.

CONCLUSION

In conclusion, IDegAsp OD was significantly better as compared to IGlax U100 in improving glycemic control and in controlling PPG excursions without compromising FPG control or safety in Indian patients. IDegAsp OD provides predictable and efficacious FPG and PPG control in insulin-naïve patients with T2DM in a single injection while significantly reducing the risk of nocturnal-confirmed hypoglycemia compared with IGlax U100 in the Indian population. In the context of high CHO utilization in India, or patients with dominant postprandial hyperglycemia, premix insulin/co-formulation can offer effective and convenient glycemic control.

Key Messages

IDegAsp OD superiorly improves glycemic control and PPG excursions without compromising FPG control than IGlax U100. IDegAsp provides effective FPG and PPG control along with significant risk reduction of nocturnal-confirmed hypoglycemia. In a high carbohydrate consumption setting or predominant postprandial hyperglycemia, premix insulin/co-formulation can offer effective and convenient glycemic control.

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Prevalence of Neurological Complications in Children with COVID-19

Hospitalized children with COVID-19 are at risk of developing febrile seizures and other neurological complications, suggests a study reported in the journal *Pediatrics*.¹

Antoon et al conducted a cross-sectional study of children hospitalized with COVID-19 aged 2 months to <18 years from March 2020 to March 2022 with an objective to identify the neurologic complications associated with COVID-19 in this age group and the factors associated with these complications, which included encephalopathy, encephalitis, febrile seizure, nonfebrile seizure, aseptic meningitis, brain abscess and bacterial meningitis.

Out of the 15,137 children included in the analysis, 1060 (7%) developed a neurologic complication. Febrile seizure was the most common neurological complication occurring in nearly 4% of patients followed by nonfebrile seizures (2.3%) and encephalopathy (2.2%). About 75% of these children had not underlying neurological disorder. They also had longer duration of hospitalization, higher ICU admission rates as well as prolonged length of ICU stay including rehospitalization and mortality rates.

Children who had a neurologic complex chronic condition were 4-times more likely to develop a neurologic complication with adjusted OR of 4.14. Younger age, infection during the Delta wave and presence of a non-neurologic complex chronic condition were associated with lower risk of such complications with adjusted ORs of 0.97, 0.71 and 0.80, respectively.

This study has shown that neurological complications are frequent in children hospitalized with COVID-19. Compared to those without neurological complication, their prognosis was also poor. Timely diagnosis of such complications can improve their outcomes. Prevention is always better than cure. All eligible children, particularly those who have underlying neurologic conditions or other at-risk groups, should be fully vaccinated on schedule. All COVID-19 preventive measures should be strictly adhered to.

Reference

1. Antoon JW, Hall M, Howard LM, et al. COVID-19 and acute neurologic complications in children. *Pediatrics*. 2022 Aug 11. [Epub ahead of print]

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